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Cancer Biology Research Literatures

Dr. Mark Herbert

World Development Institute
39-06 Main Street, Flushing, Queens, New York 11354, USA, ma708090@gmail.com

Abstract: Cancer is the general name for a group of more than 100 diseases. Although there are many kinds of cancer, all cancers start because abnormal cells grow out of control. Untreated cancers can cause serious illness and death. The body is made up of trillions of living cells. Normal body cells grow, divide, and die in an orderly fashion. During the early years of a person's life, normal cells divide faster to allow the person to grow. After the person becomes an adult, most cells divide only to replace worn-out or dying cells or to repair injuries. This article introduces recent research reports as references in the related studies.
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Key words: cancer; life; research; literature; cell

1. Introduction

Cancer is the general name for a group of more than 100 diseases. Although there are many kinds of cancer, all cancers start because abnormal cells grow out of control. Untreated cancers can cause serious illness and death. The body is made up of trillions of living cells. Normal body cells grow, divide, and die in an orderly fashion. During the early years of a person's life, normal cells divide faster to allow the person to grow. After the person becomes an adult, most cells divide only to replace worn-out or dying cells or to repair injuries.

The following introduces recent reports as references in the related studies.

Abdel-Salam, A. G., et al. (2021). "Assessment of lung cancer risk factors and mortality in Qatar: A case series study." Cancer Rep (Hoboken) **4**(1): e1302.

BACKGROUND: The global burden of cancer has exponentially increased over the last few years. In 2018 alone, approximately more than half of the 18.1 million individuals who had cancer succumbed to it. Lung cancer cases and fatalities are particularly on the rise. Therefore, exploring the factors surrounding lung cancer mortality is of utmost importance. AIMS: We investigate the clinicopathological and epidemiological characteristics of patients with lung cancer undergoing treatments, and their 5-year survival rates from a case series study in Qatar. METHODS AND RESULTS: All patients' data (between January 2010 and December 2014) in this case series study were retrieved from Al-Amal Hospital database. Kaplan-Meier survival plots, life tables and Cox regression were utilized for the statistical analysis. A total of 229 lung cancer patients were included in this study; of which 23.6% are Qatari (40 males and 14 females) and 76.4% non-Qatari (133 males and 42 females). Approximately 57.6% of our patients received at least one type of treatment. We observe a 5-year survival rate of 9.4% in our patient cohort. We also observe other predictive factors, such as distant metastasis (adjusted hazards ratio, HR = 2.414, 95% CI: 1.035-5.632), smoking status (adjusted HR = 3.909, 95% CI: 1.664-9.180) and the treatment history (adjusted HR = 0.432, 95% CI: 0.270-0.691), to be significant. CONCLUSION: Lung cancer is a prevalent health condition in Qatar, particularly owing to the rising use of tobacco in the country. The survival rate for lung cancer patients in this country is lower, compared to the global average. Moreover, several factors such as distant metastasis, smoking status, and treatment history are associated with lung cancer survival in Qatar.

Abdullah, M. M. H., et al. (2021). "Whole Grain Intakes Are Associated with Healthcare Cost Savings Following Reductions in Risk of Colorectal Cancer and Total Cancer Mortality in Australia: A Cost-of-Illness Model." Nutrients **13**(9).

Whole grain consumption has been associated with the reduced risk of several chronic diseases with significant healthcare monetary burden, including cancer. Colorectal cancer (CRC) is one of the most common cancers globally, with the highest rates reported in Australia. Three servings of whole grains provide a 15% reduction in total cancer and 17% reduction in CRC risk; however, 70% of Australians fall short of this level of intake. The aim of this study was to assess the potential savings in healthcare costs

associated with reductions in the relative risk of CRC and total cancer mortality following the whole grain Daily Target Intake (DTI) of 48 g in Australia. A three-step cost-of-illness analysis was conducted using input parameters from: (1) estimates of current and targeted whole grain intakes among proportions (5%, 15%, 50%, and 100%) of the Australian adult (>/=20 years) population; (2) estimates of reductions in relative risk (with 95% confidence intervals) of CRC and total cancer mortality associated with specific whole grain intake from meta-analysis studies; and (3) estimates of annual healthcare costs of CRC and all cancers from disease expenditure national databases. A very pessimistic (5% of population) through to universal (100% of population) adoption of the recommended DTI in Australia were shown to potentially yield savings in annual healthcare costs equal to AUD 1.9 (95% CI 1.2-2.4) to AUD 37.2 (95% CI 24.1-48.1) million for CRC and AUD 20.3 (95% CI 12.2-27.0) to AUD 405.1 (95% CI 243.1-540.1) million for total cancers. As treatment costs for CRC and other cancers are increasing, and dietary measures exchanging whole grains for refined grains are not cost preclusive nor does the approach increase energy intake, there is an opportunity to facilitate cost-savings along with reductions in disease for Australia. These results suggest specific benefits of encouraging Australians to swap refined grains for whole grains, with greater overall adherence to suggestions in dietary guidelines.

Abe, C., et al. (2021). "A longitudinal association between the traditional Japanese diet score and incidence and mortality of breast cancer-an ecological study." Eur J Clin Nutr **75**(6): 929-936.

BACKGROUND: The traditional Japanese diet is considered one of the important factors of health and longevity in Japanese people. Breast cancer is the most common cancer among women in the world. However, the association between the traditional Japanese diet and breast cancer is unclear. The purpose of this study was to investigate the longitudinal association between the traditional Japanese diet score (TJDS) with the incidence and mortality of breast cancer in an ecological study. METHODS: Food supply and breast cancer incidence and mortality by country were obtained from an international database. TJDS by country was calculated from nine food groups and the total score ranged from -9 to 9, with higher scores indicating greater adherence to a traditional Japanese diet. Longitudinal associations of interaction between TJDS and fiscal year on breast cancer incidence and mortality were investigated in 139 countries with populations of 1 million or greater. The longitudinal analysis was evaluated using four linear mixed-effect models with different adjustment covariables. RESULTS: Many countries with high scores on TJDS had lower distributions of breast cancer incidence and mortality in 1990-2017. Longitudinal analysis using a linear mixed-effect model controlled for socio-economic and lifestyle covariables showed that the interaction between TJDS and fiscal year was significantly associated with incidence of breast cancer (-0.453 +/- 0.138, $p < 0.01$) and mortality of breast cancer (-0.455 +/- 0.135, $p < 0.001$). CONCLUSIONS: This longitudinal analysis suggested that a traditional Japanese diet has been associated with lower breast cancer incidence and mortality worldwide in recent years.

Abe, C., et al. (2022). "Global Association between Traditional Japanese Diet Score and All-Cause, Cardiovascular Disease, and Total Cancer Mortality: A Cross-Sectional and Longitudinal Ecological Study." J Am Nutr Assoc: 1-8.

OBJECTIVE: Studies conducted on Japanese people have suggested that a traditional Japanese diet contributes to good health, longevity, and protection against several non-communicable diseases. However, it is unknown whether traditional Japanese dietary patterns are associated with all-cause mortality, cardiovascular disease, and cancer mortality globally. The purpose of this cross-sectional and longitudinal ecological study is to clarify the global association between the traditional Japanese diet score (TJDS) and all-cause, cardiovascular disease, and total cancer mortality. METHODS: Data on food supply and all-cause mortality, cardiovascular disease mortality, total cancer mortality, and covariables by country were obtained from a relevant internationally available database. TJDS by country was calculated from eight food groups and the total score ranged from -8 to 8, with higher scores indicating greater adherence to a traditional Japanese diet. We evaluated the cross-sectional and 10-year longitudinal association between TJDS and all-cause, cardiovascular disease, and total cancer mortality using 2009 as the baseline in 142 countries with populations of more than one million. A cross-sectional analysis and a longitudinal analysis were performed using three general linear models or three linear mixed models with different covariables. RESULTS: In cross-sectional models controlled for fully-adjusted covariables, TJDS was negatively associated with all-cause mortality (beta +/- standard error; -43.819 +/- 11.741, $p < 0.001$), cardiovascular disease mortality (-22.395 +/- 4.638, $p < 0.001$), and total cancer mortality (-3.893 +/- 1.048, $p < 0.001$). In 10-year longitudinal models controlled for fully-adjusted covariables, TJDS was significantly negatively associated with all-cause mortality (-31.563 +/- 7.695, $p < 0.001$), cardiovascular disease mortality (-16.249 +/- 4.054, $p < 0.001$), and total cancer mortality (-3.499 +/- 0.867, $p < 0.001$).

CONCLUSIONS: This cross-sectional and longitudinal ecological study suggests that the traditional Japanese diet is associated with lower all-cause mortality, cardiovascular disease mortality, and total cancer mortality, worldwide.

Abera, S. F., et al. (2020). "Lung Cancer Attributed Mortality Among 316,336 Early Stage Breast Cancer Cases Treated by Radiotherapy and/or Chemotherapy, 2000-2015: Evidence From the SEER Database." Front Oncol **10**: 602397.

OBJECTIVE: To estimate the risk of death from lung cancer in patients treated for breast cancer (BC) in relation to the general population. METHODS: BC data, covering 2000 to 2015, were extracted from the Surveillance, Epidemiology and End Results-18 (SEER-18) cancer registry database. A comparison of lung cancer attributed mortality between BC patients and the general population was performed using standardized mortality ratios (SMRs) and SMRs conditional on survival length (cSMRs). Prognostic factors of lung cancer mortality were identified using flexible parametric modelling. Our model adjusts the effect of downstream (histopathological BC tumor grade and hormone receptor status) and upstream (age at diagnosis, ethnicity, and marital status) factors. RESULTS: The median follow-up was 6.4 years (interquartile range, 3.0-10.3 years). BC cases who received only radiotherapy (cSMR = 0.93; 95%CI: 0.77-1.13), only chemotherapy (cSMR = 0.91; 0.62-1.33), and radio-and chemotherapy (cSMR = 1.04; 0.77-1.39) had no evidence of increased lung cancer mortality relative to the general population. The adjusted model identified that lung cancer mortality was higher for women who were older at diagnosis compared to those <50 years (ranging from HR50-59 = 3.41 [95%CI: 2.72-4.28] to HR70-79 = 10.53 [95%CI: 8.44-13.13]) and for cases with negative estrogen and progesterone receptors (HR =1.38; 95% CI: 1.21-1.57). Compared to married cases, widowed, divorced, single or others had a 76%, 45%, and 25% higher hazard of lung cancer mortality, respectively. Lung cancer mortality was lower for American Indian/Alaska Native and Asian/Pacific Islander ethnicities (HR = 0.51; 95% CI: 0.40-0.64) compared to BC cases with white ethnic background. CONCLUSIONS: There is no evidence for a higher lung cancer mortality in BC patients when compared to the general population.

Abubakar, M., et al. (2021). "Tumor-Associated Stromal Cellular Density as a Predictor of Recurrence and Mortality in Breast Cancer: Results from Ethnically Diverse Study Populations." Cancer Epidemiol Biomarkers Prev **30**(7): 1397-1407.

PURPOSE: Tumor-associated stroma is comprised of fibroblasts, tumor-infiltrating lymphocytes (TIL), macrophages, endothelial cells, and other cells that interactively influence tumor progression through inflammation and wound repair. Although gene-expression signatures reflecting wound repair predict breast cancer survival, it is unclear whether combined density of tumor-associated stromal cells, a morphologic proxy for inflammation and wound repair signatures on routine hematoxylin and eosin (H&E)-stained sections, is of prognostic relevance. METHODS: By applying machine learning to digitized H&E-stained sections for 2,084 breast cancer patients from China (n = 596; 24-55 years), Poland (n = 810; 31-75 years), and the United States (n = 678; 55-78 years), we characterized tumor-associated stromal cellular density (SCD) as the percentage of tumor-stroma that is occupied by nucleated cells. Hazard ratios (HR) and 95% confidence intervals (CI) for associations between SCD and clinical outcomes [recurrence (China) and mortality (Poland and the United States)] were estimated using Cox proportional hazard regression, adjusted for clinical variables. RESULTS: SCD was independently predictive of poor clinical outcomes in hormone receptor-positive (luminal) tumors from China [multivariable HR (95% CI)(fourth(Q4) vs. first(Q1) quartile) = 1.86 (1.06-3.26); P (trend) = 0.03], Poland [HR (95% CI)(Q4 vs. Q1) = 1.80 (1.12-2.89); P (trend) = 0.01], and the United States [HR (95% CI)(Q4 vs. Q1) = 2.42 (1.33-4.42); P (trend) = 0.002]. In general, SCD provided more prognostic information than most classic clinicopathologic factors, including grade, size, PR, HER2, IHC4, and TILs, predicting clinical outcomes irrespective of menopausal or lymph nodal status. SCD was not predictive of outcomes in hormone receptor-negative tumors. CONCLUSIONS: Our findings support the independent prognostic value of tumor-associated SCD among ethnically diverse luminal breast cancer patients. IMPACT: Assessment of tumor-associated SCD on standard H&E could help refine prognostic assessment and therapeutic decision making in luminal breast cancer.

Abu-Freha, N., et al. (2022). "The impact of the COVID-19 pandemic on colorectal and gastric cancer diagnosis, disease stage and mortality." Front Med (Lausanne) **9**: 954878.

BACKGROUND: Since the outbreak of COVID-19, a significant decline in endoscopic procedures has been observed. AIMS: We investigated the change of incidence, clinical characteristics, disease stage and mortality of patients with gastric cancer (GC) or colorectal cancer (CRC) diagnosed in 2020 compared to the pre-pandemic year 2019. METHODS: Demographic, clinical and laboratory data on all patients diagnosed with GC or CRC at the Soroka University Medical Center were retrospectively

collected and compared. Number of cases, time of diagnosis, clinical presentation, staging at diagnosis and mortality rates were compared. RESULTS: Two hundred sixteen patients were diagnosed with CRC in 2019, whereas only 162 were diagnosed in 2020 (25% reduction), while 36 GC diagnoses were made in 2019 compared to 24 in 2020 (33% reduction). The age-adjusted incidence was calculated to be 24.28 for CRC and 5.0 for GC in 2020 compared to 29.93 and 5.32 in 2019, respectively. CRC patients had a significantly lower rate of rectal bleeding as their presenting symptom in 2020 compared with 2019, 8.1 vs. 19% (p = 0.003), but higher rate of diarrhea as their presenting symptom, 4.3 vs. 1% (p = 0.044). No significant differences regarding other presenting symptoms, comorbidities, surgery or mortality rates were found between the groups diagnosed in 2019 or 2020. CONCLUSION: A decrease in GC and CRC incidence was observed during the year 2020; lower rate of rectal bleeding and higher rate of diarrhea as presenting symptoms were noted in 2020, but no significant difference was found regarding other presenting symptoms, disease stage, surgery or mortality.

Adams, S. A., et al. (2022). "Rural and racial disparities in colorectal cancer incidence and mortality in South Carolina, 1996 - 2016." J Rural Health **38**(1): 34-39.

PURPOSE: Colorectal cancer (CRC) is the third leading cause of cancer mortality among men and women in the United States and South Carolina (SC). Since SC has one of the highest proportions of Black (27.9%) and rural residents (33.7%), the purpose of this investigation was to describe the burden of CRC on racial disparities in rural populations. METHODS: Count data from 2012 to 2016 were obtained from the state central cancer registry using an online data retrieval system. Rural-urban status was determined using Urban Influence Codes (1-2 = urban; 3-12 = rural). Chi-square tests were calculated to examine differences in CRC stage by rurality and race. Annual percent change and annual average percent change (AAPC) were calculated to examine trends in incidence and mortality rates across rural-urban and racial groups between 1996 and 2016. RESULTS: Areas with high mortality-to-incidence ratios tended to be in rural counties. Furthermore, rural residents had higher proportions of distant stage CRC compared to urban residents, and Black populations had higher proportions of distant stage CRC compared to White populations (22.7% vs. 26.3% and 29.3% vs. 23.7%, respectively; P value < 0.05). From 1996 to 2016, Black and White urban-dwelling residents experienced a significant decline in incidence. Urban White, urban Black, and rural White populations experienced significant declines in mortality (AAPC = -2.6% vs -2.4% vs -1.6% vs -0.9%, respectively). CONCLUSIONS: Despite improvements in CRC screening in recent decades, focused evidenced-based interventions for lowering incidence and mortality among rural and Black populations in South Carolina are necessary.

Adogwa, O., et al. (2022). "Spine-specific skeletal related events and mortality in non-small cell lung cancer patients: a single-institution analysis." J Neurosurg Spine **36**(1): 125-132.

OBJECTIVE: The population prevalence of non-small cell lung cancer (NSCLC) continues to increase; however, data are limited regarding the incidence rate of skeletal related events (SREs) (i.e., surgery to the spinal column, radiation to the spinal column, radiofrequency ablation, kyphoplasty/vertebroplasty, spinal cord compression, or pathological vertebral body fractures) and their impact on overall mortality. In this study, the authors sought to estimate the incidence rates of SREs in NSCLC patients and to quantify their impact on overall mortality. METHODS: This was a single-institution retrospective study of patients diagnosed with NSCLC between 2002 and 2014. The incidence rates for bone metastasis and subsequent SREs (per 1000 person-years) by time since lung cancer diagnosis were calculated and analyses were stratified separately for each histological type. Incidence rates for mortality at 1, 2, and 3 years from diagnosis stratified by the presence of SREs were also calculated. Kaplan-Meier survival curves were constructed to describe crude survival ratios in patients with spine metastasis and SREs and those with spine metastasis but without SREs. These curves were used to estimate the 1- and 2-year survival rates for each cohort. RESULTS: We identified 320 patients with incident NSCLC (median follow-up 9.5 months). The mean +/- SD age was 60.65 +/- 11.26 years; 94.48% of patients were smokers and 60.12% had a family history of cancer. The majority of first-time SREs were pathological vertebral body compression fractures (77.00%), followed by radiation (35%), surgery (14%), and spinal cord compression (13.04%). Mortality rates were highest in NSCLC patients with spine metastasis who had at least 1 SRE. Stratifying by histological subtype, the incidence rate of mortality in patients with SRE was highest in the large cell cohort, 7.42 per 1000 person-years (95% CI 3.09-17.84 per 1000 person-years); followed by the squamous cell cohort, 2.49 per 1000 person-years (95% CI 1.87-3.32 per 1000 person-years); and lowest in the adenocarcinoma cohort, 1.68 per 1000 person-years (95% CI 1.46-1.94 per 1000 person-years). Surgery for decompression of neural structures and stabilization of the spinal column was required in 6% of patients. CONCLUSIONS: SREs in

NSCLC patients with bone metastasis are associated with an increased incidence rate of mortality.

Afework, T., et al. (2022). "Burden of mortality from cancer among adults in Addis Ababa, Ethiopia, using verbal autopsy, 2007-2017." Ecancermedicalscience **16**: 1428.

BACKGROUND: Cancer is one of the leading causes of death; worldwide, there were 10.0 million cancer deaths in 2020. In Ethiopia, 51,865 people died from the disease in the same year. We aimed to describe the burden of cancer mortality, the socio-demographic and other characteristics of deceased adults in Addis Ababa from 2007 to 2017. METHODS: This study was part of the Addis Ababa Mortality Surveillance Programme. Based on the burial-based surveillance, there were 133,170 adult deaths from 2007 to 2017. The standard verbal autopsy questionnaire was applied to collect information on the causes of death of 10% of the randomly selected deaths. RESULTS: Cancer accounted for 11% of all deaths studied. The median age of death in years was 60 (range = 47-70). Stomach cancer was the leading cause of cancer death (131, 13.6%), followed by breast cancer (116, 12.0%) and liver cancer (101, 10.5%). CONCLUSION: Cancer-related deaths accounted for a significant portion of all deaths. Premature deaths accounted for majority of the deaths. Cancer deaths were most commonly caused by stomach, breast and liver cancers. Advocating for a healthy lifestyle, effective cancer screening and effective alcohol-control regulations should be tailored to the country.

Ahmadi, M. N., et al. (2022). "Changes in physical activity and adiposity with all-cause, cardiovascular disease, and cancer mortality." Int J Obes (Lond) **46**(10): 1849-1858.

BACKGROUND: The relationship between joint changes in physical activity and adiposity with mortality is not well understood. We examined the association of changes in these two established risk factors with all-cause (ACM), cardiovascular disease (CVD), and cancer mortality. METHODS: We used longitudinal data from Taiwan's MJ Cohort, comprising 116,228 general population adults recruited from 1998-2013 with repeated measures 4.6 y (2.5) apart and followed up for mortality for 11.9 y (3.5). Physical activity, body mass index (BMI), waist circumference (WC), and body fat percentage (BF%) groups and changes were based on public health and clinical guidelines. RESULTS: Compared to stable-insufficient physical activity, increasing physical activity from any baseline level was associated with lower ACM (HR [95%CI]): 0.85 [0.74, 0.96]) and CVD mortality (0.72 [0.55, 0.93]) risk. This was approximately equal to meeting physical activity guidelines at both timepoints (eg: 0.71 [0.58, 0.88] for CVD mortality). Compared to stable-overweight/moderate adiposity, decreasing adiposity level attenuated but did not offset mortality risk for all three outcomes (eg: BMI = 0.95 [0.76, 1.16] for CVD mortality). Only maintaining a healthy adiposity level at both timepoints offset mortality risk (BMI = 0.75 [0.61, 0.89]) for CVD mortality). In the joint changes analyses, lower mortality risk was a consequence of increases in physical activity across adiposity change groups (eg: WC decrease = 0.57 [0.48, 0.67]; WC stability = 0.73 [0.66, 0.80], WC increase = 0.83 [0.72, 0.97] for ACM). Decreasing adiposity attenuated the negative associations of decreased physical activity (BF% = 1.13 [0.95, 1.35] for ACM). CONCLUSIONS: We found a lower risk for ACM, CVD, and cancer mortality from increasing physical activity and an attenuation from decreasing adiposity regardless of baseline levels. The beneficial associations of joint changes were primarily driven by physical activity, suggesting lower mortality risk may be more immediate through physical activity improvements compared to adiposity improvements alone.

Ahmed, Z. U., et al. (2021). "Explainable artificial intelligence (XAI) for exploring spatial variability of lung and bronchus cancer (LBC) mortality rates in the contiguous USA." Sci Rep **11**(1): 24090.

Machine learning (ML) has demonstrated promise in predicting mortality; however, understanding spatial variation in risk factor contributions to mortality rate requires explainability. We applied explainable artificial intelligence (XAI) on a stack-ensemble machine learning model framework to explore and visualize the spatial distribution of the contributions of known risk factors to lung and bronchus cancer (LBC) mortality rates in the conterminous United States. We used five base-learners-generalized linear model (GLM), random forest (RF), Gradient boosting machine (GBM), extreme Gradient boosting machine (XGBoost), and Deep Neural Network (DNN) for developing stack-ensemble models. Then we applied several model-agnostic approaches to interpret and visualize the stack ensemble model's output in global and local scales (at the county level). The stack ensemble generally performs better than all the base learners and three spatial regression models. A permutation-based feature importance technique ranked smoking prevalence as the most important predictor, followed by poverty and elevation. However, the impact of these risk factors on LBC mortality rates varies spatially. This is the first study to use ensemble machine learning with explainable algorithms to explore and visualize the spatial heterogeneity of the relationships between LBC mortality and risk factors in the contiguous USA.

Akaike, H., et al. (2020). "Mortality calculator as a possible prognostic predictor of overall survival after gastrectomy in elderly patients with gastric cancer." World J Surg Oncol **18**(1): 283.

BACKGROUND: The number of elderly patients with gastric cancer has been increasing. Most elderly patients have associated reduced physiologic functions that can sometimes become an obstacle to safe surgical treatment. The National Clinical Database Risk Calculator, which based on a large Japanese surgical database, provides predicted mortality and morbidity in each case as the surgical-related risks. The purpose of this study was to investigate the clinical significance of the risk for operative mortality (NRC-mortality), as calculated by the National Clinical Database Risk Calculator, during long-term follow-up after gastrectomy for elderly patients with gastric cancer. METHODS: We enrolled 73 patients aged >/= 80 years and underwent gastrectomy at our institution. Their surgical risk was evaluated based on the NRC-mortality. Several clinicopathologic factors, including NRC-mortality, were selected and analyzed as the possible prognostic factors for elderly patients who have undergone gastrectomy for gastric cancer. Statistical analysis was performed using the log-rank test and Cox proportional hazard model. RESULTS: NRC-mortality ranged from 0.5 to 10.6%, and the median value was 1.7%. Dividing the patients according to mortality, the overall survival was significantly worse in the high mortality group (>/= 1.7%, n = 38) than in the low mortality group (< 1.7%, n = 35), whereas disease-specific survival was not different between the two groups. In the Cox proportional hazard model, multivariate analysis revealed NRC-mortality, performance status, and surgical procedure as the independent prognostic factors for overall survival. For disease-specific survival, the independent prognostic factors were performance status and pathological stage but not NRC-mortality. CONCLUSION: The NRC-mortality might be clinically useful for predicting both surgical mortality and overall survival after gastrectomy in elderly patients with gastric cancer.

Akuta, N., et al. (2022). "Dynamics of Circulating miR-122 Predict Liver Cancer and Mortality in Japanese Patients with Histopathologically Confirmed NAFLD and Severe Fibrosis Stage." Oncology **100**(1): 31-38.

INTRODUCTION: It is unclear whether the relationships between changes in fibrosis and circulating microRNA-122 (miR-122) dynamics might influence the prognosis of nonalcoholic fatty liver disease (NAFLD). METHODS: This study investigates the impact of serum miR-122 dynamics and histological changes on the incidence of liver cancer and mortality in 81 Japanese NAFLD patients who underwent serial liver biopsies. The median interval between the first and second liver biopsies was 2.9 years. RESULTS: The fibrosis stage scores indicated progression, no change, and improvement (a decrease of one point or more) in 21.0%, 56.8%, and 22.2% of the patients, respectively. There were 64 patients in the high-risk group who had no improvement in stage scores. Among these, the miR-122 levels were significantly lower in 7 patients with liver cancer than those of the 54 patients who had no liver cancer at the second liver biopsy. The cumulative rates of liver cancer were significantly higher in cases with miR-122 ratios <0.5 (serum miR-122 level at second biopsy to that at first biopsy) than those with ratios >/=0.5. The cumulative survival rates in cases with miR-122 ratios <0.5 tended to be lower than those with ratios >/=0.5. Of the 64 high-risk patients, 39 indicated stage 2 or greater (severe fibrosis stage) at the first liver biopsy and also showed similar results of cumulative liver cancer and survival rates. CONCLUSIONS: Longitudinal examination of serial liver biopsies indicated that the circulating miR-122 dynamics might be useful in predicting the prognosis for NAFLD patients with severe fibrosis stage and no improvement of the stage scores.

Albhaisi, S. and R. Qayyum (2022). "The association between serum liver enzymes and cancer mortality." Clin Exp Med **22**(1): 75-81.

Interpreting levels of liver enzymes is often challenging because they may be influenced by metabolic processes beyond the liver. Given their pathophysiologic roles in inflammation and oxidative stress, higher levels of these enzymes may be associated with increased risk of mortality. However, studies have found inconsistent results. Thus, we examined the association of liver enzymes levels with cancer mortality in the general US adult population. We used the US National Health and Nutrition Examination Survey from 1999 to 2016. Kaplan-Meier survival curve comparisons were examined across quartiles of liver enzymes. Cox proportional hazards models were built to examine the relationship between cancer mortality and liver enzymes quartiles without and with adjustment for potential confounding factors. During the 338,882 person-years follow-up, 1059 participants had cancer-related deaths. There was a nonlinear U-shaped relationship between serum alanine and aspartate aminotransferase (ALT and AST) levels and cancer mortality. There was no relationship between cancer mortality and gamma-glutamyltransferase (GGT); however, each 10 IU/L increase in GGT after median was associated with 1% higher mortality risk (HR = 1.01; 95% CI = 1.00, 1.02;

P = 0.001). Only subjects with high levels of alkaline phosphatase (ALP) had higher cancer mortality (HR = 1.63; 95CI = 1.30, 2.05; P < 0.001 and HR = 1.52; 95%CI = 1.20, 1.94; P = 0.001, respectively). Only the lowest and highest serum ALT and AST levels are associated with increased cancer mortality. For ALP, the relationship is present at higher levels. The association with GGT was not robust to different analyses. The mechanisms underlying the observed relationships need further exploration.

Al-Hajeili, M., et al. (2022). "Morbidity and mortality among patients with breast cancer receiving anticancer treatment before and during the COVID-19 pandemic: A single tertiary center experience." Oncol Lett **24**(6): 454.

Breast cancer is the most common cancer type in women in Saudi Arabia (SA). Globally, cancer treatment has been affected by the recent COVID-19 pandemic. The present retrospective study reviews the 30-day morbidity and mortality rates of patients with breast cancer receiving anticancer systemic treatment before (group1) and during the peak of the COVID-19 (group 2) pandemic at a tertiary center, King Abdulaziz University Hospital (Jeddah, SA). There were no differences between the two groups regarding sex, age, breast cancer stage distribution, intention to treat or class of anticancer treatment received. Patients treated during the peak pandemic period received delayed treatment. No statistically significant difference was observed in the 30-day morbidity or mortality rates, although there was a trend towards higher rates of morbidity among patients treated during the peak of the pandemic period. In group 2, only 2.3% of the patients tested positive for COVID-19, and there was no significant difference in the 30-day morbidity and mortality rates between COVID-positive and COVID-negative patients receiving anticancer treatment. Individuals with breast cancer are a vulnerable group of patients that should be treated with special care during pandemics or other crises that affect the health care system.

Ali, B., et al. (2021). "Risk Factors for 30-Day Mortality After Head and Neck Microsurgical Reconstruction for Cancer: NSQIP Analysis." OTO Open **5**(3): 2473974X211037257.

OBJECTIVE: To identify the incidence and risk factors for 30-day postoperative mortality after microsurgical head and neck reconstruction following oncological resection. STUDY DESIGN: Retrospective case-control study. SETTING: American College of Surgeons National Surgical Quality Improvement Program (NSQIP) database. METHODS: Microsurgical head and neck reconstructive cases were identified from 2005 to 2018 using Current Procedural Terminology codes and oncologic procedures using the International Classification of Disease 9 and 10 codes. The outcome of interest was 30-day mortality. RESULTS: The 30-day postoperative mortality rate was 1.2%. Univariate logistic regression analysis identified the following associations: age >80 years, hypertension, poor functional status, preoperative wound infection, renal insufficiency, malnutrition, anemia, and prolonged operating time. Multivariable logistic regression models were used to stratify further by the degree of malnutrition and anemia. Hematocrit <30% was found to be an independent risk factor for 30-day postoperative mortality (odds ratio [OR] = 9.59, confidence interval [CI] 2.32-39.65, P < .1) with albumin <3.5 g/dL. This association was even stronger with albumin <2.5 g/dL (OR = 11.64, CI 3.06-44.25, P < .01). One-third of patients (36.6%) had preoperative anemia, of which less than 1% required preoperative transfusion, although one-quarter (24.6%) required intraoperative or 72 hours postoperative transfusion. CONCLUSIONS: Preoperative anemia is a risk factor for 30-day postoperative mortality. This association seems to get stronger with worsening anemia. Identification and optimization of such patients preoperatively may mitigate the incidence of 30-day postoperative mortality.

Ali Hassan Sajid, M., et al. (2021). "Perioperative Dexamethasone Is Associated With Higher Short-Term Mortality in Reconstructive Head and Neck Cancer Surgery. Is It Really the Case?" J Oral Maxillofac Surg **79**(5): 951-952.

Alif, S. M., et al. (2022). "Cancer and mortality in coal mine workers: a systematic review and meta-analysis." Occup Environ Med **79**(5): 347-357.

Coal mine workers are exposed to a number of workplace hazards which may increase the risk of cancer and mortality. We conducted a systematic review and meta-analysis to investigate cancer and mortality in coal mine workers We searched in Ovid Medline, PubMed, Embase and Web of Science databases using keywords and text words related to coal mines, cancer and mortality and identified 36 full-text articles using predefined inclusion criteria. Each study's quality was assessed using the Newcastle-Ottawa Scale. We performed random-effect meta-analyses including 21 of the identified articles evaluating cancer and/or mortality of coal mine workers. The meta-analysis showed an increased risk of all-cause mortality (SMR 1.14, 95% CI 1.00 to 1.30) and mortality from non-malignant respiratory disease (NMRD) (3.59, 95% CI 3.00 to 4.30) in cohorts with coal workers' pneumoconiosis (CWP). We found a somewhat increased risk of stomach cancer (1.11, 95% CI 0.97 to 1.35) and of mortality from NMRD (1.26,

95% CI 0.99 to 1.61) in the cohorts of coal miners with unknown CWP status. The meta-analysis also showed a decreased risk of prostate cancer and cardiovascular and cerebrovascular mortality among coal miners. This may be a result of the healthy worker effect and possible lower smoking rates, and perhaps also reflect the physically active nature of many jobs in coal mines. The meta-analysis for lung cancer did not show increased risk in coal miners with CWP (1.49, 95% CI 0.70 to 3.18) or for coal miners of unknown CWP status (1.03, 95% CI 0.91 to 1.18). Lower smoking rates in coal mine workers could explain why case-control studies where smoking was controlled for showed higher risks for lung cancer than were seen in cohort studies. Coal mine workers are at increased risk of mortality from NMRD but decreased risk of prostate cancer and cardiovascular and cerebrovascular mortality. Studies of coal mine workers need long-term follow-up to identify increased mortality and cancer incidence.

Alimena, S., et al. (2021). "Race- and Age-Related Disparities in Cervical Cancer Mortality." J Natl Compr Canc Netw **19**(7): 789-795.

BACKGROUND: Although the incidence of cervical cancer among younger Black women is now equivalent to that of White women, it is unknown whether the reduced incidence has affected survival rates among younger Black women. The goal of this study was to assess differences in survival by age and race. PATIENTS AND METHODS: A retrospective cohort study was performed using the National Cancer Database to analyze women with nonmetastatic cervical cancer diagnosed between 2004 and 2014. Women with unknown survival data and those who died within 3 months of diagnosis were excluded. Multivariable logistic regression models evaluated interactions between age and race (Black vs non-Black) for presentation with stage I disease and receipt of optimal treatment. A multivariable Cox regression model was used to evaluate survival differences by age and race. RESULTS: Of 55,659 women included, 16.4% were Black. Compared with their non-Black counterparts, fewer Black women presented with stage I disease (37.8% vs 47.8%; P<.01) and received optimal treatment (46.2% vs 58.3%; P<.01). Fewer Black women had private insurance if they were aged <65 years (39.6% vs 55.7%; P<.01), but not if they were aged >/=65 years (11.7% vs 12.4%; P=.43). According to multivariable logistic regression, Black women aged </=39 years were less likely to present with stage I disease, with a significant interaction term between age and race (P<.01 for interaction). Disparities in overall survival by race were greatest for Black women aged </=39 years (adjusted hazard ratio, 1.32; 95% CI, 1.20-1.46; P<.01) but decreased with increasing age interval until no disparity was noted for women aged >/=65 years (P<.01 for interaction). CONCLUSIONS: Younger Black women with cervical cancer are at risk for presenting with higher-stage disease and having worse overall survival. These findings may be related to insurance-related disparities and inadequate follow-up for abnormal Papanicolaou test results. Younger Black women with cervical cancer may be a particularly vulnerable population.

Allahqoli, L., et al. (2022). "The Global Incidence, Mortality, and Burden of Breast Cancer in 2019: Correlation With Smoking, Drinking, and Drug Use." Front Oncol **12**: 921015.

BACKGROUND: Female breast cancer (FBC) is the most common type of cancer and is associated with a considerable disease burden as well as significant mortality rates. The present study aimed to provide an update on the incidence, mortality, and burden of FBC in 2019, based on the Global Burden of Disease (GBD) Study. MATERIALS: The incidence, death rate, disability-adjusted life years (DALYs), years of life lost (YLLs), years lived with disability (YLDs), the age-standardized rates (ASR) of FBC in 204 countries, and a variety of classifications, were retrieved from the Global Burden of Disease Study. Data on tobacco use, alcohol consumption, and drug use were collected. The incidence, mortality, and burden of FBC were registered and compared between regions. Associations between age-standardized incidence rates and age-standardized mortality rates of FBC with smoking, drinking, and drug use were determined. RESULTS: The highest incidence of FBC was observed in countries with a high socioeconomic status such as those of the European continent. Despite the lower incidence of FBC in countries with a low socio-demographic index (SDI), mortality rates secondary to FBC are higher in these countries than in high-income countries. The highest age-standardized mortality rate has been reported in the Eastern Mediterranean Region (EMRO), followed by the African Region (AFRO). The highest age-standardized rates of DALY and YLL per 100,000 population in 2019 were observed in lower-income countries, while the highest ASR of YLD per 100,000 population was reported in high-income countries. CONCLUSION: The present GBD-based study provides a comprehensive review of the incidence, mortality, and burden of FBC in 2019. The incidence of FBC is higher in regions with a higher socioeconomic status, whereas mortality rates and DALYs are higher in poorly developed regions. We suggest better screening measures and early detection programs for the latter regions.

Almangush, A., et al. (2020). "Cell-in-cell phenomenon associates with aggressive characteristics and cancer-related mortality in early oral tongue cancer." BMC Cancer **20**(1): 843.

BACKGROUND: Cell-in-cell structures (caused by cell cannibalistic activity) have been related to prognosis of many cancers. This is the first multi-institutional study to assess the prognostic impact of cell-in-cell structures in a large cohort of early oral tongue squamous cell carcinomas (OTSCC). METHODS: A total of 308 cases from five Finnish University Hospitals and from the A.C. Camargo Cancer Center, Sao Paulo, Brazil, were included in this study. Cell-in-cell structures were evaluated on surgical postoperative sections that stained with hematoxylin and eosin staining. RESULTS: We found that cell-in-cell structures associated with cancer-related mortality in univariable analysis with a hazard ratio (HR) of 2.99 (95%CI 1.52-5.88; P = 0.001). This association was confirmed in multivariable analysis (HR 2.22, 95%CI 1.12-4.44; P = 0.024). In addition, statistically significant associations were observed between the cell-in-cell structures and other adverse histopathologic characteristics including deep invasion (P < 0.001), high index of tumor budding (P = 0.007), worst pattern of invasion (P < 0.001), perineural invasion (P = 0.01), and stroma-rich pattern (P = 0.001). CONCLUSIONS: Our findings demonstrate a significant relationship between cell-in-cell formation and aggressive characteristics of early OTSCC. Cell-in-cell structures have a distinct impact as a novel prognostic indicator in early OTSCC and they can be easily assessed during routine pathology practice.

Alyabsi, M. S., et al. (2022). "The 30-day hospital readmission and mortality after surgery in colorectal cancer patients." BMC Gastroenterol **22**(1): 434.

PURPOSE: Hospital readmissions in the first weeks following surgery are common, expensive, and associated with increased mortality among colorectal cancer patients. This study is designed to assess the 30-day hospital readmission after colorectal cancer surgery and evaluate the risk factors that affect hospital readmission. METHODS: The study uses data from the Ministry of National Guard-Health Affairs Cancer Registry. All colorectal cancer patients who underwent colorectal cancer surgery between January 1, 2016, and November 31, 2021, were investigated. Factors examined were age, gender, marital status, Body Mass Index, Charlson Comorbidity Index, chemotherapy, radiotherapy, tumor stage, grade, site, surgical approach, length of stay, and discharge location. Kaplan-Meier curves were constructed to assess survival rates between readmitted and non-readmitted patients, and logistic regressions were performed to assess predictors of readmission. RESULTS: A total of 356 patients underwent tumor resection and 49 patients were readmitted within 30-day of index discharge. The most common reasons for hospital readmissions were gastrointestinal (22.45%), urinary tract infection (16.33%), and surgical site infection (12.24%). In the multivariable analysis, females were 89% more likely to be readmitted compared to males (odds ratio 1.89, 95% confidence intervals 1.00-3.58). Patients with distant metastatic tumors have higher odds of readmission (odds ratio 4.52, 95% confidence intervals 1.39-14.71) compared to patients with localized disease. CONCLUSIONS: Colorectal cancer readmission is more common in patients with metastatic disease. Strategies to reduce readmission include planned transition to outpatient care, especially among patients with a high risk of readmission.

Amini, M., et al. (2022). "Global pattern of trends in incidence, mortality, and mortality-to-incidence ratio rates related to liver cancer, 1990-2019: a longitudinal analysis based on the global burden of disease study." BMC Public Health **22**(1): 604.

BACKGROUND: Liver cancer (LC) is considered as one of the most dominant malignant tumors which ranked 4(th) and in terms of global mortality and incidence, respectively. This work aimed to investigate the global temporal trends in LC mortality-to-incidence ratio (MIR) and its components, with a particular focus on examining long-term effect of human development index (HDI) on these metrics in a 30-year follow-up. METHODS: The age-standardized LC incidence and mortality data were derived from the global burden of disease (GBD) study 2019. We first leveraged joinpoint piecewise linear regression analysis to ascertain time trends in LC incidence, mortality, and MIR complement [1-MIR] and the average annual percentage change (AAPC) of the rates over the period 1990-2019. Then, the association between the metrics and HDI was explored through longitudinal multilevel models (LMMs). RESULTS: The incidence rates paralleled the mortality rates worldwide and they had similar significant monotonic decrementing trends with AAPC values of - 1.10% (95% confidence interval (CI): - 1.40, - 0.90%) and - 1.40% (- 1.50, - 1.30%), respectively from 1990 to 2019. The [1-MIR] rates were around 0 and showed an increasing pattern from 1.70 to 8.10 per 100,000 people (AAPC, 4.90%) at the same period of time. Results from the LMMs displayed that the majority of the variation lies at the country level accounted for about 88% of the total variance. Moreover, our analysis supported that the HDI was negatively associated with either incidence or mortality over time (p < 0.05). CONCLUSIONS: Our findings highlighted that the global long-term temporal trends of LC incidence and mortality decreased slightly during 1990-2019 which

may reflect improved therapeutic strategies and public health interventions. Besides, the low rates of [1-MIR] revealed the five-year relative survival rate was poor implying LC is diagnosed late in its development. Thereby, the policymakers' focus must be on early screening and detection of liver cancer.

Anderson, C., et al. (2021). "Long-term Patterns of Excess Mortality among Endometrial Cancer Survivors." Cancer Epidemiol Biomarkers Prev **30**(6): 1079-1088.

BACKGROUND: We investigated excess mortality after endometrial cancer using conditional relative survival estimates and standardized mortality ratios (SMR). METHODS: Women diagnosed with endometrial cancer during 2000-2017 (N = 183,153) were identified in the Surveillance Epidemiology and End Results database. SMRs were calculated as observed deaths among endometrial cancer survivors over expected deaths among demographically similar women in the general U.S. POPULATION: Five-year relative survival was estimated at diagnosis and each additional year survived up to 12 years post-diagnosis, conditional on survival up to that year. RESULTS: For the full cohort, 5-year relative survival was 87.7%, 96.2%, and 97.1% at 1, 5, and 10 years post-diagnosis, respectively. Conditional 5-year relative survival first exceeded 95%, reflecting minimal excess mortality compared with the general population, at 4 years post-diagnosis overall. However, in subgroup analyses, conditional relative survival remained lower for Black women (vs. White) and for those with regional/distant stage disease (vs. localized) throughout the study period. The overall SMR for all-cause mortality decreased from 5.90 [95% confidence interval (CI), 5.81-5.99] in the first year after diagnosis to 1.16 (95% CI, 1.13-1.19) at 10+ years; SMRs were consistently higher for non-White women and for those with higher stage or grade disease. CONCLUSIONS: Overall, endometrial cancer survivors had only a small survival deficit beyond 4 years post-diagnosis. However, excess mortality was greater in magnitude and persisted longer into survivorship for Black women and for those with more advanced disease. IMPACT: Strategies to mitigate disparities in mortality after endometrial cancer will be needed as the number of survivors continues to increase.

Atkins, K. M., et al. (2022). "Elevated Coronary Artery Calcium Quantified by a Validated Deep Learning Model From Lung Cancer Radiotherapy Planning Scans Predicts Mortality." JCO Clin Cancer Inform **6**: e2100095.

PURPOSE: Coronary artery calcium (CAC) quantified on computed tomography (CT) scans is a robust predictor of atherosclerotic coronary disease; however, the feasibility and relevance of quantitating CAC from lung cancer radiotherapy planning CT scans is unknown. We used a previously validated deep learning (DL) model to assess whether CAC is a predictor of all-cause mortality and major adverse cardiac events (MACEs). METHODS: Retrospective analysis of non-contrast-enhanced radiotherapy planning CT scans from 428 patients with locally advanced lung cancer is performed. The DL-CAC algorithm was previously trained on 1,636 cardiac-gated CT scans and tested on four clinical trial cohorts. Plaques >/= 1 cubic millimeter were measured to generate an Agatston-like DL-CAC score and grouped as DL-CAC = 0 (very low risk) and DL-CAC >/= 1 (elevated risk). Cox and Fine and Gray regressions were adjusted for lung cancer and cardiovascular factors. RESULTS: The median follow-up was 18.1 months. The majority (61.4%) had a DL-CAC >/= 1. There was an increased risk of all-cause mortality with DL-CAC >/= 1 versus DL-CAC = 0 (adjusted hazard ratio, 1.51; 95% CI, 1.01 to 2.26; P = .04), with 2-year estimates of 56.2% versus 45.4%, respectively. There was a trend toward increased risk of major adverse cardiac events with DL-CAC >/= 1 versus DL-CAC = 0 (hazard ratio, 1.80; 95% CI, 0.87 to 3.74; P = .11), with 2-year estimates of 7.3% versus 1.2%, respectively. CONCLUSION: In this proof-of-concept study, CAC was effectively measured from routinely acquired radiotherapy planning CT scans using an automated model. Elevated CAC, as predicted by the DL model, was associated with an increased risk of mortality, suggesting a potential benefit for automated cardiac risk screening before cancer therapy begins.

Au, P. C., et al. (2021). "Sarcopenia and mortality in cancer: A meta-analysis." Osteoporos Sarcopenia **7**(Suppl 1): S28-S33.

OBJECTIVES: The aim of this meta-analysis is to comprehensively evaluate the effects of lean mass on all-cause mortality across different cancer types. METHODS: This is a meta-analysis. Cohort studies on lean mass and mortality published before December 20, 2017 were obtained by systematic search on PubMed, Cochrane Library, and Embase. Inclusion criteria were cohort studies reporting lean mass measurements by dual-energy X-ray absorptiometry, bioimpedance analysis or computed tomography, and with all-cause mortality as the study outcome. Exclusion criteria were studies using muscle mass surrogates, anthropometric measurement of muscle, rate of change in muscle mass, and sarcopenia defined by composite criteria. Hazard ratios (HRs) and 95% confidence intervals (CIs) of low/reduced lean mass on cancer mortality were pooled with a random-effects model. Subgroup analysis stratifying studies according to cancer type and measurement index was performed. RESULTS:

Altogether 100 studies evaluated the association between lean mass and cancer mortality. The overall pooled HR on cancer mortality was 1.41 (95% CI, 1.24 to 1.59) for every standard deviation decrease in lean mass and 1.69 (95% CI, 1.56 to 1.83) for patients with sarcopenia (binary cutoffs). Overall mortality was also significantly associated with sarcopenia in across various cancer types, except for hematopoietic, breast, ovarian and endometrial, and prostate cancer. CONCLUSIONS: The robust association of decreased lean mass with increased mortality further justified the importance of developing clinical guidelines for managing sarcopenia in cancer patients. Public health initiatives aiming at promoting awareness of muscle health in susceptible individuals are urgently needed.

Aune, D., et al. (2021). "Primary sclerosing cholangitis and the risk of cancer, cardiovascular disease, and all-cause mortality: a systematic review and meta-analysis of cohort studies." Sci Rep **11**(1): 10646.

A diagnosis of primary sclerosing cholangitis (PSC) has been associated with increased risk of hepatobiliary cancers, colorectal cancer and all-cause mortality in several studies, while associations with cardiovascular disease have been inconsistent. We conducted a systematic review and meta-analysis of published cohort studies on the topic to summarize these associations. PubMed and Embase databases were searched up to January 13th, 2020. Cohort studies on PSC and risk of cancer, cardiovascular disease, or mortality were included. Summary relative risks (RRs) and 95% confidence intervals (95% CIs) were estimated using random effects models. The summary RR (95% CI) comparing persons with PSC to persons without PSC was 584.37 (269.42-1267.51, I(2) = 89%, n = 4) for cholangiocarcinoma (CCA), 155.54 (125.34-193.02, I(2) = 0%, n = 3) for hepatobiliary cancer, 30.22 (11.99-76.17, I(2) = 0%, n = 2) for liver cancer, 16.92 (8.73-32.78, I(2) = 88%, n = 4) for gastrointestinal cancer, 7.56 (2.42-23.62, I(2) = 0%, n = 3) for pancreatic cancer, 6.10 (4.19-8.87, I(2) = 14%, n = 7) for colorectal cancer (CRC), 4.13 (2.99-5.71, I(2) = 80%, n = 5) for total cancer, 3.55 (2.94-4.28, I(2) = 46%, n = 5) for all-cause mortality, and 1.57 (0.25-9.69, I(2) = 79%, n = 2) for cardiovascular disease. Strong positive associations were observed between PSC and risk of CCA, hepatobiliary cancer, liver cancer, gastrointestinal cancer, pancreatic cancer, CRC, total cancer, and all-cause mortality, but not for cardiovascular disease.

Avalon, J. C., et al. (2021). "Pre-existing cardiovascular disease increases risk of atrial arrhythmia and mortality in cancer patients treated with Ibrutinib." Cardiooncology **7**(1): 38.

BACKGROUND: Ibrutinib is a Bruton's tyrosine kinase inhibitor used in the treatment of hematological malignancies. The most common cardiotoxicity associated with ibrutinib is atrial arrhythmia (atrial fibrillation and flutter). It is known that patients with cardiovascular disease (CVD) are at an increased risk for developing atrial arrhythmia. However, the rate of atrial arrhythmia in patients with pre-existing CVD treated with ibrutinib is unknown. OBJECTIVE: This study examined whether patients with pre-existing CVD are at a higher risk for developing atrial arrhythmias compared to those without prior CVD. METHODS: A single-institution retrospective chart review of patients with no prior history of atrial arrhythmia treated with ibrutinib from 2012 to 2020 was performed. Patients were grouped into two cohorts: those with CVD (known history of coronary artery disease, heart failure, pulmonary hypertension, at least moderate valvular heart disease, or device implantation) and those without CVD. The primary outcome was incidence of atrial arrhythmia, and the secondary outcomes were all-cause mortality, risk of bleeding, and discontinuation of ibrutinib. The predictors of atrial arrhythmia (namely atrial fibrillation) were assessed using logistic regression. A Cox-Proportional Hazard model was created for mortality. RESULTS: Patients were followed for a median of 1.1 years. Among 217 patients treated with ibrutinib, the rate of new-onset atrial arrhythmia was nearly threefold higher in the cohort with CVD compared to the cohort without CVD (17% vs 7%, p = 0.02). Patients with CVD also demonstrated increased adjusted all-cause mortality (OR 1.9, 95% CI 1.06-3.41, p = 0.01) and decreased survival probability (43% vs 54%, p = 0.04) compared to those without CVD over the follow-up period. There were no differences in risk of bleeding or discontinuation between the two cohorts. CONCLUSIONS: Pre-existing cardiovascular disease was associated with significantly higher rates of atrial arrhythmia and mortality in patients with hematological malignancies managed with ibrutinib.

Avery, C. L., et al. (2021). "Comparison of 20-Year Obesity-Associated Cancer Mortality Trends With Heart Disease Mortality Trends in the US." JAMA Netw Open **4**(5): e218356.

IMPORTANCE: Heart disease and cancer are the 2 major diseases associated with mortality risk in the United States. Four decades of improvements in heart disease mortality slowed after 2011; this slowing has been associated with the obesity epidemic. The same pattern has not been observed for total cancer mortality. However, trends in total cancer mortality may obscure patterns specific to obesity-associated cancers. OBJECTIVE: To investigate whether trends in obesity-associated cancer mortality mirror the slowed

mortality improvements observed for heart disease associated with the obesity epidemic. DESIGN, SETTING, AND PARTICIPANTS: This cross-sectional study compared US mortality trends for International Statistical Classification of Diseases and Related Health Problems, Tenth Revision-defined cancer (total cancer, obesity-associated cancer, and cancer not associated with obesity) and heart disease deaths from January 1, 1999, to December 31, 2018. Data were included on decedents with complete information on the underlying cause of death, age, sex, race, and ethnicity. EXPOSURES: Changes in age-adjusted cause-specific mortality rates between 1999-2011 and 2011-2018 were compared. MAIN OUTCOMES AND MEASURES: Annual relative rates of change in age-adjusted mortality rates (AAMRs) in the overall population and stratified by sex, race, and ethnicity were estimated using Poisson regression. Differences in AAMR annual relative rates of change before and after 2011 were evaluated using Wald tests. RESULTS: A total of 50 163 483 decedents met the inclusion criteria (50.1% female decedents, 79.9% non-Hispanic White decedents, and 11.7% non-Hispanic Black decedents; mean [SD] age, 72.8 [18.5] years). In contrast with heart disease mortality, for which improvements slowed between 1999-2011 and 2011-2018, decreases in total cancer AAMR relative change accelerated between 1999-2011 (-1.48 [95% CI, -1.43 to -1.52]) and 2011-2018 (-1.77 [95% CI, -1.67 to -1.86]) (P < .001). For obesity-associated cancer mortality, which accounted for approximately 33% of total cancer deaths annually, decreases in annual AAMR relative change decelerated from -1.19 (95% CI, -1.13 to -1.26) in 1999-2011 to -0.83 (95% CI, -0.70 to -0.96) in 2011-2018 (P < .001). The largest decelerations in obesity-associated cancer mortality were observed for female decedents (-1.45 [95% CI, -1.36 to -1.53] in 1999-2011 and -0.91 [95% CI, -0.75 to -1.07] in 2011-2018; P < .001) and non-Hispanic White individuals (-1.16 [95% CI, -1.09 to -1.22] in 1999-2011 and -0.68 [95% CI, -0.55 to -0.81] in 2011-2018; P < .001). CONCLUSIONS AND RELEVANCE: Slowing improvements in obesity-associated cancer mortality were obscured when considering total cancer mortality. These findings potentially signal a changing profile of cancer-associated mortality that may parallel trends previously observed for heart disease as the consequences of the obesity epidemic are understood.

Baar, W., et al. (2022). "Risk Factors for Postoperative Pulmonary Complications Leading to Increased In-Hospital Mortality in Patients Undergoing Thoracotomy for Primary Lung Cancer Resection: A Multicentre Retrospective Cohort Study of the German Thorax Registry." J Clin Med **11**(19).

Postoperative pulmonary complications (PPCs) represent the most frequent complications after lung surgery, and they increase postoperative mortality. This study investigated the incidence of PPCs, in-hospital mortality rate, and risk factors leading to PPCs in patients undergoing open thoracotomy lung resections (OTLRs) for primary lung cancer. The data from 1426 patients in this multicentre retrospective study were extracted from the German Thorax Registry and presented after univariate and multivariate statistical processing. A total of 472 patients showed at least one PPC. The presence of two PPCs was associated with a significantly increased mortality rate of 7% (p < 0.001) compared to that of patients without or with a single PPC. Three or more PPCs increased the mortality rate to 33% (p < 0.001). Multivariate stepwise logistic regression analysis revealed male gender (OR 1.4), age > 60 years (OR 1.8), and current or previous smoking (OR 1.6), while the pre-operative risk factors were still CRP levels > 3 mg/dl (OR 1.7) and FEV1 < 60% (OR 1.4). Procedural independent risk factors for PPCs were: duration of surgery exceeding 195 min (OR 1.6), the amount of intraoperative blood loss (OR 1.6), partial ligation of the pulmonary artery (OR 1.5), continuing invasive ventilation after surgery (OR 2.9), and infusion of intraoperative crystalloids exceeding 6 mL/kg/h (OR 1.9). The incidence of PPCs was significantly lower in patients with continuous epidural or paravertebral analgesia (OR 0.7). Optimising perioperative management by implementing continuous neuroaxial techniques and optimised fluid therapy may reduce the incidence of PPCs and associated mortality.

Baasland, I., et al. (2022). "Cervical cancer mortality in Norway according to screening attendance and age." Acta Obstet Gynecol Scand **101**(9): 952-959.

INTRODUCTION: The association between cervical cancer screening and reduction of cervical cancer has been dealt with in much research. However, little has been published on the association between screening and cervical cancer mortality. We assessed cervical cancer deaths according to screening history, histopathology, and age among women in, under, and above screening age. MATERIAL AND METHODS: In this nationwide, registry-based case-control study from Norway, we included 817 cervical cancer deaths in women diagnosed with cervical cancer in the period 1998-2009. We matched each case with 10 population-based controls free from cervical cancer, obtained by density-based sampling. Odds ratios (ORs) with 95% confidence intervals (CIs) for the association between screening attendance and cervical cancer mortality were estimated using conditional logistic regression models. RESULTS: Of all fatal cervical cancers, 35% were diagnosed among women over screening age and

altogether, 83% were either in age groups not covered by the screening program or in non-attenders of screening age. The estimated risk reduction associated with a cytology test in the preceding 3.5 years was 80% in screening age 25-69 years (OR 0.20; 95% CI 0.16-0.24) with the largest reduction in squamous cell carcinomas (84%) but also a substantial estimated risk reduction of 65% for adenocarcinomas. The associated risk reduction was strongest in women aged 45-69 years, with ORs in the range 0.09-0.18, compared with ORs 0.42-1.35 in women aged 25-39 years. CONCLUSIONS: To reduce the mortality of cervical cancer, screening programs should focus on increasing adherence to the program, as half of all the fatal cases were in the non-attender group. Further assessments regarding the potential preventive impact of extending screening to women over the current screening age should be considered.

Bach, L., et al. (2021). "Depression and sleep disorders are associated with early mortality in women with breast cancer in the United Kingdom." J Psychiatr Res **143**: 481-484.

BACKGROUND: The aim of this study was to estimate the association between common mental disorders and mortality in breast cancer patients. METHODS: This retrospective cohort study included women aged 18-80 for whom an initial diagnosis of breast cancer was documented in one of 200 general practices in the UK between January 2008 and December 2012. The main outcome of this study was the mortality within 5 years of the index date as a function of depression, anxiety disorder, and sleep disorders, using Cox regression models. RESULTS: A total of 6656 women (mean age: 57.9 (standard deviation: 12.0 years)) were included in the study. Within 5 years of the index date, 461 (6.9%) of women were deceased. Depression (HR: 1.44 (95% CI: 1.17-1.78)), and sleep disorders (HR: 1.37 (95% CI: 1.02-1.84)) were significantly associated with death within 5 years. CONCLUSIONS: It is important to treat BC patients with chronic diseases holistically and to take psychological comorbidities seriously as factors influencing the survival of patients in order to counteract the considerable mortality rate of BC patients.

Bagheri, A., et al. (2021). "Total, Dietary, and Supplemental Magnesium Intakes and Risk of All-Cause, Cardiovascular, and Cancer Mortality: A Systematic Review and Dose-Response Meta-Analysis of Prospective Cohort Studies." Adv Nutr **12**(4): 1196-1210.

A meta-analysis of prospective studies was conducted to examine the association of total, supplemental, and dietary magnesium intakes with risk of all-cause, cancer, and cardiovascular disease (CVD) mortality and identify the dose-response relations involved in these association. We performed a systematic search of PubMed, Scopus, Google Scholar, and ISI Web of Knowledge up to April 2020. Prospective cohort studies that reported risk estimates for the association between total, supplemental, and dietary magnesium intakes and risk of mortality were included. Random effects models were used. Nineteen publication with a total of 1,168,756 participants were included in the current meta-analysis. In total, 52,378 deaths from all causes, 23,478 from CVD, and 11,408 from cancer were identified during the follow-up period of 3.5 to 32 years. Dietary magnesium intake was associated with a lower risk of all-cause [pooled effect size (ES): 0.87; 95% CI: 0.79, 0.97; P = 0.009; I2 = 70.7%; P < 0.001] and cancer mortality (pooled ES: 0.80; 95% CI: 0.67, 0.97; P = 0.023; I2 = 55.7%; P = 0.027), but not with CVD mortality (pooled ES: 0.93; 95% CI: 0.82, 1.07; P = 0.313; I2 = 72.3%; P < 0.001). For supplemental and total magnesium intakes, we did not find any significant associations with risks of all-cause, CVD, and cancer mortality. However, linear dose-response meta-analysis indicated that each additional intake of 100 mg/d of dietary magnesium was associated with a 6% and 5% reduced risk of all-cause and cancer mortality, respectively. In conclusion, higher intake of dietary magnesium was associated with a reduced risk of all-cause and cancer mortality, but not CVD mortality. Supplemental and total magnesium intakes were not associated with the risk of all-cause, CVD, and cancer mortality. These findings indicate that consumption of magnesium from dietary sources may be beneficial in reducing all-cause and cancer mortality and thus have practical importance for public health.

Bahadoer, R. R., et al. (2021). "One-year excess mortality and treatment in surgically treated patients with colorectal cancer: A EURECCA European comparison." Eur J Surg Oncol **47**(7): 1651-1660.

BACKGROUND: Mortality in the first postoperative year represents an accurate reflection of the perioperative risk after colorectal cancer surgery. This research compares one-year mortality after surgery divided into three age-categories (18-64, 65-74, >/=75 years), focusing on time trends and comparing treatment strategies. MATERIAL: Population-based data of all patients diagnosed and treated surgically for stage I-III primary colorectal cancer from 2007 to 2016, were collected from Belgium, the Netherlands, Norway, and Sweden. Stratified for age-category and stage, treatment was evaluated, and 30-day, one-year and one-year excess mortality were calculated for colon and rectal cancer separately. Results were evaluated over two-year time periods. RESULTS: Data

of 206,024 patients were analysed. Postoperative 30-day and one-year mortality reduced significantly over time in all countries and age-categories. Within the oldest age category, in 2015-2016, one-year excess mortality varied from 9% in Belgium to 4% in Sweden for colon cancer and, from 9% in Belgium to 3% in the other countries for rectal cancer. With increasing age, patients were less likely to receive additional therapy besides surgery. In Belgium, colon cancer patients were more often treated with adjuvant chemotherapy ($p < 0.001$). For neoadjuvant treatment of rectal cancer, patients in Belgium and Norway were mostly treated with chemoradiotherapy. In the Netherlands and Sweden, radiotherapy alone was preferred ($p < 0.001$). CONCLUSIONS: Despite improvement over time in all countries and age-categories, substantial variation exists in one-year postoperative mortality. Differences in one-year excess postoperative mortality could be due to differences in treatment strategies, highlighting the consequences of under- and over-treatment on cancer survival.

Bahadoer, R. R., et al. (2022). "The survival gap between young and older patients after surgical resection for colorectal cancer remains largely based on early mortality: A EURECCA comparison of four European countries." J Geriatr Oncol **13**(6): 803-812.

BACKGROUND: A decade ago, it was demonstrated that the difference in survival between older patients and younger patients with colorectal cancer (CRC) was mainly due to mortality in the first postoperative year. Over the last few years, improvements - especially in perioperative care - have increased survival. The current research investigates whether a survival gap between younger and older patients with CRC still exists on a national level in four European countries. METHODS: Population-based data from Belgium, the Netherlands, Norway, and Sweden were collected from patients that underwent surgical resection for primary stage I-III CRC between 2007 and 2016. Relative survival and conditional relative survival (CS), with the condition of surviving the first postoperative year, were calculated for colon and rectal cancer separately, stratified for country and age category (<65, 65-75, >/=75 years). In addition, relative excess risk of death (RER) was estimated, and one-year excess mortality was calculated. RESULTS: Data of 206,024 patients were analyzed. In general, compared to patients <65 years, patients >/=75 years had a worse survival during the first year after surgery, which was most pronounced in Belgium (RER colon cancer 2.5 [95% confidence interval (CI) 2.3-2.8] and RER rectal cancer 2.6 [95% CI 2.3-2.9]). After surviving the first year, CS was mostly not statistically different between patients <65 years and patients >/=75 years with stage I-II, with the exception of stage II colon cancer in Belgium. However, CS remained worse in the largest part of the patients >/=75 years with stage III colon or rectal cancer (except for rectal cancer in Norway). CONCLUSIONS: Although differences exist between the countries, the survival gap between young and older patients is based mainly on early mortality and remains only for stage III disease after surviving the first year.

Bai, R., et al. (2022). "Incidence and mortality trends of nasopharynx cancer from 1990 to 2019 in China: an age-period-cohort analysis." BMC Public Health **22**(1): 1351.

BACKGROUND: Nasopharynx cancer (NPC) is a great health burden in China. This study explored the long-term trends of NPC incidence and mortality in China. METHODS: We retrospectively analyzed data from the Global Burden of Disease Study 2019 using an age-period-cohort framework. RESULTS: The age-standardized incidence rate (ASIR) of NPC increased by 72.7% and age-standardized mortality rate (ASMR) of NPC decreased by 51.7% for both sexes between 1990 and 2019. For males, the local drift for incidence was higher than 0 ($P < 0.05$) in those aged 20 to 79 years. For females, the local drift was higher than 0 ($P < 0.05$) in those aged 30 to 59 years, and lower than 0 ($P < 0.05$) in those aged 65 to 84 years. The local drift for mortality rates were less than 0 ($P < 0.05$) in every age group for both sexes. The estimated period relative risks (RRs) for incidence of NPC were increased monotonically for males, and increased for females after 2000. The increasing trend of cohort RRs of incidence was ceased in recent birth cohorts. Both period and cohort effects of NPC mortality in China decreased monotonically. CONCLUSIONS: Over the last three decades, the ASMR and crude mortality rate (CMR) of NPC has decreased, but the ASIR and crude incidence rate (CIR) increased in China. Although the potential mortality risk of NPC decreased, the risk of NPC incidence was found to increase as the period move forward, and suggested that control and prevention efforts should be enhanced.

Bai, X., et al. (2022). "Time tracking and multidimensional influencing factors analysis on female breast cancer mortality: Evidence from urban and rural China between 1994 to 2019." Front Public Health **10**: 1000892.

BACKGROUND: There are huge differences in female breast cancer mortality between urban and rural China. In order to better prevent breast cancer equally in urban and rural areas, it is critical to trace the root causes of past inequities and predict how future differences will change. Moreover, carcinogenic factors from micro-individual to macro-environment also need to be analyzed in detail. However, there is no

systematic research covering these two aspects in the current literature. METHODS: Breast cancer mortality data in urban and rural China from 1994 to 2019 are collected, which from China Health Statistical Yearbook. The Age-Period-Cohort model is used to examine the effects of different age groups, periods, and birth cohorts on breast cancer mortality. Nordpred project is used to predict breast cancer mortality from 2020 to 2039. RESULTS: The age effect gradually increases and changes from negative to positive at the age of 40-44. The period effect fluctuates very little and shows the largest difference between urban and rural areas in 2019. The birth cohort effect gradually decreases with urban-rural effects alternating between strong and weak. In the predicted results, the urban-rural mortality gap becomes first narrow and then wide and shows a trend of younger death. CONCLUSIONS: From the perspective of a temporal system, the changing trend of breast cancer mortality is highly consistent with the history of social and economic structural changes in China. From the perspective of the theory of social determinants of health, individuals, families, institutions and governments need to participate in the prevention of breast cancer.

Baker, J. R., et al. (2021). "Prediagnostic Blood Selenium Status and Mortality among Patients with Colorectal Cancer in Western European Populations." Biomedicines **9**(11).

A higher selenium (Se) status has been shown to be associated with lower risk for colorectal cancer (CRC), but the importance of Se in survival after CRC diagnosis is not well studied. The associations of prediagnostic circulating Se status (as indicated by serum Se and selenoprotein P (SELENOP) measurements) with overall and CRC-specific mortality were estimated using multivariable Cox proportional hazards regression among 995 CRC cases (515 deaths, 396 from CRC) in the European Prospective Investigation into Cancer and Nutrition (EPIC) cohort. Se and SELENOP serum concentrations were measured on average 46 months before CRC diagnosis. Median follow-up time was 113 months. Participants with Se concentrations in the highest quintile (>/=100 microg/L) had a multivariable-adjusted hazard ratio (HR) of 0.73 (95% CI: 0.52-1.02; P(trend) = 0.06) for CRC-specific mortality and 0.77 (95% CI: 0.57-1.03; P(trend) = 0.04) for overall mortality, compared with the lowest quintile (</=67.5 microg/L). Similarly, participants with SELENOP concentrations in the highest (>/=5.07 mg/L) compared with the lowest quintile (</=3.53 mg/L) had HRs of 0.89 (95% CI: 0.64-1.24; P(trend) = 0.39) for CRC-specific mortality and 0.83 (95% CI: 0.62-1.11; P(trend) = 0.17) for overall mortality. Higher prediagnostic exposure to Se within an optimal concentration (100-150 microg/L) might be associated with improved survival among CRC patients, although our results were not statistically significant and additional studies are needed to confirm this potential association. Our findings may stimulate further research on selenium's role in survival among CRC patients especially among those residing in geographic regions with suboptimal Se availability.

Balakrishna, R., et al. (2022). "Consumption of Nuts and Seeds and Health Outcomes Including Cardiovascular, Diabetes and Metabolic Disease, Cancer, and Mortality: an Umbrella Review." Adv Nutr.

Consumption of nuts and seeds is associated with a range of health outcomes. Summarizing the best evidence on essential health outcomes from the consumption of nuts is essential to provide optimal recommendations. Our objective is to comprehensively assess health outcomes associations related to the consumption of nuts and seeds, using a culinary definition including tree nuts and peanuts (registered in PROSPERO: CRD42021258300). Health outcomes of interest include cardiovascular disease, cancer, diabetes, obesity, respiratory disease, mortality, and their biomarker for disease. We present associations for high versus low consumption, per serving, and dose-response relationships. Medline, Embase, Cochrane, and Epistemonikos were searched and screened for systematic reviews and meta-analyses. Evidence was extracted from 89 articles on the consumption of nuts and relevant health outcomes, including 23 articles with meta-analysis on disease and mortality, 66 articles on biomarkers for disease, and 9 articles on allergy/adverse outcomes. Intake of nuts was associated with reduced risk of cardiovascular diseases and related risk factors, with moderate quality of evidence. An intake of 28 grams of nuts per day compared to not eating nuts was associated with a 21% relative risk reduction of cardiovascular disease (including coronary heart disease incidence and mortality, atrial fibrillation, and stroke mortality), 11% risk reduction of cancer deaths, and 22% reduction in all-cause mortality. Nut consumption was also inversely associated with mortality from respiratory diseases, infectious diseases, and diabetes: however, associations between nut consumption and diabetes incidence were mixed. Meta-analyses of trials on biomarkers for disease generally mirrored meta-analyses from observational studies on cardiovascular disease, cancers, and diabetes. Allergy and related adverse reactions to nuts were observed among 1-2% of adult populations, with substantial heterogeneity between studies. Overall, the current evidence supports dietary recommendations to consume a handful of nuts

and seeds per day for people without allergies to these foods.

Bang, G. A., et al. (2020). "Clinical epidemiology and mortality risk factors of gastric cancer in a sub-Saharan African setting: a retrospective analysis of 120 cases in Yaounde (Cameroon)." Pan Afr Med J **37**: 104.

INTRODUCTION: in sub-Saharan Africa, there is scare published data on cancer in general and gastric cancer in particular. METHODS: we conducted a multicenter retrospective analysis of the medical records of patients followed for gastric cancer in 5 hospital departments in the city of Yaounde (Cameroon) over 6 years. RESULTS: we recorded a total of 120 patients with a mean age of 53.4 +/- 13.7 years. There were 62 females (51.7%). The most common risk factors for gastric cancer in our patients was Helicobacter pylori infection (59 cases, 49.1%). Seventy-six patients (63.3%) consulted within 1 to 6 months of symptoms on set at the forefront of which chronic epigastralgia (74.1%). At endoscopy, the tumor was mostly located at the antrum and was locally advanced or metastatic in 25.8% and 58.4 of cases respectively. Adenocarcinoma was the main histologic type found in 105 (87.5%) cases. Curative treatment could only be implemented in 26.7% of patients. We noted a total of 85 deaths (70.8%) with a mean survival time of 5.91 +/- 7.51 months. Survival rate at 3 and 5 years was 10.1% and 4.6%, respectively. On multivariable analysis, variables independently associated with overall survival included: WHO stage 3 performance status (p = 0.042), palpable epigastric mass on examination (p = 0.042), pyloric localization (p = 0.007), and liver metastasis (p = 0.012). CONCLUSION: clinical epidemiology of gastric cancer in our study is comparable to those of other African studies with a predominance of locally advanced/metastatic forms. Prognosis is grim with diagnostic delay behind all of the identified mortality risk factors.

Banna, G. L., et al. (2022). "Risk of SARS-CoV2-Related Mortality in Non-Small Cell Lung Cancer Patients Treated with First-Line Immunotherapy Alone or in Combination with Chemotherapy." Cancer Invest **40**(5): 406-412.

BACKGROUND: The impact of systemic anticancer treatments on SARS-CoV-2-related mortality is still debatable. METHODS: By a retrospective analysis of patients with non-small-cell lung cancer (NSCLC) treated with first-line Pembrolizumab or in combination with chemotherapy (ChT) during the first surge of the pandemic. RESULTS: The adjusted risk of death was higher in patients treated with ChT + Pembrolizumab (HR 4.6, 1.2-17.4, p = 0.02). The SARS-CoV-2-related mortality rate was higher in patients treated with ChT + Pembrolizumab (p = 0.03), >/=70 years (p = 0.03) and current smokers (p = 0.17). CONCLUSIONS: The addition of ChT to immunotherapy could be associated with increased risk of mortality and higher SARS-CoV-2-related mortality rate.

Bao, X., et al. (2022). "Plasma prostasin: a novel risk marker for incidence of diabetes and cancer mortality." Diabetologia **65**(10): 1642-1651.

AIMS/HYPOTHESIS: Diabetes is associated with an increased risk of cancer. Prostasin is an epithelial sodium channel stimulator that has been associated with suppression of tumours, glucose metabolism and hyperglycaemia-associated tumour pathology. However, the association between prostasin, diabetes and cancer mortality has not been well investigated in humans. We aim to investigate the associations between plasma prostasin and diabetes, and to explore whether prostasin has an effect on cancer mortality risk in individuals with hyperglycaemia. METHODS: Plasma prostasin was measured using samples from the Malmo Diet and Cancer Study Cardiovascular Cohort, and statistical analysis was performed from both sex-specific quartiles and per 1 SD. The cross-sectional association between plasma prostasin and diabetes was first studied in 4658 participants (age 57.5 +/- 5.9 years, 39.9% men). After excluding 361 with prevalent diabetes, the associations of prostasin with incident diabetes and cancer mortality risk were assessed using Cox regression analysis. The interactions between prostasin and blood glucose levels as well as other covariates were tested. RESULTS: The adjusted OR for prevalent diabetes in the 4th vs 1st quartile of prostasin concentrations was 1.95 (95% CI 1.39, 2.76) (p for trend <0.0001). During mean follow-up periods of 21.9 +/- 7.0 and 23.5 +/- 6.1 years, respectively, 702 participants developed diabetes and 651 died from cancer. Prostasin was significantly associated with the incidence of diabetes. The adjusted HR for diabetes in the 4th vs 1st quartile of prostasin concentrations was 1.76 (95% CI 1.41, 2.19) (p for trend <0.0001). Prostasin was also associated with cancer mortality There was a significant interaction between prostasin and fasting blood glucose for cancer mortality risk (p for interaction =0.022), with a stronger association observed in individuals with impaired fasting blood glucose levels at baseline (HR per 1 SD change 1.52; 95% CI 1.07, 2.16; p=0.019). CONCLUSIONS/INTERPRETATION: Plasma prostasin levels are positively associated with diabetes risk and with cancer mortality risk, especially in individuals with high blood glucose levels, which may shed new light on the relationship between diabetes and cancer.

Barcelo, A., et al. (2021). "The role of education on Cancer amenable mortality among non-Hispanic blacks & non-Hispanic whites in the United States (1989-2018)." BMC Cancer **21**(1): 907.

BACKGROUND: Cancer mortality in the U.S. has fallen in recent decades; however, individuals with lower levels of education experienced a smaller decline than more highly educated individuals. This analysis aimed to measure the influence of education lower than a high school diploma, on cancer amenable mortality among Non-Hispanic Whites (NHW) and Non-Hispanic Blacks (NHB) in the U.S. from 1989 to 2018. METHODS: We analyzed data from 8.2 million death certificates of men and women who died from cancer between 1989 and 2018. We examined 5-year and calendar period intervals, as well as annual percent changes (APC). APC was adjusted for each combination of sex, educational level, and race categories (8 models) to separate the general trend from the effects of age. RESULTS: Our study demonstrated an increasing mortality gap between the least and the most educated NHW and NHB males and females who died from all cancers combined and for most other cancer types included in this study. The gap between the least and the most educated was broader among NHW males and females than among NHB males and females, respectively, for most malignancies. CONCLUSIONS: In summary, we reported an increasing gap in the age-adjusted cancer mortality among the most and the least educated NHW and NHB between 25 and 74 years of age. We demonstrated that although NHB exhibited the greatest age-adjusted mortality rates for most cancer locations, the gap between the most and the least educated was shown for NHW.

Barco, I., et al. (2022). "COVID-19 Incidence and Mortality in Patients Operated on for Breast Cancer. Comparison with the General Population." Clin Breast Cancer.

BACKGROUND: Breast Cancer (BC) remains the most diagnosed malignancy and the most common cause of cancer-related mortality in women worldwide. Covid-19 mortality in BC patients has been linked to comorbid conditions rather than to cancer treatment itself, although this was not confirmed by a meta-analysis. Also, during Covid-19 outbreaks, a great deal of health care resources is reassigned to critical Covid-19 patients. PATIENTS AND METHODS: During 5 consecutive trimesters (from 1/12/2020 to 31/3/2021) 2511 BC patients older than 20 years from our institution were surveyed. 1043 of them had received a Covid test and these made our study group, which was conveniently compared with the Covid-19 tested background feminine Catalan population. RESULTS: 13.1% of our patients presented with a positive Covid-19 test, whereas confirmed COVID-19 infection amounted to 7.1% of the feminine Catalan tested population. The COVID-19-specific mortality rate was 11.7% (16/137) in the study group, which compares with a 4.7% rate for the overall population. Most deaths occurred in patients over 70. CONCLUSION: Three clinical factors were significantly associated with Covid-19 mortality in BC, namely lack of hormone therapy, distant metastases, and BC dwelling in nursing homes. BC patients are at a higher risk of Covid-19 infection and mortality in comparison with the reference group without BC.

Battisti, N. M. L., et al. (2021). "Observational cohort study in older women with early breast cancer: Use of radiation therapy and impact on health-related quality of life and mortality." Radiother Oncol **161**: 166-176.

BACKGROUND: Radiotherapy reduces in-breast recurrence risk in early breast cancer (EBC) in older women. This benefit may be small and should be balanced against treatment effect and holistic patient assessment. This study described treatment patterns according to fitness and impact on health-related quality-of-life (HRQoL). METHODS: A multicentre, observational study of EBC patients aged >/= 70 years, undergoing breast-conserving surgery (BCS) or mastectomy, was undertaken. Associations between radiotherapy use, surgery, clinico-pathological parameters, fitness based on geriatric parameters and treatment centre were determined. HRQoL was measured using the European Organisation for the Research and Treatment of Cancer (EORTC) questionnaires. RESULTS: In 2013-2018 2811 women in 56 UK study centres underwent surgery with a median follow-up of 52 months. On multivariable analysis, age and tumour risk predicted radiotherapy use. Among healthier patients (based on geriatric assessments) with high-risk tumours, 534/613 (87.1%) having BCS and 185/341 (54.2%) having mastectomy received radiotherapy. In less fit individuals with low-risk tumours undergoing BCS, 149/207 (72.0%) received radiotherapy. Radiotherapy effects on HRQoL domains, including breast symptoms and fatigue were seen, resolving by 18 months. CONCLUSION: Radiotherapy use in EBC patients >/= 70 years is affected by age and recurrence risk, whereas geriatric parameters have limited impact regardless of type of surgery. There was geographical variation in treatment, with some fit older women with high-risk tumours not receiving radiotherapy, and some older, low-risk, EBC patients receiving radiotherapy after BCS despite evidence of limited benefit. The impact on HRQoL is transient.

Bereza-Carlson, P., et al. (2022). "Preoperative Risk Score for Early Mortality After Up-Front Pancreatic Cancer Surgery: A Nationwide Cohort Study." World J Surg **46**(11): 2769-2777.

BACKGROUND: Pancreatic ductal adenocarcinoma is a highly fatal malignancy. The aim was to identify preoperative factors for early mortality in up-front resectable patients following pancreatoduodenectomy (PD) and develop an early mortality risk score. METHODS: Patients registered in the Swedish National Registry for Pancreatic and Periampullary Cancer were included. Relevant preoperative factors (n = 21) were investigated. Early mortality was defined as death within 12 months after surgery. Based on the identified risk factor odds ratios (ORs), the Score Predicting Early Mortality (SPEM) was developed. RESULTS: In total, 2183 PDs were performed, and 926 patients met the study criteria. The mean age was 68 (SD +/- 8.8) years, and 48% were female. A total of 233 (24%) patients died within 12 months. In the multivariable analyses, age > 75 years (OR 1.7; 95% CI 1.1-2.4; p = 0.008), CRP >/= 15 mg/L (OR 2.0; 95% CI 1.3-3.1; p = 0.001), CA 19-9 > 500 U/mL (OR 1.8; 95% CI 1.0-3.2; p = 0.040), diabetes mellitus (OR 1.40; 95% CI 1.00-2.1; p = 0.042), and active smoking (OR 1.47; 95%CI 1.00-2.00; p = 0.050) were found to be independent risk factors for early mortality. CONCLUSION: Five independent preoperative risk factors for early mortality following PD were identified and together formed SPEM. The score might be a useful tool in establishing individualized treatment plans.

Berger, J. M., et al. (2022). "SARS-CoV-2-related mortality and treatment delays for cancer patients in Austria : Findings of a multicentric nationwide study." Wien Klin Wochenschr **134**(9-10): 371-376.

BACKGROUND: Cancer patients infected with severe acute respiratory syndrome coronavirus type 2 (SARS-CoV-2) have an increased risk of mortality. Here, we investigated predictive factors for coronavirus disease 2019 (COVID-19) associated mortality in patients with neoplastic diseases treated throughout Austria. METHODS: In this multicentric nationwide cohort study, data on patients with active or previous malignant diseases and SARS-CoV-2 infections diagnosed between 13 March 2020 and 06 April 2021 were collected. Collected data included the stage of the malignant disease and outcome parameters 30 days after the diagnosis of SARS-CoV-2 infection. RESULTS: The cohort consisted of 230 individuals of which 75 (32.6%) patients were diagnosed with hematologic malignancies and 155 (67.4%) with solid tumors. At a median follow-up of 31 days after COVID-19 diagnosis, 38 (16.5%) patients had died due to COVID-19. Compared to survivors, patients who died were older (62.4 vs. 71.4 years, p < 0.001) and had a higher ECOG performance status (0.7 vs. 2.43, p < 0.001). Furthermore, higher neutrophil counts (64.9% vs. 73.8%, p = 0.03), lower lymphocyte counts (21.4% vs. 14%, p = 0.006) and lower albumin levels (32.5 g/l vs. 21.6 g/l, p < 0.001) were observed to be independent risk factors for adverse outcomes. No association between mortality and systemic antineoplastic therapy was found (p > 0.05). In 60.6% of the patients, therapy was postponed due to quarantine requirements or hospital admission. CONCLUSION: Mortality of Austrian cancer patients infected with SARS-CoV-2 is comparable to that of other countries. Furthermore, risk factors associated with higher mortality were evident and similar to the general population. Treatment delays were frequently observed.

Bergwall, S., et al. (2021). "Leisure-time physical activities and the risk of cardiovascular mortality in the Malmo diet and Cancer study." BMC Public Health **21**(1): 1948.

BACKGROUND: The association between leisure-time physical activity and cardiovascular mortality has been previously studied, but few studies have focused on specific activities and intensities. METHODS: The association between different leisure-time physical activities and cardiovascular mortality was investigated among 25,876 individuals without diabetes or cardiovascular disease from the population-based Malmo Diet and Cancer Study cohort. The individuals estimated the average duration spent on 17 physical activities at baseline in 1991-1996 and after 5 years. Cardiovascular mortality was obtained from a register during a mean of 20 years of follow-up. RESULTS: A total leisure-time physical activity of 15-25 metabolic equivalent task (MET) hours/week was associated with a decreased risk of cardiovascular mortality (HR 15-25 vs < 7.5 MET-h/week =0.80, 95% CI 0.69-0.93), with no further risk reduction at higher levels. Several high-intensity activities (i.e., lawn tennis and running) and moderate-intensity activities (i.e., golf, cycling and gardening) were associated with a reduced risk. Individuals who engaged in high-intensity physical activity for an average of 2.29 MET h/week (30 min/week) had an 18% (95% CI 0.72-0.93) reduced risk of cardiovascular mortality compared with non-participants, and no further risk reductions were observed at higher levels. Decreased risk was observed among individuals who had started (HR 0.56, 95% CI 0.32-0.97) or continued (HR 0.49, 95% CI 0.36-0.66) high-intensity activities at the five-year follow-up. CONCLUSIONS: Moderate- and high-intensity leisure-time physical activities reduced the risk of cardiovascular mortality. With regard to total leisure-time physical activity, the largest risk reduction was

observed for 15-25 MET-h/week (equivalent to walking for approximately 5 h/week).

Bermudi, P. M. M., et al. (2020). "Spatial pattern of mortality from breast and cervical cancer in the city of Sao Paulo." Rev Saude Publica **54**: 142.

OBJECTIVE: To verify the spatial pattern of mortality from breast and cervical cancer in areas of primary health care, considering socioeconomic conditions. METHODS: This is an ecological study, from January 2000 to December 2016. The study area is the municipality of Sao Paulo, Brazil, and its 456 coverage areas of primary health units. Information on deaths of women aged 20 years or over were geocoded according to residence address. We calculated mortality rates, standardized by age, and smoothed by the local empirical Bayesian method, and grouped into three or two years to reduce the random fluctuation of the data. In addition, bivariate global and local Moran indexes were calculated to verify the existence of spatial agglomeration of standardized mortality rates with a domain of socioeconomic condition, elaborated based on the Indice Paulista de Vulnerabilidade Social (IPVS - Sao Paulo Index of Social Vulnerability). RESULTS: The success rate of geocoding was 98.9%. Mortality from breast cancer, without stratification by time, showed a pattern with higher rates located in central regions with better socioeconomic conditions. It showed a decrease at the end of the period and a change in spatial pattern, with increased mortality in peripheral regions. On the other hand, mortality from cervical cancer remained with the highest rates in peripheral regions with worse socioeconomic conditions, despite being reduced over time. CONCLUSION: The spatial pattern of mortality from the studied cancers, over time, suggests association with the best socioeconomic conditions of the municipality, either as protection (cervical) or risk (breast). This knowledge may direct resources to prevent and promote health in the territories.

Bernard, A., et al. (2022). "[Comparison of mortality of lung cancer resections in France to other European countries]." Rev Mal Respir **39**(8): 669-675.

BACKGROUND: France is characterized by the dispersion of its technical surgical platforms, and it seemed interesting for us to obtain information on quality of care compared to other European countries, which often have different organizations and practices. The objective of the study was to compare the 30-day mortality of patients operated on for bronchial cancer in France with that of other European countries. METHOD: We conducted a literature review on practices in different European countries. The terms used for the selection were: lung cancer surgery, 30-day mortality in different hospitals in European countries. RESULTS: We selected 9 articles corresponding to 9 European countries. The correlation coefficient between the number of lung resections per year and the population of the country was 0.967. The linear regression model between number of annual lung resections and population showed that except for Great Britain, most of the countries were close to the linear regression line. Germany and France had a mortality rate of 2.887% and 2.937% respectively, whereas the average is 2.13%. Following sensitivity analysis, the mortality rates for Germany and France remained higher than the average. CONCLUSION: France is among the European countries with the highest postoperative mortality rates. These results should induce surgical teams to adopt quality-of-care measures focusing on outcome analysis.

Bernardo, S., et al. (2021). "Outcomes of excessive alcohol drinkers without baseline evidence of chronic liver disease after 15 years follow-up: Heavy burden of cancer and liver disease mortality." PLoS One **16**(5): e0252218.

BACKGROUND: Most long-term heavy drinkers do not have clinically evident chronic liver disease (CLD). However, at any time-point, their risk of developing CLD remains unknown. We aimed to evaluate the long-term outcomes of a group of heavy drinkers, without evidence of CLD at baseline. METHODS: A cohort of 123 long-term heavy drinkers without CLD were prospectively recruited in 2002 and retrospectively followed until 2018. RESULTS: At baseline (2002), median alcohol consumption was 271+/-203g/day during 21.5+/-20 years, 65% being abstinent during the previous 1.75+/-5 months. Patients were followed for 14+/-3 years. During follow-up, 53% reported any alcohol intake. Alcohol consumption during follow-up associated weakly with either 1- or 6-months previous abstinence at baseline. Until 2018, progression to CLD occurred in 6%, associating with years of alcohol intake during follow-up (OR 1.15 [1.01-1.31]) and baseline alkaline-phosphatase (OR 1.05 [1.01-1.10]). During follow-up, being abstinent for at least 1 year positively associated with CLD-free survival. 27% died (55% of cancer-mostly oropharyngeal cancer, 27% of cardiovascular disease, and 9% of liver disease), with a mean age of 71 years [69-74] (10 years less than the expected in the Portuguese population). Achieving abstinence for at least 1 year positively associated with overall survival, while smoking, and hepatic steatosis at baseline associated negatively. CONCLUSION: Long-term heavy drinkers seemed to have a decreased life expectancy compared with the overall Portuguese population. Cancer was the main cause of death. Our results suggest that progression to CLD depends mostly on continued alcohol intake. Alcohol abstinence, even

if temporary, seems to decrease the risks of CLD and mortality.

Bertero, E., et al. (2022). "Cancer Incidence and Mortality According to Pre-Existing Heart Failure in a Community-Based Cohort." JACC CardioOncol **4**(1): 98-109.

BACKGROUND: Studies assessing whether heart failure (HF) is associated with cancer and cancer-related mortality have yielded conflicting results. OBJECTIVES: This study assessed cancer incidence and mortality according to pre-existing HF in a community-based cohort. METHODS: Among individuals >/=50 years of age from the Puglia region in Italy with administrative health data from 2002 to 2018, no cancer within 3 years before the baseline evaluation, and >/=5-year follow-up, the study matched 104,020 subjects with HF at baseline with 104,020 control subjects according to age, sex, drug-derived complexity index, Charlson comorbidity index, and follow-up duration. Cancer incidence and mortality were defined based on International Classification of Diseases-Ninth Revision codes in hospitalization records or death certificates. RESULTS: The incidence rate of cancer in HF patients and control subjects was 21.36 (95% CI: 20.98-21.74) and 12.42 (95% CI: 12.14-12.72) per 1000 person-years, respectively, with the HR being 1.76 (95% CI: 1.71-1.81). Cancer mortality was also higher in HF patients than control subjects (HR: 4.11; 95% CI: 3.86-4.38), especially in those <70 years of age (HR: 7.54; 95% CI: 6.33-8.98 vs HR: 3.80; 95% CI: 3.44-4.19 for 70-79 years of age; and HR: 3.10; 95% CI: 2.81-3.43 for >/=80 years of age). The association between HF and cancer mortality was confirmed in a competing risk analysis (subdistribution HR: 3.48; 95% CI: 3.27-3.72). The HF-related excess risk applied to the majority of cancer types. Among HF patients, prescription of high-dose loop diuretic was associated with higher cancer incidence (HR: 1.11; 95% CI: 1.03-1.21) and mortality (HR: 1.35; 95% CI: 1.19-1.53). CONCLUSIONS: HF is associated with an increased risk of cancer and cancer-related mortality, which may be heightened in decompensated states.

Bertke, S. J., et al. (2021). "Lung Cancer Mortality and Styrene Exposure in the Reinforced-Plastics Boatbuilding Industry: Evaluation of Healthy Worker Survivor Bias." Am J Epidemiol **190**(9): 1784-1792.

The evidence for styrene's being a human lung carcinogen has been inconclusive. Occupational cohorts within the reinforced-plastics industry are an ideal population in which to study this association because of their relatively high levels of exposure to styrene and lack of concomitant exposures to other known carcinogens. However, healthy worker survivor bias (HWSB), where healthier workers stay employed longer and thus have higher exposure potential, is a likely source of confounding bias for exposure-response associations, in part due to styrene's acute effects. Through December 31, 2016, we studied a cohort of 5,163 boatbuilders exposed to styrene in Washington State who were employed between 1959 and 1978; prior regression analyses had demonstrated little evidence for an exposure-response relationship between styrene exposure and lung cancer mortality. Based on estimates of necessary components of HWSB, we found evidence for a potentially large HWSB. Using g-estimation of a structural nested model to account for HWSB, we estimated that 1 year of styrene exposure at more than 30 parts per million accelerated time to lung cancer death by 2.29 years (95% confidence interval: 1.53, 2.94). Our results suggest possibly strong HWSB in our small cohort and indicate that large, influential studies of styrene-exposed workers may suffer from similar biases, warranting a reassessment of the evidence of long-term health effects of styrene exposure.

Beynon, R. A., et al. (2022). "Epigenetic biomarkers of ageing are predictive of mortality risk in a longitudinal clinical cohort of individuals diagnosed with oropharyngeal cancer." Clin Epigenetics **14**(1): 1.

BACKGROUND: Epigenetic clocks are biomarkers of ageing derived from DNA methylation levels at a subset of CpG sites. The difference between age predicted by these clocks and chronological age, termed "epigenetic age acceleration", has been shown to predict age-related disease and mortality. We aimed to assess the prognostic value of epigenetic age acceleration and a DNA methylation-based mortality risk score with all-cause mortality in a prospective clinical cohort of individuals with head and neck cancer: Head and Neck 5000. We investigated two markers of intrinsic epigenetic age acceleration (IEAAHorvath and IEAAHannum), one marker of extrinsic epigenetic age acceleration (EEAA), one optimised to predict physiological dysregulation (AgeAccelPheno), one optimised to predict lifespan (AgeAccelGrim) and a DNA methylation-based predictor of mortality (ZhangScore). Cox regression models were first used to estimate adjusted hazard ratios (HR) and 95% confidence intervals (CI) for associations of epigenetic age acceleration with all-cause mortality in people with oropharyngeal cancer (n = 408; 105 deaths). The added prognostic value of epigenetic markers compared to a clinical model including age, sex, TNM stage and HPV status was then evaluated. RESULTS: IEAAHannum and AgeAccelGrim were associated with mortality risk after adjustment for clinical and lifestyle factors (HRs per standard deviation [SD] increase in age

acceleration = 1.30 [95% CI 1.07, 1.57; p = 0.007] and 1.40 [95% CI 1.06, 1.83; p = 0.016], respectively). There was weak evidence that the addition of AgeAccelGrim to the clinical model improved 3-year mortality prediction (area under the receiver operating characteristic curve: 0.80 vs. 0.77; p value for difference = 0.069). CONCLUSION: In the setting of a large, clinical cohort of individuals with head and neck cancer, our study demonstrates the potential of epigenetic markers of ageing to enhance survival prediction in people with oropharyngeal cancer, beyond established prognostic factors. Our findings have potential uses in both clinical and non-clinical contexts: to aid treatment planning and improve patient stratification.

Bjornebo, L., et al. (2022). "Association of 5alpha-Reductase Inhibitors With Prostate Cancer Mortality." JAMA Oncol **8**(7): 1019-1026.

IMPORTANCE: There is evidence that 5alpha-reductase inhibitors (5-ARIs), a standard treatment of benign prostate hyperplasia, are associated with a decrease in the incidence of prostate cancer (PCa). However, studies to date have had conflicting results regarding the association with prostate cancer mortality (PCM). OBJECTIVE: To evaluate the association of treatment with 5-ARIs with PCM in men without a prior diagnosis of PCa. DESIGN, SETTING, AND PARTICIPANTS: This population-based cohort study was conducted in Stockholm, Sweden, between January 1, 2007, and December 31, 2018, and included 429 977 men with a prostate-specific antigen (PSA) test within the study period. Study entry was set to 1 year after the first PSA test. Data were analyzed from September 2021 to December 2021. EXPOSURES: After their initial PSA test, men with 2 or more newly dispensed prescriptions of 5-ARI, finasteride, or dutasteride were considered 5-ARI users (n = 26 190). MAIN OUTCOMES AND MEASURES: Primary outcome was PCM. Cox proportional hazards regression models were used to calculate multivariable-adjusted hazard ratios (HRs) and 95% CIs for all-cause mortality and PCM. RESULTS: The study cohort included 349 152 men. The median (IQR) age for those with 2 or more filled prescriptions of 5-ARI was 66 (61-73) years and 57 (50-64) years for those without. The median follow-up time was 8.2 (IQR, 4.9-10) years with 2 257 619 person-years for the unexposed group and 124 008 person-years for the exposed group. The median exposure to treatment with 5-ARI was 4.5 (IQR, 2.1-7.4) years. During follow-up, 35 767 men (8.3%) died, with 852 deaths associated with PCa. The adjusted multivariable survival analysis showed a lower risk of PCM in the 5-ARI group with longer exposure times (0.1-2.0 years: adjusted HR, 0.89; 95% CI, 0.64-1.25; >8 years: adjusted HR, 0.44; 95% CI, 0.27-0.74). No statistically significant differences were seen in all-cause mortality between the exposed and unexposed group. Men treated with 5-ARIs underwent more PSA tests and biopsies per year than the unexposed group (median of 0.63 vs 0.33 and 0.22 vs 0.12, respectively). CONCLUSIONS AND RELEVANCE: The results of this cohort study suggest that there was no association between treatment with 5-ARI and increased PCM in a large population-based cohort of men without a previous PCa diagnosis. Additionally, a time-dependent association was seen with decreased risk of PCM with longer 5-ARI treatment. Further research is needed to determine whether the differences are because of intrinsic drug effects or PCa testing differences.

Bjornsdottir, H. H., et al. (2020). "A national observation study of cancer incidence and mortality risks in type 2 diabetes compared to the background population over time." Sci Rep **10**(1): 17376.

We examined changing patterns in cancer incidence and deaths in diabetes compared to the background population. A total of 457,473 patients with type 2 diabetes, included between 1998 and 2014, were matched on age, sex, and county to five controls from the population. Incidence, trends in incidence and post-cancer mortality for cancer were estimated with Cox regression and standardised incidence rates. Causes of death were estimated using logistic regression. Relative importance of risk factors was estimated using Heller's relative importance model. Type 2 diabetes had a higher risk for all cancer, HR 1.10 (95% CI 1.09-1.12), with highest HRs for liver (3.31), pancreas (2.19) and uterine cancer (1.78). There were lesser increases in risk for breast (1.05) and colorectal cancers (1.20). Type 2 diabetes patients experienced a higher HR 1.23 (1.21-1.25) of overall post-cancer mortality and mortality from prostate, breast, and colorectal cancers. By the year 2030 cancer could become the most common cause of death in type 2 diabetes. Persons with type 2 diabetes are at greater risk of developing cancer and lower chance of surviving it. Notably, hazards for specific cancers (e.g. liver, pancreas) in type 2 patients cannot be explained by obesity alone.

Blanco, B. A., et al. (2021). "The Impact of Residential Segregation on Pancreatic Cancer Diagnosis, Treatment, and Mortality." Ann Surg Oncol **28**(6): 3147-3155.

BACKGROUND: Disparities in pancreatic cancer outcomes between black and white patients are well documented. This study aimed to use a more novel index to examine the impact of racial segregation on the diagnosis, management, and outcomes of pancreatic cancer in black patients compared with white patients.

METHODS: Black and white adults with pancreatic cancer in urban counties were identified using data from the 2018 submission of the Surveillance, Epidemiology and End Results (SEER) Program and the 2010 Census. The racial index of dissimilarity (IoD), a validated proxy of racial segregation, was used to assess the evenness with which whites and blacks are distributed across census tracts in each county. Multivariate Poisson regression was performed, and stepwise models were constructed for each of the outcomes. Overall survival was studied using the Kaplan-Meier method. RESULTS: The study enrolled 60,172 adults with a diagnosis of pancreatic cancer between 2005 and 2015. Overall, the black patients (13.8% of the cohort) lived in more segregated areas (IoD, 0.67 vs 0.61; $p < 0.05$). They were less likely to undergo surgery for localized disease (relative risk [RR], 0.80; 95% confidence interval [CI], 0.76-0.83) and more frequently had a diagnosis of advanced-stage disease (RR, 1.09; 95% CI, 1.01-1.19) with increasing segregation. They also had shorter survival times (9.8 vs 11.4 months; $p < 0.05$). CONCLUSIONS: Disparities in advanced-stage disease at diagnosis, surgery for localized disease, and overall survival are directly related to the degree of residential segregation, a proxy for structural racism. In searching for solutions to this problem, it is important to account for the historical marginalization of black Americans.

Blay, J. Y., et al. (2021). "Delayed care for patients with newly diagnosed cancer due to COVID-19 and estimated impact on cancer mortality in France." ESMO Open **6**(3): 100134.

BACKGROUND: The impact of the first coronavirus disease 2019 (COVID-19) wave on cancer patient management was measured within the nationwide network of the Unicancer comprehensive cancer centers in France. PATIENTS AND METHODS: The number of patients diagnosed and treated within 17 of the 18 Unicancer centers was collected in 2020 and compared with that during the same periods between 2016 and 2019. Unicancer centers treat close to 20% of cancer patients in France yearly. The reduction in the number of patients attending the Unicancer centers was analyzed per regions and cancer types. The impact of delayed care on cancer-related deaths was calculated based on different hypotheses. RESULTS: A 6.8% decrease in patients managed within Unicancer in the first 7 months of 2020 versus 2019 was observed. This reduction reached 21% during April and May, and was not compensated in June and July, nor later until November 2020. This reduction was observed only for newly diagnosed patients, while the clinical activity for previously diagnosed patients increased by 4% similar to previous years. The reduction was more pronounced in women, in breast and prostate cancers, and for patients without metastasis. Using an estimated hazard ratio of 1.06 per month of delay in diagnosis and treatment of new patients, we calculated that the delays observed in the 5-month period from March to July 2020 may result in an excess mortality due to cancer of 1000-6000 patients in coming years. CONCLUSIONS: In this study, the delays in cancer patient management were observed only for newly diagnosed patients, more frequently in women, for breast cancer, prostate cancer, and nonmetastatic cancers. These delays may result is an excess risk of cancer-related deaths in the coming years.

Blazek, K., et al. (2022). "The impact of skin cancer prevention efforts in New South Wales, Australia: Generational trends in melanoma incidence and mortality." Cancer Epidemiol **81**: 102263.

BACKGROUND: In Australia, skin cancer awareness campaigns have focused on raising the awareness and consequences of skin cancer and highlighting the importance of utilising sun protection. METHODS: Trends in melanoma incidence and mortality have been explored elsewhere in Australia and this study sought to examine the trends in NSW. Anonymised incidence and mortality data for in situ and invasive melanoma from 1988 to 2014 were obtained from the NSW Cancer Registry. Trends of melanoma incidence and mortality were analysed using segmented regression to allow for changes over time. Birth cohort patterns were assessed using age-period-cohort models. RESULTS: Over the period, incidence of in situ melanoma increased in all age groups although the rates were lowest in those under 40 years of age. Incidence of invasive melanoma was either stable or decreased in people under 60, while it increased in those aged 60 and above, particularly in men. Age-period-cohort analysis revealed decreasing age-specific incidence of invasive melanoma under 40 years of age. Melanoma mortality over the period was stable or decreased in all groups except in men aged 60 or over. Overall, mortality rates generally declined or remained stable particularly in recent years. CONCLUSION: It is encouraging that rates of invasive melanoma are declining in the younger age cohorts - which could be attributed to both primary prevention efforts with individuals protecting their skin as well as early detection through self assessment and clinician performed skin checks. In addition, whilst it is important to monitor the increasing rates of in situ melanoma, the increase is likely due to early detection and treatment of melanoma that could have progressed to invasive melanoma and therefore detection whilst still in situ is an improved outcome. Overall, the results demonstrate the need to continue to improve the understanding of and compliance with primary skin

cancer prevention measures in order to reduce population UVR exposure and overall melanoma incidence.

Bledsoe, A. C., et al. (2022). "Mortality and cancer in eosinophilic gastrointestinal disorders distal to the esophagus: nationwide cohort study 1990-2017." J Gastroenterol **57**(10): 735-747.

BACKGROUND: Eosinophilic gastrointestinal disorders (EGIDs) include inflammatory conditions with enteric infiltration of eosinophils and resulting symptoms. This study aims to examine a population-based sample of patients for prevalence, mortality, and cancer risk in EGIDs distal to the esophagus. METHODS: Nationwide, population-based cohort study. EGID was identified through relevant biopsy codes from Sweden's all 28 pathology departments through the ESPRESSO cohort. Individuals with EGID were then matched to general population reference individuals with similar age and sex. Study participants were linked to Swedish healthcare registers. Through Cox regression, we calculated adjusted hazard ratios (aHRs) adjusting for sex, age, county, calendar period, and education. RESULTS: In total, 2429 patients (56% female) were found to have EGID distal to the esophagus, representing a prevalence of about 1/4800 in the Swedish population. Mean age was 44 years with 11% children at the time of diagnosis. Mortality was increased 17% in patients with EGIDs compared to reference individuals (aHR = 1.17; 95%CI = 1.04-1.33). Excess mortality was seen in gastric and small bowel eosinophilic disease, but not colonic disease (aHR = 1.81; 95%CI = 1.32-2.48, aHR = 1.50; 95%CI = 1.18-1.89, and aHR = 0.99; 95%CI = 0.85-1.16, respectively). Cause specific mortality was driven by cancer-related death (aHR = 1.33; 95%CI = 1.05-1.69). However, this study failed to show an increase in incident cancers (aHR = 1.14; 95%CI = 0.96-1.35). Comparison of EGID individuals with their siblings yielded similar aHRs. CONCLUSIONS: This study found an increased risk of death in patients with EGIDs distal to the esophagus, with cancer death driving the increase. Proximal gut disease seems to confer the greatest risk. There was no increase in incident cancers.

Bliton, J., et al. (2021). "Clinical Stage of Cancer Affects Perioperative Mortality for Gastrointestinal Cancer Surgeries." J Surg Res **260**: 1-9.

BACKGROUND: The impact of the stage of cancer on perioperative mortality remains obscure. The purpose of this study was to investigate whether cancer stage influences 30-d mortality for gastric, pancreatic, and colorectal cancers. METHODS: Data were collected from the National Cancer Database for patients undergoing resections for cancers of the stomach, pancreas, colon, or rectum between 2004 and 2015. The main analysis was conducted among patients with cancer stages 1-3. A sensitivity analysis also included cancer stage 4. Descriptive statistics were used to compare the patients' baseline characteristics. Generalized linear mixed models were used to evaluate the relationship between stage and 30-d mortality, controlling for other disease-, patient- and hospital-level factors. Pseudo R2 statistics (%Delta pseudo R(2)) were used to quantify the relative explanatory capacity of the variables to the model for 30-d mortality. All analyses were performed using SAS 9.4. RESULTS: The cohort included 24,468, 28,078, 176,285, and 64,947 patients with stomach, pancreas, colon, and rectal cancers, respectively. After adjusting for other variables, 30-d mortality was different by stage for all cancer types examined. The factor most strongly associated with 30-d mortality was age (%Delta pseudo R(2) range 14%-39%). The prognostic impact of cancer stage (Stages 1, 2, or 3) on 30-d mortality was comparable to that of the Charlson comorbidity index. CONCLUSIONS: Cancer stage contributes to explaining differences observed in short-term mortality for gastrointestinal cancers. Short-term mortality models would benefit by including more granular cancer stage, beyond disseminated status alone.

Bo, Y., et al. (2022). "Combined effects of chronic PM2.5 exposure and habitual exercise on cancer mortality: a longitudinal cohort study." Int J Epidemiol **51**(1): 225-236.

BACKGROUND: Exercise may increase the inhalation and deposition of air pollutants, which may counteract its beneficial effects. We thus examined the combined effects of chronic exposure to fine particulate matter (PM2.5) and habitual exercise on the risk of death from cancer in Taiwan. PATIENTS AND METHODS: A total of 384 128 adults (>/=18 years of age) were recruited for a medical screening programme between 2001 and 2016, yielding 842 384 medical-examination records. All participants were followed up until 31 May 2019. Vital data were obtained from the National Death Registry of Taiwan and the ambient PM2.5 exposure was estimated using a satellite-based spatiotemporal model. Information on habitual exercise was collected using a standard self-administered questionnaire. The time-dependent Cox-regression model was used to evaluate the combined effects. RESULTS: A greater amount of habitual exercise was associated with lower risk of death from cancer, whilst a higher level of PM2.5 exposure was associated with a higher risk of death from cancer. The inverse associations of habitual exercise with death from cancer were not modified by chronic exposure to PM2.5. The participants in the group with a high level

of exercise and a low level of PM2.5 exposure exhibited a 35% lower risk of death from cancer than those in the group with a low level of exercise and a high level of PM2.5 exposure (95% confidence interval: 28%, 42%). CONCLUSIONS: Increased levels of exercise and reduced exposure levels of PM2.5 are associated with a lower risk of death from cancer. Habitual exercise reduces the risk of death from cancer regardless of the levels of chronic PM2.5 exposure. Our results indicate that habitual exercise is a suitable health-promotion strategy even for people who reside in moderately polluted regions.

Boice, J. D., Jr., et al. (2022). "Mortality from leukemia, cancer and heart disease among U.S. nuclear power plant workers, 1957-2011." Int J Radiat Biol **98**(4): 657-678.

BACKGROUND: The aim of the Million Person Study of Low-Dose Health Effects (MPS) is to examine the level of radiation risk for chronic exposures received gradually over time and not acutely as was the case for the Japanese atomic bomb survivors. Nuclear power plant (NPP) workers comprise nearly 15 percent of the MPS. Leukemia, selected cancers, Parkinson's disease, ischemic heart disease (IHD) and other causes of death are evaluated. METHODS AND MATERIAL: The U.S. Nuclear Regulatory Commission's Radiation Exposure Information and Reporting System (REIRS) and the Landauer, Inc. dosimetry databases identified 135,193 NPP workers first monitored 1957-1984. Annual personal dose equivalents [Hp(10)] were available for each worker. Radiation records from all places of employment were sought. Vital status was determined through 2011. Mean absorbed doses to red bone marrow (RBM), esophagus, lung, colon, brain and heart were estimated by adjusting the recorded Hp(10) for each worker by scaling factors, accounting for exposure geometry and energy of the incident gamma radiation. Standardized mortality ratios (SMR) were calculated. Radiation risks were estimated using Cox proportional hazards models. RESULTS: Nearly 50% of workers were employed for more than 20 years. The mean duration of follow-up was 30.2 y. Overall, 29,124 total deaths occurred, 296 from leukemia other than chronic lymphocytic leukemia (CLL), 3382 from lung cancer, 140 from Parkinson's disease and 5410 from IHD. The mean dose to RBM was 37.9 mGy (maximum 1.0 Gy; percent >100 mGy was 9.2%), 43.2 mGy to lung, 43.7 mGy to colon, 33.2 mGy to brain, and 43.9 mGy to heart. The SMRs (95% CI) were 1.06 (0.94; 1.19) for leukemia other than CLL, 1.10 (1.07; 1.14) for lung cancer, 0.90 (0.76; 1.06) for Parkinson's disease, and 0.80 (0.78; 0.82) for IHD. The excess relative risk (ERR) per 100 mGy for leukemia other than CLL was 0.15 (90% CI -0.001; 0.31). For all solid cancers the ERR per 100 mGy (95% CI) was 0.01 (-0.03; 0.05), for lung cancer -0.04 (-0.11; 0.02), for Parkinson's disease 0.24 (-0.02; 0.50), and for IHD -0.01 (-0.06; 0.04). CONCLUSION: Prolonged exposure to radiation increased the risk of leukemia other than CLL among NPP workers. There was little evidence for a radiation association for all solid cancers, lung cancer or ischemic heart disease. Increased precision will be forthcoming as the different cohorts within the MPS are combined, such as industrial radiographers and medical radiation workers who were assembled and evaluated in like manner.

Bolormaa, E., et al. (2022). "Income-based disparity in the risk distant-stage cervical cancer and mortality after introduction of a national cancer screening program." Epidemiol Health: e2022066.

OBJECTIVES: To assess the socioeconomic gradient in the risk of distant-stage cervical cancer (CC) at presentation and mortality within five years after introducing a national cancer screening program (NCSP). METHODS: All new CC cases from 2007 to 2017 were retrieved from the Korea Central Cancer Registry data linked to the National Health Information Database of National Health Insurance Service in South Korea. The cumulative incidence of CCs, adjusted odds ratios (OR) of distant metastases at presentation, and adjusted all-cause mortality hazard ratios (HR) within five years were assessed according to income gradients. RESULTS: The age-standardized cumulative incidence of CC ranged from 48.9 to 381.5 per 100,000 women, with the richest quintile having the highest incidence. Of 31,391 new cases, 8.6% had distant metastasis on presentation, most frequently among medical aid beneficiaries (9.9%). The OR for the distant stage was higher when the income level was lower (1.46, 95% confidence interval [CI]: 1.28, 1.67, for the lowest compared to the richest) or the women were medical aid beneficiaries (1.50, 95% CI: 1.24, 1.82). The five-year mortality was higher in the lower-income quintiles and among medical aid beneficiaries than in the richest quintile. CONCLUSION: The incidence of CC was higher in the richest quintile than in the lower-income quintiles, while the risk of distant-stage CC and mortality was higher when the level of income was lower in the context of the NCSP. A more focused approach is needed to further reduce the disparity in the timely diagnosis and treatment of CC patients.

Bonner, S., et al. (2022). "Neighborhood Deprivation, Hospital Quality and Mortality After Cancer Surgery." Ann Surg.

OBJECTIVE: To evaluate if receipt of complex cancer surgery at high quality hospitals is associated with a reduction in disparities between

individuals living in the most and least deprived neighborhoods. BACKGROUND: The association between social risk factors and worse surgical outcomes for patients undergoing high-risk cancer operations is well documented. To what extent neighborhood socioeconomic deprivation as an isolated social risk factor known to be associated with worse outcomes can be mitigated by hospital quality is less known. METHODS: Using 100% Medicare fee-for-service claims, we analyzed data on 212,962 Medicare beneficiaries >age 65 undergoing liver resection, rectal resection, lung resection, esophagectomy and pancreaticoduodenectomy for cancer between 2014 and 2018. Clinical risk-adjusted 30-day post-operative mortality rates were used to stratify hospitals into quintiles of quality. Beneficiaries were stratified into quintiles based on census tract Area Deprivation Index. The association of hospital quality and neighborhood deprivation with 30-day mortality was assessed using logistic regression. RESULTS: There were 212,962 patients in the cohort including 109,419(51.4%) men with mean (SD) age of 73.8(5.9) years old. At low-quality hospitals, patients living in the most deprived areas had significantly higher risk-adjusted mortality than those from the least deprived areas for all procedures; esophagectomy: 22.3% versus 20.7%; P<0.003, liver resection 19.3% versus 16.4%; P<0.001, pancreatic resection 15.9% versus 12.9%; P<0.001, lung resection 8.3% versus 7.8%; P<0.001, rectal resection 8.8% versus 8.1%; P<0.001. Surgery at a high-quality hospitals was associated with no significant differences in mortality between individuals living in the most compared to least deprived neighborhoods for esophagectomy, rectal resection, liver resection and pancreatectomy. For example, the adjusted odds of mortality between individuals living in the most deprived compared to least deprived neighborhoods following esophagectomy at low quality hospitals (OR 1.22; 95% CI 1.14-1.31; P<0.001) was higher than at high quality hospitals (OR 0.98, 95%CI 0.94-1.02; P=0.03). CONCLUSION AND RELEVANCE: Receipt of complex cancer surgery at a high-quality hospital was associated with no significant differences in mortality between individuals living in the most deprived neighborhoods compared to least deprived. Initiatives to increase access referrals to high quality hospitals for patients from high deprivation levels may improve outcomes and contribute to mitigating disparities.

Bonney, A., et al. (2022). "Impact of low-dose computed tomography (LDCT) screening on lung cancer-related mortality." Cochrane Database Syst Rev **8**(8): CD013829.

BACKGROUND: Lung cancer is the most common cause of cancer-related death in the world, however lung cancer screening has not been implemented in most countries at a population level. A previous Cochrane Review found limited evidence for the effectiveness of lung cancer screening with chest radiography (CXR) or sputum cytology in reducing lung cancer-related mortality, however there has been increasing evidence supporting screening with low-dose computed tomography (LDCT). OBJECTIVES: To determine whether screening for lung cancer using LDCT of the chest reduces lung cancer-related mortality and to evaluate the possible harms of LDCT screening. SEARCH METHODS: We performed the search in collaboration with the Information Specialist of the Cochrane Lung Cancer Group and included the Cochrane Lung Cancer Group Trial Register, Cochrane Central Register of Controlled Trials (CENTRAL, the Cochrane Library, current issue), MEDLINE (accessed via PubMed) and Embase in our search. We also searched the clinical trial registries to identify unpublished and ongoing trials. We did not impose any restriction on language of publication. The search was performed up to 31 July 2021. SELECTION CRITERIA: Randomised controlled trials (RCTs) of lung cancer screening using LDCT and reporting mortality or harm outcomes. DATA COLLECTION AND ANALYSIS: Two review authors were involved in independently assessing trials for eligibility, extraction of trial data and characteristics, and assessing risk of bias of the included trials using the Cochrane RoB 1 tool. We assessed the certainty of evidence using GRADE. Primary outcomes were lung cancer-related mortality and harms of screening. We performed a meta-analysis, where appropriate, for all outcomes using a random-effects model. We only included trials in the analysis of mortality outcomes if they had at least 5 years of follow-up. We reported risk ratios (RRs) and hazard ratios (HRs), with 95% confidence intervals (CIs) and used the I(2) statistic to investigate heterogeneity. MAIN RESULTS: We included 11 trials in this review with a total of 94,445 participants. Trials were conducted in Europe and the USA in people aged 40 years or older, with most trials having an entry requirement of >/= 20 pack-year smoking history (e.g. 1 pack of cigarettes/day for 20 years or 2 packs/day for 10 years etc.). One trial included male participants only. Eight trials were phase three RCTs, with two feasibility RCTs and one pilot RCT. Seven of the included trials had no screening as a comparison, and four trials had CXR screening as a comparator. Screening frequency included annual, biennial and incrementing intervals. The duration of screening ranged from 1 year to 10 years. Mortality follow-up was from 5 years to approximately 12 years. None of the included trials were at low risk of bias across all domains. The certainty of evidence was moderate to low across different outcomes, as assessed

by GRADE. In the meta-analysis of trials assessing lung cancer-related mortality, we included eight trials (91,122 participants), and there was a reduction in mortality of 21% with LDCT screening compared to control groups of no screening or CXR screening (RR 0.79, 95% CI 0.72 to 0.87; 8 trials, 91,122 participants; moderate-certainty evidence). There were probably no differences in subgroups for analyses by control type, sex, geographical region, and nodule management algorithm. Females appeared to have a larger lung cancer-related mortality benefit compared to males with LDCT screening. There was also a reduction in all-cause mortality (including lung cancer-related) of 5% (RR 0.95, 95% CI 0.91 to 0.99; 8 trials, 91,107 participants; moderate-certainty evidence). Invasive tests occurred more frequently in the LDCT group (RR 2.60, 95% CI 2.41 to 2.80; 3 trials, 60,003 participants; moderate-certainty evidence). However, analysis of 60-day postoperative mortality was not significant between groups (RR 0.68, 95% CI 0.24 to 1.94; 2 trials, 409 participants; moderate-certainty evidence). False-positive results and recall rates were higher with LDCT screening compared to screening with CXR, however there was low-certainty evidence in the meta-analyses due to heterogeneity and risk of bias concerns. Estimated overdiagnosis with LDCT screening was 18%, however the 95% CI was 0 to 36% (risk difference (RD) 0.18, 95% CI -0.00 to 0.36; 5 trials, 28,656 participants; low-certainty evidence). Four trials compared different aspects of health-related quality of life (HRQoL) using various measures. Anxiety was pooled from three trials, with participants in LDCT screening reporting lower anxiety scores than in the control group (standardised mean difference (SMD) -0.43, 95% CI -0.59 to -0.27; 3 trials, 8153 participants; low-certainty evidence). There were insufficient data to comment on the impact of LDCT screening on smoking behaviour. AUTHORS' CONCLUSIONS: The current evidence supports a reduction in lung cancer-related mortality with the use of LDCT for lung cancer screening in high-risk populations (those over the age of 40 with a significant smoking exposure). However, there are limited data on harms and further trials are required to determine participant selection and optimal frequency and duration of screening, with potential for significant overdiagnosis of lung cancer. Trials are ongoing for lung cancer screening in non-smokers.

Borowicz, S., et al. (2021). "HAI-1 is an independent predictor of lung cancer mortality and is required for M1 macrophage polarization." PLoS One **16**(6): e0252197.

Non-small cell lung cancer (NSCLC) is the leading cause of cancer-related death worldwide. Though immune checkpoint inhibitors (ICIs) have revolutionized lung cancer therapy in recent years, there are several factors limiting the therapeutic efficacy of ICI-based immunotherapy in lung cancer. Recent evidence suggests that one such mechanism is the phenotypic shift of tumor-infiltrating macrophages away from an anti-tumor M1 phenotype and towards an anti-inflammatory and tumor-permissive M2 phenotype. Though this phenomenon is well documented, the means through which the lung tumor microenvironment (TME) usurps macrophage function are poorly described. Hepatocyte growth factor (HGF) is a known driver of both lung cancer pathobiology as well as M2 polarization, and its signaling is antagonized by the tumor suppressor gene HAI-1 (SPINT1). Using a combination of genomic databases, primary NSCLC specimens, and in vitro models, we determined that patients with loss of HAI-1 have a particularly poor prognosis, hallmarked by increased HGF expression and an M2-dominant immune infiltrate. Similarly, conditioned media from HAI-1-deficient tumor cells led to a loss of M1 and increased M2 polarization in vitro, and patient NSCLC tissues with loss of HAI-1 showed a similar loss of M1 macrophages. Combined, these results suggest that loss of HAI-1 is a potential means through which tumors acquire an immunosuppressive, M2-dominated TME, potentially through impaired M1 macrophage polarization. Hence, HAI-1 status may be informative when stratifying patients that may benefit from therapies targeting the HGF pathway, particularly as an adjuvant to ICI-based immunotherapy.

Borza, T., et al. (2022). "The course of depressive symptoms and mortality in older patients with cancer." Aging Ment Health **26**(6): 1153-1160.

OBJECTIVE: The Geriatric Depression Scale (GDS-15), a self-report questionnaire, emphasizes the psychological dimension of depression. We aimed to investigate whether GDS-15 scores were associated with mortality in older patients with cancer and describe the course of individual symptoms on the GDS-15. METHODS: An observational, multicenter, prospective study of 288 patients 70 years or older with cancer followed over 24 months. The patients were assessed with the GDS-15 at inclusion, and after four and 12 months. An extended Cox regression model assessed the association between time-dependent GDS-15 scores and mortality. RESULTS: After adjusting for cancer-related prognostic factors, a one-point increase in GDS-15 sum score increased risk of death by 12%. GDS-15 mean score increased during the first four months of the study, as did odds for the presence of the GDS-15 symptoms 'feel you have more problems with memory than most', 'not feel full of energy', and 'think that most people are better off than you'. The most prevalent and persistent GDS-15 symptom was 'prefer

to stay at home, rather than going out and doing new things', and 'not to be in good spirits most of the time' was the least prevalent. CONCLUSIONS: More severe depressive symptoms, as measured by the GDS-15, were associated with higher mortality in older patients with cancer. The importance of emotional distress and how to alleviate it should be investigated further in these patients.

Breekveldt, E. C. H., et al. (2022). "Colorectal cancer incidence, mortality, tumour characteristics, and treatment before and after introduction of the faecal immunochemical testing-based screening programme in the Netherlands: a population-based study." Lancet Gastroenterol Hepatol **7**(1): 60-68.

BACKGROUND: In 2014, a population-based colorectal cancer (CRC) screening programme was stepwise implemented in the Netherlands comprising faecal immunochemical testing once every 2 years, with a cutoff value for positivity of 47 mug haemoglobin per g faeces. We aimed to assess CRC incidence, mortality, tumour characteristics, and treatment before and after introduction of this screening programme. METHODS: We did a retrospective, observational, population-based study in the Netherlands and gathered CRC incidence data from the Netherlands Cancer Registry from Jan 1, 2010, to Dec 31, 2019, in people aged 55 years or older. Patients with a CRC diagnosis between Jan 1, 2014, and Dec 31, 2018, in the Netherlands Cancer Registry were linked with the nationwide registry of histopathology and cytopathology (PALGA) to identify mode of detection (ie, screening-detected vs clinically detected). We calculated age-standardised CRC incidence rates and used data from Statistics Netherlands to calculate CRC-related mortality in 2010-19. We compared localisation, stage distribution, and treatment of screening-detected CRCs with clinically detected CRCs diagnosed in 2014-18 in patients aged 55-75 years. FINDINGS: Between Jan 1, 2010, and Dec 31, 2019, 125 215 CRCs were diagnosed in individuals aged 55 years or older and were included in the analyses for CRC incidence. Before the introduction of the screening programme, the age-standardised CRC incidence rate was 214.3 per 100 000 population in 2013 in people aged 55 years or older. After the introduction of the screening programme, this rate initially increased to 259.2 per 100 000 population in 2015, and subsequently decreased to 181.5 per 100 000 population in 2019. Age-standardised incidence rates for advanced CRCs (stage III and IV) were 117.0 per 100 000 population in 2013 and increased to 122.8 per 100 000 population in 2015; this rate then decreased to 94.7 per 100 000 population in 2018. Age-standardised CRC mortality decreased from 87.5 deaths per 100 000 population in 2010 to 64.8 per 100 000 population in 2019. Compared with clinically detected CRCs, screening-detected CRCs were more likely to be located in the left side of the colon (48.6% vs 35.2%) and to be detected at an early stage (I or II; 66.7% vs 46.2%). Screening-detected CRCs were more likely to be treated by local excision compared with clinically detected CRCs, and this finding persisted when stage I CRCs were analysed separately. INTERPRETATION: After introduction of this national screening programme, a decrease in overall and advanced-stage CRC incidence was observed. In view of this observation, together with the observed shift to detection at earlier stages and more screening-detected CRCs being treated by local excision, we might cautiously conclude that, in the long-term, faecal immunochemical testing-based screening could ultimately lead to a decrease in CRC-related morbidity and mortality. FUNDING: None.

Brehmer, M. (2022). "Register-based research. Accurate data and analysis, crucial for correct conclusions. Comment on "Incidence, mortality, and relative survival of patients with cancer of the bladder and upper urothelial tract in the Nordic countries between 1990 and 2019"." Scand J Urol: 1-2.

Brenner, A. V., et al. (2022). "Comparison of All Solid Cancer Mortality and Incidence Dose-Response in the Life Span Study of Atomic Bomb Survivors, 1958-2009." Radiat Res **197**(5): 491-508.

Recent analysis of all solid cancer incidence (1958-2009) in the Life Span Study (LSS) revealed evidence of upward curvature in the radiation dose response among males but not females. Upward curvature in sex-averaged excess relative risk (ERR) for all solid cancer mortality (1950-2003) was also observed in the 0-2 Gy dose range. As reasons for non-linearity in the LSS are not completely understood, we conducted dose-response analyses for all solid cancer mortality and incidence applying similar methods [1958-2009 follow-up, DS02R1 doses, including subjects not-in-city (NIC) at the time of the bombing] and statistical models. Incident cancers were ascertained from Hiroshima and Nagasaki cancer registries, while cause of death was ascertained from death certificates throughout Japan. The study included 105,444 LSS subjects who were alive and not known to have cancer before January 1, 1958 (80,205 with dose estimates and 25,239 NIC subjects). Between 1958 and 2009, there were 3.1 million person-years (PY) and 22,538 solid cancers for incidence analysis and 3.8 million PY and 15,419 solid cancer deaths for mortality analysis. We fitted sex-specific ERR models adjusted for smoking to both types of data. Over the entire range of doses, solid cancer mortality dose-response

exhibited a borderline significant upward curvature among males (P = 0.062) and significant upward curvature among females (P = 0.010); for solid cancer incidence, as before, we found a significant upward curvature among males (P = 0.001) but not among females (P = 0.624). The sex difference in magnitude of dose-response curvature was statistically significant for cancer incidence (P = 0.017) but not for cancer mortality (P = 0.781). The results of analyses in the 0-2 Gy range and restricted lower dose ranges generally supported inferences made about the sex-specific dose-response shape over the entire range of doses for each outcome. Patterns of sex-specific curvature by calendar period (1958-1987 vs. 1988-2009) and age at exposure (0-19 vs. 20-83) varied between mortality and incidence data, particularly among females, although for each outcome there was an indication of curvature among 0-19-year-old male survivors in both calendar periods and among 0-19-year-old female survivors in the recent period. Collectively, our findings indicate that the upward curvature in all solid cancer dose response in the LSS is neither specific to males nor to incidence data; its evidence appears to depend on the composition of sites comprising all solid cancer group and age at exposure or time. Further follow up and site-specific analyses of cancer mortality and incidence will be important to confirm the emerging trend in dose-response curvature among young survivors and unveil the contributing factors and sites.

Burch, A. E., et al. (2022). "A population health assessment of screening mammography on breast cancer mortality in North Carolina." Breast Cancer Res Treat **196**(3): 647-656.

PURPOSE: To identify predictors of screening mammography use and the effect of screening mammography on breast cancer mortality in North Carolina. METHODS: This cross-sectional study integrated publicly available data from government and private data repositories to model predictors of screening mammography and breast cancer mortality in North Carolina. RESULTS: In North Carolina during 2008-2010, on average, 68.1% of women aged 40-74 years underwent a screening mammogram in the previous two years (range: 38.7%-82.1). The ordinary least squares (OLS) regression demonstrated counties experiencing persistent poverty have mammography screening rates that are 4.3% less, on average, than counties without persistent poverty (estimate (SE) = -4.283 (2.105), p = 0.045). As the percentage of women with a college education increases, the mammography screening rates increase by approximately 0.3% (estimate (SE) = 0.319 (0.078), P < .001) and as the health literacy score increases, the mammography screening rate decreases by 0.3% (estimate (SE) = -0.318 (0.104), p = 0.003). These variables explain 7.0% of the variability in mammographic screening rates. The OLS regression analysis demonstrated that age-adjusted breast cancer incidence (Estimate (SE) = 0.074 (0.024), p = 0.003) and health literacy score (estimate (SE) = - 0.175 (0.083), p = 0.039) are significantly related to breast cancer mortality. CONCLUSIONS: Demographic, socioeconomic, and environmental variables explain only a small percentage of the variability in the rates of screening mammography and breast cancer mortality in North Carolina. Advances in the available treatments are likely the major contributor to improving breast cancer mortality.

Burgess, L., et al. (2022). "Association of the USPSTF Grade D Recommendation Against Prostate-Specific Antigen Screening With Prostate Cancer-Specific Mortality." JAMA Netw Open **5**(5): e2211869.

IMPORTANCE: The 2012 US Preventive Services Task Force (USPSTF) Grade D recommendation against prostate-specific antigen (PSA) screening for all men has been controversial, with data documenting a shift to a higher stage of disease at diagnosis. The association between the Grade D recommendation and prostate cancer-specific mortality (PCSM) among contemporary cohorts, however, is unclear. OBJECTIVE: To evaluate PCSM rates between 1999 and 2019, comparing trends in rates before and after the change in the 2012 USPSTF screening guideline to assess its association with PCSM. EXPOSURE: The 2012 USPSTF Grade D recommendation against PSA screening for all men. DESIGN, SETTING, AND PARTICIPANTS: This cross-sectional study used Centers for Disease Control and Prevention Wide-ranging Online Data for Epidemiologic Research maintained by the National Center for Health Statistics to collect data on cause of death for all individuals who died of prostate cancer in the US from 1999 to 2019. Analysis was performed from January to August 2021. MAIN OUTCOMES AND MEASURES: Trends in PCSM rates were calculated from 1999 to 2012 and from 2014 to 2019, with a washout year of 2013, using linear regression, with year and binary indicator of pre-2013 and post-2013 status as interaction terms. Trends were further analyzed by age, race and ethnicity, urbanization category, and US Census region. Other measures included diagnosis of localized or metastatic prostate cancer and overall cancer mortality. RESULTS: A total of 618 095 patients died of prostate cancer in the US from 1999 to 2019. Age-adjusted PCSM decreased linearly at a rate of -0.273 per 100 000 population per year from 1999 to 2012 and stalled at a rate of -0.009 per 100 000 per year from 2014 to 2019 (P < .001). This finding was significant among men aged 60 years or older, especially among men aged 60 to 69 years,

men aged 80 years or older, and among Black men. Men aged 60 to 64 years had a decreasing, age-adjusted PCSM rate of -0.0088 per 100 000 population per year prior to 2013 followed by an increasing rate of 0.0014 per 100 000 per year. Men aged 65 to 69 years had a decreasing, age-adjusted PCSM rate of -0.024 per 100 000 population per year prior to 2013 followed by an increasing rate of 0.0011 per 100 000 population per year. Men aged 80 years or older had the largest absolute difference between rates before and after 2013 compared with all other age groups, with a difference of 0.06 for men aged 80 to 84 years and 0.07 for men 85 aged years or older. Black men had a decreasing, age-adjusted PCSM rate of -0.700 per 100 000 population per year prior to 2013 followed by a flattened rate of -0.091 per 100 000 population per year. Changes were observed across races and ethnicities, urbanization categories, and US Census regions and were accompanied by increased diagnoses of metastatic disease, which are inconsistent with mortality trends across all malignant neoplasms. CONCLUSIONS AND RELEVANCE: This cross-sectional study using comprehensive PCSM data through 2019 demonstrated decreasing PCSM rates that flattened or increased after the 2012 USPSTF Grade D recommendation, suggesting that decreased PSA screening may be a factor associated with this change. This change was seen across ages, races and ethnicities, urbanization categories, and US Census regions. The updated 2018 USPSTF guideline supporting shared decision-making may reverse these trends in the coming years.

Burghgraef, T. A., et al. (2022). "Predicting Mortality Within 90 Days Of First Intervention In Patients With Left-Sided Obstructive Colon Cancer." Dis Colon Rectum.

BACKGROUND: Acute resection for left-sided obstructive colon carcinoma is thought to be associated with higher mortality risk than a bridge to surgery approach using decompressing stoma or self-expandable metal stent, but prediction models are lacking. OBJECTIVE: Determine the influence of treatment strategy on mortality within 90-days from first intervention using a prediction model in patients presenting with left-sided obstructive colon carcinoma. DESIGN: A national multicenter cohort study, using data of a prospective national audit. SETTINGS: The study was performed in 75 Dutch hospital. PATIENTS: Patients were included if they underwent a resection with curative intent for left-sided obstructive colon carcinoma between 2009 and 2016. INTERVENTIONS: First intervention was either acute resection, bridge to surgery with self-expandable metallic stent, or bridge to surgery with decompressing stoma. MAIN OUTCOME MEASURES: The main outcome measure was 90-day mortality after first intervention. Risk factors were identified using multivariable logistic analysis. Subsequently a risk model was developed. RESULTS: In total 2395 patients were included, with first intervention consisting of acute resection in 1848 (77%) patients, stoma as bridge to surgery in 332 (14%) patients, and stent as bridge to surgery in 215 (9%) patients. Overall, 152 patients (6.3%) died within 90-days from first intervention. A decompressing stoma was independently associated with a lower 90-day mortality risk (HR: 0.27, CI: 0.094-0.62). Other independent predictors for mortality were age, ASA classification, tumor location, and index levels of serum creatinine and C-reactive protein. The constructed risk model had an area under the curve of 0.84 (CI: 0.81-0.87). LIMITATIONS: Only patients that underwent surgical resection were included. CONCLUSIONS: Treatment strategy had a significant impact on 90-day mortality. A decompressing stoma considerably lowers the risk of mortality, especially in older and frail patients. A risk model was developed, which needs further external validation. See Video Abstract at http://links.lww.com/DCR/B975.

Burisch, J., et al. (2022). "Surgery, cancer and mortality among patients with ulcerative colitis diagnosed 1962-1987 and followed until 2017 in a Danish population-based inception cohort." Aliment Pharmacol Ther **55**(3): 339-349.

BACKGROUND: Long-term data on the natural disease course of unselected patients with ulcerative colitis (UC) are limited. AIMS: To determine the long-term course and prognosis of UC, including patients' risks of surgery, cancer and mortality, in a population-based cohort followed for over 50 years METHODS: All incident patients with UC diagnosed between 1962 and 1987 in Copenhagen County, Denmark were included in a population-based cohort. We extracted information about IBD-related surgeries, cancers and mortality from patient files from 1962 to 1987, and from the Danish National Patient Registry, Cancer Registry, and Register of Causes of Death during 1988-2017. Patients were matched with up to 50 individuals from the general population. RESULTS: We followed 1161 patients for a median of 34 years (range: 0.1-56.0). Median age at diagnosis was 33 years (range: 2-88). The cumulative probability of colectomy 10, 20, 30, 40 and 50 years after diagnosis was 22% (95% CI: 20%-25%), 27% (95% CI: 25%-30%), 31% (95% CI: 28%-34%), 34% (95% CI: 31%-37%), and 40% (95% CI: 36%-44%), respectively. The risk of small intestinal, colon, rectal and anal cancer was higher than among controls, as was cancer of the skin, pancreas and thyroid. All-cause mortality was lower than controls (adjusted RR: 0.90,

95% CI: 0.82-0.99). CONCLUSION: In this population-based cohort of UC patients diagnosed between 1962 and 1987, 40% underwent colectomy within 50 years of diagnosis. Physicians need to be aware that UC patients are at increased risk of intestinal and extra-intestinal cancers. However, UC patients' risk of mortality is comparable to that of the background population.

Burnell, M., et al. (2021). "UKCTOCS update: applying insights of delayed effects in cancer screening trials to the long-term follow-up mortality analysis." Trials **22**(1): 173.

BACKGROUND: During trials that span decades, new evidence including progress in statistical methodology, may require revision of original assumptions. An example is the continued use of a constant-effect approach to analyse the mortality reduction which is often delayed in cancer-screening trials. The latter led us to re-examine our approach for the upcoming primary mortality analysis (2020) of long-term follow-up of the United Kingdom Collaborative Trial of Ovarian Cancer Screening (LTFU UKCTOCS), having initially (2014) used the proportional hazards (PH) Cox model. METHODS: We wrote to 12 experts in statistics/epidemiology/screening trials, setting out current evidence, the importance of pre-specification, our previous mortality analysis (2014) and three possible choices for the follow-up analysis (2020) of the mortality outcome: (A) all data (2001-2020) using the Cox model (2014), (B) new data (2015-2020) only and (C) all data (2001-2020) using a test that allows for delayed effects. RESULTS: Of 11 respondents, eight supported changing the 2014 approach to allow for a potential delayed effect (option C), suggesting various tests while three favoured retaining the Cox model (option A). Consequently, we opted for the Versatile test introduced in 2016 which maintains good power for early, constant or delayed effects. We retained the Royston-Parmar model to estimate absolute differences in disease-specific mortality at 5, 10, 15 and 18 years. CONCLUSIONS: The decision to alter the follow-up analysis for the primary outcome on the basis of new evidence and using new statistical methodology for long-term follow-up is novel and has implications beyond UKCTOCS. There is an urgent need for consensus building on how best to design, test, estimate and report mortality outcomes from long-term randomised cancer screening trials. TRIAL REGISTRATION: ISRCTN22488978 . Registered on 6 April 2000.

Burton, A., et al. (2021). "Primary liver cancer in the UK: Incidence, incidence-based mortality, and survival by subtype, sex, and nation." JHEP Rep **3**(2): 100232.

BACKGROUND & AIMS: The incidence of primary liver cancer (PLC) is increasing in Western Europe. To understand trends over time and the current burden in the UK, a detailed analysis of the epidemiology of PLC and its subtypes was conducted. METHODS: Data on PLCs diagnosed during 1997-2017 were obtained from population-based, nationwide registries in the UK. European age-standardised incidence (ASR) and incidence-based mortality rates (ASMR) per 100,000 person-years were calculated overall and by sex and UK-nation. Annual percentage change in rates was estimated using Joinpoint regression. One-, 2-, and 5-year age-standardised net survival was estimated. RESULTS: A total of 82,024 PLCs were diagnosed. Both hepatocellular carcinoma (HCC) incidence and mortality rates trebled (ASR 1.8-5.5 per 100,000, ASMR 1.3-4.0). The rate of increase appeared to plateau around 2014/2015. Scottish men consistently had the highest HCC incidence rates. PLC survival increased, driven by a substantial increase in the proportion that are HCC (as prognosis is better than other PLCs) and in HCC survival (change in 1-year survival 24-47%). Intrahepatic cholangiocarcinoma was the most common PLC in women and 1-year survival improved from 22.6% to 30.5%. CONCLUSIONS: PLC incidence has been increasing rapidly but, as most risk factors are modifiable, it is largely a preventable cancer. This rate of increase has slowed in recent years, possibly attributable to effective treatment for hepatitis C. As other risk factors such as obesity and diabetes remain prevalent in the UK, it is unlikely the considerable burden of this disease will abate. While improvements in survival have been made, over half of patients are not alive after 1 year, therefore further progress in prevention, early detection, and treatment innovation are needed. LAY SUMMARY: Many more people are getting liver cancer, particularly the subtype hepatocellular carcinoma, than 20 years ago. Men in Scotland are most likely to get liver cancer and to die from it. Survival after liver cancer diagnosis is getting longer but still less than half are alive after 1 year.

Burtscher, J., et al. (2021). "Moderate Altitude Residence Reduces Male Colorectal and Female Breast Cancer Mortality More Than Incidence: Therapeutic Implications?" Cancers (Basel) **13**(17).

BACKGROUND: Living at moderate altitude may be associated with health benefits, including reduced mortality from male colorectal and female breast cancer. We aimed to determine altitude-dependent incidence and mortality rates of those cancers and put them in the context of altitude-associated lifestyle differences. METHODS: Incidence cases and deaths of male colorectal cancer (n = 17,712 and 7462) and female breast cancer (n = 33,803 and

9147) from altitude categories between 250 to about 2000 m were extracted from official Austrian registries across 10 years (2008-2017). Altitude-associated differences in health determinants were derived from the Austrian Health Interview Survey (2014). RESULTS: The age-standardized incidence and mortality rates of male colorectal cancer decreased by 24.0% and 44.2%, and that of female breast cancer by 6.5% and 26.2%, respectively, from the lowest to the highest altitude level. Higher physical activity levels and lower body mass index for both sexes living at higher altitudes were found. CONCLUSIONS: Living at a moderate altitude was associated with a reduced incidence and (more pronounced) mortality from colorectal and breast cancer. Our results suggest a complex interaction between specific climate conditions and lifestyle behaviours. These observations may, in certain cases, support decision making when changing residence.

Butler, S. S., et al. (2021). "Risk of cardiovascular mortality with androgen deprivation therapy in prostate cancer: A secondary analysis of the Prostate, Lung, Colorectal, and Ovarian (PLCO) Randomized Controlled Trial." Cancer **127**(13): 2213-2221.

BACKGROUND: For men with radiation-managed prostate cancer, there is conflicting evidence regarding the association between androgen deprivation therapy (ADT) and cardiovascular mortality (CVM), particularly among those who have with preexisting comorbidities. The objective of this study was to analyze the association between ADT and CVM across patient comorbidity status using prospectively collected data from a large clinical trial. METHODS: In total, 1463 men were identified who were diagnosed with clinically localized, intermediate-risk/high-risk prostate cancer (T2b-T4, Gleason 7-10, or prostate-specific antigen >10 ng/mL) from 1993 to 2001 and managed with either radiation therapy (RT) alone or RT plus ADT during the randomized Prostate, Lung, Colon, and Ovarian (PLCO) Cancer Screening Trial. Adjusted hazard ratios (aHRs) for cause-specific mortality (prostate cancer-specific mortality vs other-cause mortality-including the primary end point of CVM [death from ischemic heart disease, cerebrovascular accident, or other circulatory disease]) were determined using Fine and Gray competing-risk regression analysis and stratified by comorbidity history. RESULTS: There was no difference in the risk of 5-year CVM between ADT plus RT and RT alone (2.3% vs 3.3%, respectively; aHR, 0.69; 95% CI, 0.38-1.24; P = .21) overall or on subgroup analysis among men with a history of >/=1 preexisting comorbidities (3.2% vs 5.3%, respectively; aHR, 0.83; 95% CI, 0.43-1.60; P = .58), >/=2 preexisting comorbidities (6.9% vs 8.3%, respectively; aHR, 0.95; 95% CI, 0.40-2.25; P = .90), or cardiovascular disease/risk factors (3.6% vs 4.3%, respectively; aHR, 0.85; 95% CI, 0.44-1.65; P = .63). These results were all similar when each component of CVM was analyzed separately-either cardiac, stroke, or other vascular mortality (P > .05). CONCLUSIONS: This study provides prospectively collected evidence that the use of ADT plus RT, compared with RT alone, is not associated with an increased risk of CVM, even among subgroups of men who have preexisting comorbidities and cardiovascular disease.

Byrne, J., et al. (2022). "Impact of era of diagnosis on cause-specific late mortality among 77 423 five-year European survivors of childhood and adolescent cancer: The PanCareSurFup consortium." Int J Cancer **150**(3): 406-419.

Late mortality of European 5-year survivors of childhood or adolescent cancer has dropped over the last 60 years, but excess mortality persists. There is little information concerning secular trends in cause-specific mortality among older European survivors. PanCareSurFup pooled data from 12 cancer registries and clinics in 11 European countries from 77 423 five-year survivors of cancer diagnosed before age 21 between 1940 and 2008 followed for an average age of 21 years and a total of 1.27 million person-years to determine their risk of death using cumulative mortality, standardized mortality ratios (SMR), absolute excess risks (AER), and multivariable proportional hazards regression analyses. At the end of follow-up 9166 survivors (11.8%) had died compared to 927 expected (SMR 9.89, 95% confidence interval [95% CI] 9.69-10.09), AER 6.47 per 1000 person-years, (95% CI 6.32-6.62). At 60 to 68 years of attained age all-cause mortality was still higher than expected (SMR = 2.41, 95% CI 1.90-3.02). Overall cumulative mortality at 25 years from diagnosis dropped from 18.4% (95% CI 16.5-20.4) to 7.3% (95% CI 6.7-8.0) over the observation period. Compared to the diagnosis period 1960 to 1969, the mortality hazard ratio declined for first neoplasms (P for trend <.0001) and for infections (P < .0001); declines in relative mortality from second neoplasms and cardiovascular causes were less pronounced (P = .1105 and P = .0829, respectively). PanCareSurFup is the largest study with the longest follow-up of late mortality among European childhood and adolescent cancer 5-year survivors, and documents significant mortality declines among European survivors into modern eras. However, continuing excess mortality highlights survivors' long-term care needs.

Caba, Y., et al. (2021). "The Impact of Dementia on Cancer Treatment Decision-Making, Cancer

Treatment, and Mortality: A Mixed Studies Review." JNCI Cancer Spectr **5**(3).

Dementia and cancer occur commonly in older adults. Yet, little is known about the effect of dementia on cancer treatment and outcomes in patients diagnosed with cancer, and no guidelines exist. We performed a mixed studies review to assess the current knowledge and gaps on the impact of dementia on cancer treatment decision-making, cancer treatment, and mortality. A search in PubMed, Medline, and PsycINFO identified 55 studies on older adults with a dementia diagnosis before a cancer diagnosis and/or comorbid cancer and dementia published in English from January 2004 to February 2020. We described variability using range in quantitative estimates, ie, odds ratios (ORs), hazard ratios (HRs), and risk ratios (RR) when appropriate and performed narrative review of qualitative data. Patients with dementia were more likely to receive no curative treatment (including hospice or palliative care) (OR, HR, and RR range = 0.40-4.4, n = 8), while less likely to receive chemotherapy (OR and HR range = 0.11-0.68, n = 8), radiation (OR range = 0.24-0.56, n = 2), and surgery (OR range = 0.30-1.3, n = 4). Older adults with cancer and dementia had higher mortality than those with cancer alone (HR and OR range = 0.92-5.8, n = 33). Summarized findings from qualitative studies consistently revealed that clinicians, caregivers, and patients tended to prefer less aggressive care and gave higher priority to quality of life over life expectancy for those with dementia. Current practices in treatment-decision making for patients with both cancer and dementia are inconsistent. There is an urgent need for treatment guidelines for this growing patient population that considers patient and caregiver perspectives.

Cabral, J. F., et al. (2022). "Trend analysis of lung cancer incidence and mortality in Grande Cuiaba, Mato Grosso, Brazil, 2000 to 2016." Rev Bras Epidemiol **25**(Supl 1): e220014.

OBJECTIVE: To analyses lung cancer incidence and mortality trends to gender and age group in Grande Cuiaba between 2000 to 2016. METHODS: Study of times series applying incidence data from the Population-Based Cancer Registry of Cuiaba, and mortality data from Mortality Information System. Annual Percentage Change and the Average Annual Percentage Change were calculated in the incidence and mortality rate through the Joinpoint regression. RESULTS: It was observed between men a decrease of -2,2% in the overall incidence of lung cancer during the term of 2000-2016 and by age range: 40 to 49 years (-4,2%), 60 to 69 years (-2,0%) and 70 to 79 years (-9,4%), in this last age group it was between 2000-2009. The general mortality was stable on historical series, nonetheless, a decline between men of 50 to 59 years (-3,5%) among 2006 to 2016 and of 70 to 79 years among 2002-20011 (-6,3%) were observed. The incidence trends among female individuals maintained stable whereas the overall mortality trends had an increase of 7,2% between 2000-2012 and decrease of -34,1% between 2012-2016. Amid women from 50 to 79 years, there was a raise, ranging from 3,5% to 3,9% between 2000-2016. CONCLUSIONS: There is an evident disparity between the trends analysis of incidence and mortality of lung cancer among men and women, that can be explained by changes in smoking over time, for example, the adherence or not of the smoking withdraw program besides social, cultural, economics differences and even biological.

Cahuana Pinto, R. S. M., et al. (2021). "Incidence of lung cancer and mortality among civil construction industry workers: A protocol for a systematic review and meta-analysis." PLoS One **16**(4): e0250377.

BACKGROUND: The construction sector is one of the most stable growth industries in the world. However, many studies have suggested an association between occupational exposure in civil construction and lung cancer risk. Thus, this study aims to assess lung cancer risk in civil construction workers occupationally exposed to physical and chemical agents through a systematic review and meta-analysis. METHODS/DESIGN: Studies will be identified by searching PUBMED, Embase, SCOPUS, WEB OF SCIENCE and the reference list of included articles. Eligible study designs will be cohort, cross-sectional, and case-control studies that report occupational exposure to physical or chemical agents and lung cancer risk through mortality or incidence outcomes. A meta-analysis will be used to combine odds ratios (ORs) from case-control studies and relative risks (RR) from cohort studies. Two reviewers will independently screen articles, extract data, and assess scientific quality using standardized forms and ROBINS-E tool if available. Otherwise, the New-Castle Ottawa rating scale will be used. Any of those will also be used in combination with the GRADE approach for quality of evidence. Overall risk estimates and their corresponding 95% confidence intervals (CIs) will be obtained using the random-effects model meta-analysis. This systematic review and meta-analysis will be conducted following the Meta-analysis of Observational Studies in Epidemiology (MOOSE) guidelines. Results will be reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement. DISCUSSION: This review will identify and synthesize studies investigating the association between occupational exposure in the construction industry and lung cancer. The findings will help governmental entities and researchers with evidence-based decision-making

because they will integrate and validate the evidence on construction workers' health effects due to occupational exposure. SYSTEMATIC REVIEW REGISTRATION: PROSPERO CRD42020164209.

Cai, C., et al. (2021). "Gut microbiota imbalance in colorectal cancer patients, the risk factor of COVID-19 mortality." Gut Pathog **13**(1): 70.

BACKGROUND: COVID-19 pandemic is sweeping across the world. Previous studies have shown that gut microbiota is associated with COVID-19, and operational taxonomic unit (OTU) composed of Blautia genus, Lactobacillus genus, and Ruminococcus genus of Firmicutes is correlated with the severity of COVID-19. Gut microbiota imbalance in colorectal cancer patients may lead to the variation of OTU. RESULTS: Based on the GMrepo database, the gut microbiota of 1374 patients with colorectal neoplasms and 27,329 healthy people was analyzed to investigate the differences in the abundance of microbes between colorectal neoplasms patients and healthy people. Furthermore, We collected feces samples from 12 patients with colorectal cancer and 8 healthy people in Xiangya hospital for metabolomic analysis to investigate the potential mechanisms. Our study showed that the abundance of Blautia and Ruminococcus was significantly increased in colorectal neoplasms, which may increase the severity of COVID-19. The gender and age of patients may affect the severity of COVID-19 by shaping the gut microbiota, but the BMI of patients does not. CONCLUSIONS: Our work draws an initial point that gut microbiota imbalance is a risk factor of COVID-19 mortality and gut microbiota may provide a new therapeutic avenue for colorectal cancer patients.

Cai, G., et al. (2021). "Immunological alternation in COVID-19 patients with cancer and its implications on mortality." Oncoimmunology **10**(1): 1854424.

Patients with malignancy were reportedly more susceptible and vulnerable to Coronavirus Disease 2019 (COVID-19), and witnessed a greater mortality risk in COVID-19 infection than noncancerous patients. But the role of immune dysregulation of malignant patients on poor prognosis of COVID-19 has remained insufficiently investigated. Here we conducted a retrospective cohort study that included 2,052 patients hospitalized with COVID-19 (Cancer, n = 93; Non-cancer, n = 1,959), and compared the immunological characteristics of both cohorts. We used stratification analysis, multivariate regressions, and propensity-score matching to evaluate the effect of immunological indices. In result, COVID-19 patients with cancer had ongoing and significantly elevated inflammatory factors and cytokines (high-sensitivity C-reactive protein, procalcitonin, interleukin (IL)-2 receptor, IL-6, IL-8), as well as decreased immune cells (CD8 + T cells, CD4 + T cells, B cells, NK cells, Th and Ts cells) than those without cancer. The mortality rate was significantly higher in cancer cohort (24.7%) than non-cancer cohort (10.8%). By stratification analysis, COVID-19 patients with immune dysregulation had poorer prognosis than those with the relatively normal immune system both in cancer and non-cancer cohort. By logistic regression, Cox regression, and propensity-score matching, we found that prior to adjustment for immunological indices, cancer history was associated with an increased mortality risk of COVID-19 ($p < .05$); after adjustment for immunological indices, cancer history was no longer an independent risk factor for poor prognosis of COVID-19 ($p > .30$). In conclusion, COVID-19 patients with cancer had more severely dysregulated immune responses than noncancerous patients, which might account for their poorer prognosis. Clinical Trial: This study has been registered on the Chinese Clinical Trial Registry (No. ChiCTR2000032161).

Cai, H., et al. (2020). "Association of age and cause-special mortality in patients with stage I/ II colon cancer: A population-based competing risk analysis." PLoS One **15**(10): e0240715.

PURPOSE: This study aimed to determine the probability and prognostic factors of colon cancer-specific mortality (CCSM) and noncancer-specific mortality (NCSM) for patients with stage I/II colon cancer and evaluate the association of age on cause-specific mortality. MATERIALS AND METHODS: From Surveillance, Epidemiology, and End Results (SEER) database, we identified 33152 patients with stage I/II colon cancer undergoing surgery between 2004 and 2011. The cumulative incidence of CCSM and NCSM was calculated, and competing risk analysis was performed to investigate prognostic factors for cause-specific mortality. RESULTS: In patients <50, 50-75, and >75 years of age, 5-year cumulative incidence of CCSM was 5.7%, 7.8%, and 16.1%, respectively (overall, 10.6%); 5-year cumulative incidence of NCSM was 2.2%, 7.1%, and 26.9%, respectively (overall, 13.8%). The probability of CCSM and NCSM increased with advanced age. The 5-year cumulative incidence of CCSM was higher than NCSM in patients <50 years of age, whereas lower in patients >75 years of age. The probability of CCSM and NCSM was similar in patients 50-75 years of age. Competing-risk multivariable analysis demonstrated that increasing age was a strong predictor of CCSM (per year increase, SHR 1.03,95% confidence interval [CI]: 1.03-1.04). Age was most predictive of NCSM: (per year increase, SHR 1.08, 95% CI: 1.08-1.08). CONCLUSION: Age was significantly associated with

an increased cumulative incidence of CCSM and NCSM of patients with stage I/II colon cancer underwent surgery. NCSM was a significant competing event and should be adequately considered when performing survival analysis.

Cai, J., et al. (2021). "[Trend analysis on morbidity and mortality of pancreatic cancer in China, 2005-2015]." Zhonghua Liu Xing Bing Xue Za Zhi **42**(5): 794-800.

Objective: To analyze the trend of morbidity and mortality of pancreatic cancer in China from 2005 to 2015 and estimate the related age, period and cohort effect, respectively. Methods: Joinpoint regression analysis was used to analyze the trend of morbidity rate and mortality rate of pancreatic cancer during 2005-2015 and calculate the annual percentage change and average annual percentage change based on the data in the annual report of China Cancer Registry. Population aged 20-84 years was fitted by the Age-Period-Cohort model to estimate the effect parameters of age, period and cohort. Results: The trend variations of the crude morbidity rate and crude mortality rate of pancreatic cancer were consistent. The morbidity rate of pancreatic cancer firstly increased before 2008 and then decreased. The morbidity rate and mortality rate of pancreatic cancer were higher in men than women, and higher in urban areas than in rural areas. From 2005 to 2015, the overall age-standardized morbidity rate of pancreatic cancer increased by 2.78% annually and the overall age standardized mortality rate of pancreatic cancer increased by 2.24% annually. The age standardized morbidity of pancreatic cancer in rural men changed more rapidly, with an average annual increase of 3.74%, and the age standardized mortality rate of pancreatic cancer in urban men changed more rapidly, with an average annual increase of 3.57%. The age effect on the morbidity and mortality of pancreatic cancer increased with age, and the effect was most obvious in age group 70-80 years, the period effect increased over time and the cohort effect decreased with year, but rebound or fluctuation was observed after 1976. Conclusions: The morbidity rate and mortality rate of pancreatic cancer in China increased slightly in past decades. Strategies on effective prevention and control of pancreatic cancer should be developed in the future.

Calip, G. S., et al. (2022). "Impact of time to distant recurrence on breast cancer-specific mortality in hormone receptor-positive breast cancer." Cancer Causes Control **33**(5): 793-799.

Women with hormone receptor (HR)-positive early-stage breast cancer (BC) have five-year survival rates of > 90% but remain at serious risk for developing distant metastases beyond five years from diagnosis. This retrospective cohort study used data from the Surveillance, Epidemiology, and End Results (SEER) registries to examine associations between distant recurrence-free interval (DRFI) and risk of BC-specific mortality following distant relapse. The analysis includes 1,057 women with second primary stage IV BC who were initially diagnosed with AJCC stages I-III HR-positive BC between1990 and 2016. Overall, 65% of women had a preceding DRFI of >/= 5 years. Five-year BC-specific survival following development of distant recurrence was 52% for women with DRFI >/= 5 years compared to 31% in women with DRFI of < 5 years. In multivariable analyses, risks of cancer-specific mortality following distant recurrence were lower in women with DRFI of 5 years or more (subdistribution hazard ratio = 0.72, 95% CI 0.58-0.89, p = 0.002). The results of this study may inform patient-clinician discussions surrounding prognosis and treatment selection among HR-positive patients who develop a distant recurrence of disease.

Canton-Bulnes, M. L., et al. (2022). "Determinants of mortality in cancer patients with unscheduled admission to the Intensive Care Unit: A prospective multicenter study." Med Intensiva (Engl Ed) **46**(12): 669-679.

OBJECTIVES: To analyze clinical features associated to mortality in oncological patients with unplanned admission to the Intensive Care Unit (ICU), and to determine whether such risk factors differ between patients with solid tumors and those with hematological malignancies. DESIGN: An observational study was carried out. SETTING: A total of 123 Intensive Care Units across Spain. PATIENTS: All cancer patients with unscheduled admission due to acute illness related to the background oncological disease. INTERVENTIONS: None. MAIN VARIABLES: Demographic parameters, severity scores and clinical condition were assessed, and mortality was analyzed. Multivariate binary logistic regression analysis was performed. RESULTS: A total of 482 patients were included: solid cancer (n=311) and hematological malignancy (n=171). Multivariate regression analysis showed the factors independently associated to ICU mortality to be the APACHE II score (OR 1.102; 95% CI 1.064-1.143), medical admission (OR 3.587; 95% CI 1.327-9.701), lung cancer (OR 2.98; 95% CI 1.48-5.99) and mechanical ventilation after the first 24h of ICU stay (OR 2.27; 95% CI 1.09-4.73), whereas no need for mechanical ventilation was identified as a protective factor (OR 0.15; 95% CI 0.09-0.28). In solid cancer patients, the APACHE II score, medical admission, antibiotics in the previous 48h and lung cancer were identified as independent mortality indicators, while no need for mechanical ventilation was identified as a protective factor. In the multivariate analysis, the APACHE II score and

mechanical ventilation after 24h of ICU stay were independently associated to mortality in hematological cancer patients, while no need for mechanical ventilation was identified as a protective factor. Neutropenia was not identified as an independent mortality predictor in either the total cohort or in the two subgroups. CONCLUSIONS: The risk factors associated to mortality did not differ significantly between patients with solid cancers and those with hematological malignancies. Delayed intubation in patients requiring mechanical ventilation might be associated to ICU mortality.

Cardoso, R., et al. (2021). "Colorectal cancer incidence, mortality, and stage distribution in European countries in the colorectal cancer screening era: an international population-based study." Lancet Oncol **22**(7): 1002-1013.

BACKGROUND: Colorectal cancer screening programmes and uptake vary substantially across Europe. We aimed to compare changes over time in colorectal cancer incidence, mortality, and stage distribution in relation to colorectal cancer screening implementation in European countries. METHODS: Data from nearly 3.1 million patients with colorectal cancer diagnosed from 2000 onwards (up to 2016 for most countries) were obtained from 21 European countries, and were used to analyse changes over time in age-standardised colorectal cancer incidence and stage distribution. The WHO mortality database was used to analyse changes over time in age-standardised colorectal cancer mortality over the same period for the 16 countries with nationwide data. Incidence rates were calculated for all sites of the colon and rectum combined, as well as the subsites proximal colon, distal colon, and rectum. Average annual percentage changes (AAPCs) in incidence and mortality were estimated and relevant patterns were descriptively analysed. FINDINGS: In countries with long-standing programmes of screening colonoscopy and faecal tests (ie, Austria, the Czech Republic, and Germany), colorectal cancer incidence decreased substantially over time, with AAPCs ranging from -2.5% (95% CI -2.8 to -2.2) to -1.6% (-2.0 to -1.2) in men and from -2.4% (-2.7 to -2.1) to -1.3% (-1.7 to -0.9) in women. In countries where screening programmes were implemented during the study period, age-standardised colorectal cancer incidence either remained stable or increased up to the year screening was implemented. AAPCs for these countries ranged from -0.2% (95% CI -1.4 to 1.0) to 1.5% (1.1 to 1.8) in men and from -0.5% (-1.7 to 0.6) to 1.2% (0.8 to 1.5) in women. Where high screening coverage and uptake were rapidly achieved (ie, Denmark, the Netherlands, and Slovenia), age-standardised incidence rates initially increased but then subsequently decreased. Conversely, colorectal cancer incidence increased in most countries where no large-scale screening programmes were available (eg, Bulgaria, Estonia, Norway, and Ukraine), with AAPCs ranging from 0.3% (95% CI 0.1 to 0.5) to 1.9% (1.2 to 2.6) in men and from 0.6% (0.4 to 0.8) to 1.1% (0.8 to 1.4) in women. The largest decreases in colorectal cancer mortality were seen in countries with long-standing screening programmes. INTERPRETATION: We observed divergent trends in colorectal cancer incidence, mortality, and stage distribution across European countries, which appear to be largely explained by different levels of colorectal cancer screening implementation. FUNDING: German Cancer Aid (Deutsche Krebshilfe) and the German Federal Ministry of Education and Research.

Cardoso, R., et al. (2021). "Incidence and Mortality of Proximal and Distal Colorectal Cancer in Germany-Trends in the Era of Screening Colonoscopy." Dtsch Arztebl Int **118**(16): 281-287.

BACKGROUND: The use of colonoscopy has increased and colorectal cancer (CRC) incidence has decreased after the introduction of screening colonoscopy in Germany. However, it remains unknown to what extent progress has been achieved in the prevention of cancer in the proximal colon, distal colon, and rectum. METHODS: We analyzed trends in CRC incidence (2000-2016) and mortality (2000-2018) in Germany by sex, age, and tumor location. RESULTS: The age-standardized incidence of CRC declined by 22.4% (from 65.3 to 50.7 per 100 000) in men and by 25.5% (from 42.7 to 31.8 per 100 000) in women. CRC mortality declined by 35.8% (from 29.6 to 19.0 per 100 000) in men and by 40.5% (19.0 to 11.3 per 100 000) in women. Despite demographic changes, the annual numbers of CRC cases and deaths still decreased from about 60 400 to 58 300 and from around 28 700 to 24 200, respectively. The decline in incidence was greatest in groups aged >/= 55 years. While the incidence of cancer in the distal colon and rectum decreased by 34.5% and 26.2%, respectively, in men and by 41.0% and 27.9% in women, the incidence of proximal colon cancer remained stable in men and decreased by only 7.0% in women. However, a major shift towards earlier stages was observed for the proximal cancers. CONCLUSION: The results support the assumption that the increased use of colo - noscopy has contributed to substantial reductions in the incidence of distal CRC incidence and the mortality from cancers in the entire colon and rectum.

Carethers, J. M. (2021). "Racial and ethnic disparities in colorectal cancer incidence and mortality." Adv Cancer Res **151**: 197-229.

The occurrence of colorectal cancer (CRC) shows a large disparity among recognized races and

ethnicities in the U.S., with Black Americans demonstrating the highest incidence and mortality from this disease. Contributors for the observed CRC disparity appear to be multifactorial and consequential that may be initiated by structured societal issues (e.g., low socioeconomic status and lack of adequate health insurance) that facilitate abnormal environmental factors (through use of tobacco and alcohol, and poor diet composition that modifies one's metabolism, microbiome and local immune microenvironment) and trigger cancer-specific immune and genetic changes (e.g., localized inflammation and somatic driver gene mutations). Mitigating the disparity by prevention through CRC screening has been demonstrated; this has not been adequately shown once CRC has developed. Acquiring additional knowledge into the science behind the observed disparity will inform approaches towards abating both the incidence and mortality of CRC between U.S. racial and ethnic groups.

Carioli, G., et al. (2022). "Cancer mortality predictions for 2021 in Latin America." Eur J Cancer Prev **31**(3): 217-227.

We estimated cancer mortality statistics for the current year in seven major Latin American countries, with a focus on colorectal cancer. We retrieved official death certification data and population figures from the World Health Organization and the Pan American Health Organization databases. We analysed mortality from all neoplasms combined and for selected cancer sites. We estimated numbers of deaths and age-standardized mortality rates for the year 2021 using a logarithmic Poisson count data joinpoint model. Total cancer mortality is predicted to decline in all countries considered for both sexes, with the exception of Argentinian women. The lowest total mortality rates were predicted in Mexico (65.4/100 000 men and 62.3 in women), the highest ones were in Cuba (133.3/100 000 men and 91.0 in women). Stomach cancer rates have been decreasing since 1970 in all countries; colorectal cancer started to decline over recent calendar periods. Rates for this cancer were unfavourable in the youngest age group. Lung cancer trends declined in males and remained comparatively low in all countries except Cuba. In Cuba, lung cancer rates in women overtook those for breast. Mortality from cancers of the breast, (cervix) uterus, ovary, prostate and bladder, as well as leukemia mostly showed favourable trends. A marked variability in rates across Latin American countries persists, and rates were relatively high for stomach, uterus, prostate and lung cancers, as compared to Europe and North America, suggesting the need to improve preventive strategies. Colorectal cancer mortality was relatively low in Latin America, except in Argentina, and short-term predictions remain moderately favourable.

Carioli, G., et al. (2021). "European cancer mortality predictions for the year 2021 with focus on pancreatic and female lung cancer." Ann Oncol **32**(4): 478-487.

BACKGROUND: We predicted cancer mortality statistics for 2021 for the European Union (EU) and its five most populous countries plus the UK. We also focused on pancreatic cancer and female lung cancer. MATERIALS AND METHODS: We obtained cancer death certifications and population data from the World Health Organization and Eurostat databases for 1970-2015. We predicted numbers of deaths and age-standardised (world population) rates for 2021 for total cancers and 10 major cancer sites, using a joinpoint regression model. We calculated the number of avoided deaths over the period 1989-2021. RESULTS: We predicted 1 267 000 cancer deaths for 2021 in the EU, corresponding to age-standardised rates of 130.4/100 000 men (-6.6% since 2015) and 81.0/100 000 for women (-4.5%). We estimated further falls in male lung cancer rates, but still trending upward in women by +6.5%, reaching 14.5/100 000 in 2021. The breast cancer predicted rate in the EU was 13.3/100 000 (-7.8%). The rates for stomach and leukaemias in both sexes and for bladder in males are predicted to fall by >10%; trends for other cancer sites were also favourable, except for the pancreas, which showed stable patterns in both sexes, with predicted rates of 8.1/100 000 in men and 5.6/100 000 in women. Rates for pancreatic cancer in EU men aged 25-49 and 50-64 years declined, respectively, by 10% and 1.8%, while for those aged 65+ years increased by 1.3%. Rates fell for young women only (-3.4%). Over 1989-2021, about 5 million cancer deaths were avoided in the EU27 compared with peak rates in 1988. CONCLUSION: Overall cancer mortality continues to fall in both sexes. However, specific focus is needed on pancreatic cancer, which shows a sizeable decline for young men only. Tobacco control remains a priority for the prevention of pancreatic and other tobacco-related cancers, which account for one-third of the total EU cancer deaths, especially in women, who showed less favourable trends.

Carlsson, S. V., et al. (2022). "Young Age on Starting Prostate-specific Antigen Testing Is Associated with a Greater Reduction in Prostate Cancer Mortality: 24-Year Follow-up of the Goteborg Randomized Population-based Prostate Cancer Screening Trial." Eur Urol.

BACKGROUND: The risk of death from prostate cancer (PC) depends on age, but the age at which to start prostate-specific antigen (PSA) screening remains uncertain. OBJECTIVE: To study the

relationship between risk reduction for PC mortality and age at first PSA screening. DESIGN, SETTING, AND PARTICIPANTS: The randomized Goteborg-1 trial invited men for biennial PSA screening between the ages of 50 and 70 yr (screening, n = 10 000) or no invitation but exposure to opportunistic PSA testing (control, n = 10 000). INTERVENTION: Regular versus opportunistic PSA screening or no PSA. OUTCOME MEASUREMENTS AND STATISTICAL ANALYSIS: We modeled the nonlinear association between starting age and the absolute risk reduction in PC mortality in three settings: (1) intention-to-screen (randomized arms); (2) historical control (screening group and 1990-1994 registry data); and (3) attendees only (screening attendees and matched controls). We tested whether the effect of screening on PC mortality depends on the age at starting screening by comparing survival models with and without an interaction between trial arm and age (intention-to-screen and attendees only). RESULTS AND LIMITATIONS: Younger age on starting PSA testing was associated with a greater reduction in PC mortality. Starting screening at age 55 yr approximately halved the risk of PC death compared to first PSA at age 60 yr. The test of association between starting age and the effect of screening on PC mortality was slightly greater than the conventional level of statistical significance (p = 0.052) for the entire cohort, and statistically significant among attendees (p = 0.002). This study is limited by the low number of disease-specific deaths for men starting screening before age 55 yr and the difficulty in discriminating between the effect of starting age and screening duration. CONCLUSIONS: Given that prior screening trials included men aged up to 70 yr on starting screening, our results suggest that the effect size reported in prior trials underestimates that of currently recommended programs starting at age 50-55 yr. PATIENT SUMMARY: In this study from the Goteborg-1 trial, we looked at the effect of prostate-specific antigen (PSA) screening in reducing men's risk of dying from prostate cancer given the age at which they begin testing. Starting at a younger age reduced the risk of prostate cancer death by a greater amount. We recommend that PSA screening should start no later than at age 55 yr.

Chatignoux, E., et al. (2021). "How to produce sound predictions of incidence at a district level using either health care or mortality data in the absence of a national registry: the example of cancer in France." Int J Epidemiol **50**(1): 279-292.

BACKGROUND: In many countries, epidemiological surveillance of chronic diseases is monitored by local registries (LR) which do not necessarily cover the whole national territory. This gap has fostered interest in using non-registry databases (e.g., health care or mortality databases) available for the whole territory as proxies for incidence at the local level. However, direct counts from these databases do not provide reliable incidence measures. Accordingly, specific methods are needed to correct proxies and assess their epidemiological usefulness. METHODS: This study's objective was to implement a three-stage turnkey methodology using national non-registry data to predict incidence in geographical areas without an LR as follows: constructing a calibration model to make predictions including accurate prediction intervals; accuracy assessment of predictions and rationale for the criteria to assess which predictions were epidemiologically useful; mapping after spatial smoothing of the latter predictions. The methodology was applied to a real-world setting, whereby we aimed to predict cancer incidence, by gender, at the district level in France over the 2007-15 period for 24 different cancer sites, using several health care indicators and mortality. In the present paper, the spatial smoothing performed on predicted incidence of epidemiological interest is illustrated for two examples. RESULTS: Predicted incidence of epidemiological interest was possible for 27/34 solid site-gender combinations and for only 2/8 haematological malignancies-gender combinations. Mapping of smoothed predicted incidence provided a clear picture of the main contrasts in incidence between districts. CONCLUSIONS: The methodology implemented provides a comprehensive framework to produce valuable predictions of incidence at a district level, using proxy measures and existing LR.

Chavez-MacGregor, M., et al. (2022). "Evaluation of COVID-19 Mortality and Adverse Outcomes in US Patients With or Without Cancer." JAMA Oncol **8**(1): 69-78.

IMPORTANCE: As the COVID-19 pandemic continues, understanding the clinical outcomes of patients with cancer and COVID-19 has become critically important. OBJECTIVE: To compare the outcomes of patients with or without cancer who were diagnosed with COVID-19 and to identify the factors associated with mortality, mechanical ventilation, intensive care unit (ICU) stay, and hospitalization. DESIGN, SETTING, AND PARTICIPANTS: This cohort study obtained data from the Optum de-identified COVID-19 electronic health record data set. More than 500 000 US adults who were diagnosed with COVID-19 from January 1 to December 31, 2020, were analyzed. EXPOSURES: The patient groups were (1) patients without cancer, (2) patients with no recent cancer treatment, and (3) patients with recent cancer treatment (within 3 months before COVID-19 diagnosis) consisting of radiation therapy or systemic

therapy. MAIN OUTCOMES AND MEASURES: Mortality, mechanical ventilation, ICU stay, and hospitalization within 30 days of COVID-19 diagnosis were the main outcomes. Unadjusted rates and adjusted odds ratios (ORs) of adverse outcomes were presented according to exposure group. RESULTS: A total of 507 307 patients with COVID-19 were identified (mean [SD] age, 48.4 [18.4] years; 281 165 women [55.4%]), of whom 493 020 (97.2%) did not have cancer. Among the 14 287 (2.8%) patients with cancer, 9991 (69.9%) did not receive recent treatment and 4296 (30.1%) received recent treatment. In unadjusted analyses, patients with cancer, regardless of recent treatment received, were more likely to have adverse outcomes compared with patients without cancer (eg, mortality rate: 1.6% for patients without cancer, 5.0% for patients with no recent cancer treatment, and 7.8% for patients with recent cancer treatment). After adjustment, patients with no recent cancer treatment had similar or better outcomes than patients without cancer (eg, mortality OR, 0.93 [95% CI, 0.84-1.02]; mechanical ventilation OR, 0.61 [95% CI, 0.54-0.68]). In contrast, a higher risk of death (OR, 1.74; 95% CI, 1.54-1.96), ICU stay (OR, 1.69; 95% CI, 1.54-1.87), and hospitalization (OR, 1.19; 95% CI, 1.11-1.27) was observed in patients with recent cancer treatment. Compared with patients with nonmetastatic solid tumors, those with metastatic solid tumors and hematologic malignant neoplasms had worse outcomes (eg, mortality OR, 2.36 [95% CI, 1.96-2.84]; mechanical ventilation OR, 0.87 [95% CI, 0.70-1.08]). Recent chemotherapy and chemoimmunotherapy were also associated with worse outcomes (eg, chemotherapy mortality OR, 1.84 [95% CI, 1.51-2.26]). CONCLUSIONS AND RELEVANCE: This cohort study found that patients with recent cancer treatment and COVID-19 had a significantly higher risk of adverse outcomes, and patients with no recent cancer treatment had similar outcomes to those without cancer. The findings have risk stratification and resource use implications for patients, clinicians, and health systems.

Che, W., et al. (2022). "Association between age and the presence and mortality of breast cancer synchronous brain metastases in the United States: A neglected SEER analysis." Front Public Health **10**: 1000415.

BACKGROUND: The extent of the relationship between age and the presence of breast cancer synchronous brain metastases (BCSBMs) and mortality has not yet been well-identified or sufficiently quantified. We aimed to examine the association of age with the presence of BCSBMs and all-cause and cancer-specific mortality outcomes using the SEER database. METHODS: Age-associated risk of the presence and survival of BCSBMs were evaluated on a continuous scale (restricted cubic spline, RCS) with logistic or Cox regression models. The main endpoints were the presence of BCSBMs and all-cause mortality or cancer-specific mortality. Cox proportional hazards regression and competing risk models were used in survival analysis. RESULTS: Among 374,132 adult breast cancer patients, 1,441 (0.38%) had BMs. The presence of BCSBMs displayed a U-shaped relationship with age, with the highest point of the curve occurring at the age of 62. In both the younger (age </= 61) and older (age >/= 62) groups, the observed curve showed a nearly linear relationship between age and the presence of BCSBMs. The relationship between age and all-cause mortality (ASM) and cancer-specific mortality (CSM) was linear. Older age at diagnosis was associated with a higher risk of ASM (HR 1.019, 95% CI: 1.013-1.024, p < 0.001) and CSM (HR 1.016, 95% CI: 1.010-1.023, p < 0.001) in multivariable Cox models. Age (sHR 1.007, 95% CI 1-1.013, p = 0.049) was substantially related to a significantly increased risk of CSM in competing risk models. CONCLUSION: Age had a non-linear U-shaped relationship with the presence of BCSBMs and a linear relationship with BCSBMs mortality.

Cheema, H. A., et al. (2022). "Vitamin D supplementation for the prevention of total cancer incidence and mortality: An updated systematic review and meta-analysis." Heliyon **8**(11): e11290.

INTRODUCTION: Previous randomized controlled trials (RCTs) and meta-analyses of RCTs evaluating vitamin D supplementation for the prevention of cancer incidence and mortality have found inconsistent results and no meta-analysis has assessed the quality of the evidence available. We, therefore, aimed to perform an updated meta-analysis by including recent large-scale RCTs and assessing the quality of the pooled evidence. METHODS: We searched several databases and trial registers from inception to April 2022. We used a random-effects model to estimate pooled risk ratios (RRs) and 95% confidence intervals (CIs). We used the Grades of Recommendation, Assessment, Development, and Evaluation (GRADE) considerations to evaluate the certainty of evidence. RESULTS: We included 13 RCTs in our study. Vitamin D supplementation had no effect on the risk of total cancer incidence (RR 0.99, 95% CI: 0.94-1.04; I (2) = 0%), total cancer mortality (RR 0.93, 95% CI: 0.84-1.03; I (2) = 24%) and total mortality (RR 0.92, 95% CI: 0.82-1.04; I (2) = 36%). The overall quality of evidence was high for all outcomes. DISCUSSION: Vitamin D supplementation is ineffective in reducing total cancer incidence and mortality in largely vitamin D-replete older adult

populations. Future research should be based on populations with a higher prevalence of vitamin D deficiency and should involve more extended follow-up periods. STUDY PROTOCOL: PROSPERO database, CRD42021285401.

Chen, C., et al. (2020). "Self-Reported Lower Gastrointestinal Endoscopy Use and Changes in Colorectal Cancer Mortality Rates in European Countries." Clin Transl Gastroenterol **11**(10): e00243.

INTRODUCTION: To quantify the association of self-reported lower gastrointestinal endoscopy use measured in 2004/05 with colorectal cancer (CRC) mortality changes over 2004-2015 in Europe. METHODS: An ecological analysis was performed using endoscopy utilization data from the Survey of Health, Aging, and Retirement in 11 European countries in 2004/05 and CRC mortality data from the World Health Organization Mortality Database over 2004-2015. Mortality trends were compared through annual mortality changes from joinpoint regression models. Cross-national variations in mortality trends with respect to endoscopy use were tested for statistical significance by negative binomial regression models. RESULTS: The proportion of respondents who reported having had an endoscopy within 10 years varied widely across countries, from 6.1% to 25.1%. Large disparities in CRC mortality trends were also observed, with annual mortality change ranging from a decline of 3.3% to an increase of 0.9% for men and from a decline of 3.3% to a decline of 0.6% for women. Endoscopy uptake was negatively associated with the magnitude of annual mortality change over 2004-2015 (rate ratio for a 10-year mortality change per 10% higher endoscopy use, 0.88; 95% confidence interval, 0.82-0.94). DISCUSSION: This analysis provides quantitative evidence on the contributions of endoscopy use to CRC mortality declines in European countries over the past decade. A considerable fraction of protection is likely to be delivered through endoscopic removal of adenomas and sessile serrated lesions. With many European countries having recently implemented CRC screening programs, an increase in endoscopy use and a subsequent reduction in CRC mortality would be expected.

Chen, F., et al. (2022). "Long-Time Trend of Colorectal Cancer Mortality Attributable to High Processed Meat Intake in China and a Bayesian Projection from 2020 to 2030: A Model-Based Study." Int J Environ Res Public Health **19**(17).

Colorectal cancer is among the leading causes of cancer worldwide. Processed meat was known to be positively associated with a higher risk of gastrointestinal cancer. This study focused on the long-time trends of colorectal cancer mortality attributable to high processed meat intake in China from 1990 to 2019 and the projection for the next decade based on data obtained from the Global Burden of Disease 2019 study. We used an age-period-cohort model to fit the long-time trend. The joinpoint model was conducted to estimate the average and annual change of the attributable mortality. The Bayesian age-period-cohort model was used to project the crude attributable mortality from 2020 to 2030. An upward trend in colorectal cancer mortality attributable to high processed meat intake was observed for both sexes in China from 1990 to 2019, with an overall net drift of 4.009% for males and 2.491% for females per year. Projection analysis suggested that the burden of colorectal cancer incidence and mortality would still be high. Our findings suggested that colorectal cancer death attributable to high processed meat intake is still high in China, and elderly males were at higher risk. Gradually decreasing the intake of processed meat could be an effective way to reduce colorectal cancer mortality.

Chen, G., et al. (2021). "Development and Validation of Web-Based Nomograms for Predicting Cause-Specific Mortality in Surgically Resected Nonmetastatic Invasive Breast Cancer: A Population-Based Study." Ann Surg Oncol **28**(11): 6537-6550.

BACKGROUND: This study aims to build nomograms to predict overall survival (OS) and breast cancer-specific death (BCSD) in resected nonmetastatic invasive breast cancer. PATIENTS AND METHODS: Patients extracted from surveillance, epidemiology, and end results database between 2010 and 2014 were analyzed. Through multivariate Cox regression and Fine and Gray competing risks regression, independent predictive factors were identified and integrated to build nomograms for predicting OS and BCSD. The models were validated by bootstrap resampling and an independent cohort. Additionally, the models' performance was measured by the Harrell's C-index, calibrate curve, and time-dependent receiver operating characteristic (ROC) curves. RESULTS: In total, 110,180 cases were identified and enrolled in the analysis, with 83,450 in the training cohort and 26,730 in the validation cohort. Several independent predictive factors for OS and BCSD were identified and integrated to construct the nomograms. The C-indexes in the training cohort and validation cohort were 0.759 and 0.772 for predicting OS, and 0.857 and 0.856 for predicting BCSD, respectively. The nomogram models were well calibrated, and the time-dependent ROC curves verified the superiority of our models for clinical usefulness. Significant differences in the OS and BCSD curves were also observed when stratifying patients

into several different risk groups. For convenient access, we deployed these proposed nomograms into web-based calculators. CONCLUSIONS: We established and validated novel nomograms for individualized prediction of OS and BCSD in resected nonmetastatic invasive breast cancer. These nomograms perform better than previous models and could be easily accessed easily by clinicians.

Chen, H., et al. (2022). "Cancer Mortality Patterns by Birthplace and Generation Status of Mexican Latinos: The Multiethnic Cohort." J Natl Cancer Inst **114**(7): 959-968.

BACKGROUND: Latinos are the largest minority group in the United States. We assessed cancer mortality by birthplace and generation status of Mexican Latinos in the Multiethnic Cohort. METHODS: We included 26 751 Latinos of Mexican origin and 6093 non-Latino Whites aged 45-74 years at cohort entry (1993-1996) from the California Multiethnic Cohort component. The Mexican Latinos comprised 42% first-generation Mexico-born immigrants, 42% second-generation (28% US-born with both parents Mexico-born and 14% US-born with 1 parent US-born and 1 parent Mexico-born), and 16% third-generation or more who were US-born with both parents US-born. Multivariable Cox models were used to calculate covariate adjusted hazard ratios and 95% confidence intervals for overall and site-specific cancer mortality by birthplace and generation status. All statistical tests were 2-sided. RESULTS: Cancer death rate was highest among the US-born with 1 parent US-born and 1 parent Mexico-born (age-adjusted rate = 471.0 per 100 000 person-years) and US-born with both parents US-born (age-adjusted rate = 469.0 per 100 000 person-years) groups. The US-born with both parents Mexico-born group had a 30% (hazard ratio = 1.30, 95% confidence interval = 1.18 to 1.44) higher risk of cancer death than the first-generation Mexico-born immigrants group, showing US birthplace was associated with an elevated cancer mortality. For cancer-specific mortality, US birthplace was positively associated with colorectal, liver and lung, and ovarian cancer (P values ranged from .04 to .005). Among US-born Mexican Latinos, generation status was not statistically significantly associated with overall cancer or site-specific cancer mortality. CONCLUSIONS: Our findings suggest that US birthplace is a risk factor for cancer death in Mexican Americans. Identification of the contributing factors is important to curtail patterns of increasing cancer mortality in US-born Mexican Latinos.

Chen, J. G., et al. (2021). "Liver cancer mortality over six decades in an epidemic area: what we have learned." PeerJ **9**: e10600.

BACKGROUND AND AIMS: Liver cancer is one of the most dominant malignant tumors in the world. The trends of liver cancer mortality over the past six decades have been tracked in the epidemic region of Qidong, China. Using epidemiological tools, we explore the dynamic changes in age-standardized rates to characterize important aspects of liver cancer etiology and prevention. METHODS: Mortality data of liver cancer in Qidong from 1958 to 1971 (death retrospective survey) and from 1972 to 2017 (cancer registration) were tabulated for the crude rate (CR), and age-standardized rate and age-birth cohorts. The average annual percentage change was calculated by the Joinpoint Regression Program. RESULTS: The natural death rate during 1958-2017 decreased from 9 per thousand to 5.4 per thousand and then increased to 8 per thousand as the population aged; cancer mortality rates rose continuously from 57/10(5) to 240/10(5). Liver cancer mortality increased from 20/10(5) to 80/10(5), and then dropped to less than 52/10(5) in 2017. Liver cancer deaths in 1972-2017 accounted for 30.53% of all cancers, with a CR of 60.48/10(5), age-standardized rate China (ASRC) of 34.78/10(5), and ASRW (world) of 45.71/10(5). Other key features were the CR for males and females of 91.86/10(5) and 29.92/10(5), respectively, with a sex ratio of 3.07:1. Period analysis showed that the ASRs for mortality of the age groups under 54 years old had a significant decreasing trend. Importantly, birth cohort analysis showed that the mortality rate of liver cancer in 40-44, 35-39, 30-34, 25-29, 20-24, 15-19 years cohort decreased considerably, but the rates in 70-74, and 75+ increased. CONCLUSIONS: The crude mortality rate of liver cancer in Qidong has experienced trends from lower to higher levels, and from continued increase at a high plateau to most recently a gradual decline, and a change greatest in younger people. Many years of comprehensive prevention and intervention measures have influenced the decline of the liver cancer epidemic in this area. The reduction of intake levels of aflatoxin might be one of the most significant factors as evidenced by the dramatic decline of exposure biomarkers in this population during the past three decades.

Chen, L., et al. (2020). "Impact of Minimally Invasive Esophagectomy in Post-Operative Atrial Fibrillation and Long-Term Mortality in Patients Among Esophageal Cancer." Cancer Control **27**(1): 1073274820974013.

AIMS: Postoperative Atrial fibrillation (POAF) after esophagectomy may prolong stay in intensive care and increase risk of perioperative complications. A minimally invasive approach is becoming the preferred option for esophagectomy, yet its implications for POAF risk remains unclear. The

association between POAF and minimally invasive esophagectomy (MIE) was examined in this study. METHODS: We used a dataset of 575 patients who underwent esophagectomy. Multivariate logistic regression analysis was performed to examine the association between MIE and POAF. A cox proportional hazards model was applied to assess the long-term mortality (MIE vs open esophagectomy, OE). RESULTS: Of the 575 patients with esophageal cancer, 62 developed POAF. MIE was negatively associated with the occurrence of POAF (Odds ratio: 0.163, 95%CI: 0.033-0.801). No significant difference was observed in long-term mortality (Odds ratio: 2.144, 95%CI: 0.963-4.775). CONCLUSIONS: MIE may reduced the incidence of POAF without compromising the survival of patients with esophageal cancer. Moreover, the specific mechanism of MIE providing this possible advantage needs to be determined by larger prospective cohort studies with specific biomarker information from laboratory tests.

Chen, L., et al. (2020). "The role of surgery type in postoperative atrial fibrillation and in-hospital mortality in esophageal cancer patients with preserved left ventricular ejection fraction." World J Surg Oncol **18**(1): 244.

BACKGROUND: Postoperative atrial fibrillation (POAF) is one of the most common complications of esophagectomy, which may extend the inpatient hospital stay. Minimally invasive esophagectomy (MIE) has been increasingly used in clinical practice; however, its POAF risk and short-term mortality remain unclear. This study aimed to examine the POAF risk and in-hospital mortality rate between patients receiving MIE and open esophagectomy (OE). METHODS: Esophageal cancer patients who underwent MIE or OE from a retrospective cohort study were evaluated. A multivariate logistic regression model was built to assess the associations between esophagectomy (MIE vs. OE) and various outcomes (POAF, in-hospital mortality). Covariates included age, sex, body mass index, neoadjuvant therapy, tumor stage, surgery incision type, comorbidities, cardia conditions, peri-operative medication, and complications. RESULTS: Of the 484 patients with esophageal cancer, 63 received MIE. A total of 53 patients developed POAF. Compared to patients receiving OE, MIE patients had 81% reduced odds of POAF (adjusted odds ratio [aOR] 0.185, 95% CI 0.039-0.887, P = 0.035). No statistically significant association was found for in-hospital mortality (aOR 0.709, 95% CI 0.114-4.409, P = 0.712). CONCLUSIONS: MIE is associated with a lower risk of POAF, compared to traditional surgery. No significant short-term survival benefit was found for MIE.

Chen, L., et al. (2022). "Factors leading to the risk of stroke mortality: a cross-sectional study with lung cancer patient-based large sample." Eur J Cancer Prev **31**(1): 14-18.

To identify the risk factors for stroke mortality among lung cancer patients on the basis of the Surveillance, Epidemiology, and End Results (SEER) database. The clinical data of lung cancer patients diagnosed between 2004 and 2016 were collected in the SEER database. The stroke mortality of lung cancer patients was compared with the general population using standardized mortality ratios (SMRs). COX proportional hazard model was applied to analyze the risk factors for stroke mortality among lung cancer patients. Among 82 454 patients, 4821 (5.85%) died of stroke. The stroke mortality rate in lung cancer patients significantly increased compared with the general population [SMR: 1.73, 95% confidential interval (95% CI), 1.69-1.78]. Differences were pronounced between the patients with stroke death and those without regarding all the basic characteristics ($P < 0.001$). Multivariate COX analysis showed that the risk factors for stroke mortality among lung cancer patients included increasing age, males, the black, grade II-III, distant metastasis and higher American Joint Committee on Cancer (AJCC) TNM stage, whereas adenocarcinoma was found to be a protective factor compared with squamous cell carcinoma. Increasing age, males, the black, grade II-III, distant metastasis and higher TNM stage are associated with an increased risk of stroke mortality among lung cancer patients, but adenocarcinoma with a lowered risk.

Cho, B., et al. (2021). "Evaluation of Racial/Ethnic Differences in Treatment and Mortality Among Women With Triple-Negative Breast Cancer." JAMA Oncol **7**(7): 1016-1023.

IMPORTANCE: To our knowledge, there is no consensus regarding differences in treatment and mortality between non-Hispanic African American and non-Hispanic White women with triple-negative breast cancer (TNBC). Little is known about whether racial disparities vary by sociodemographic, clinical, and neighborhood factors. OBJECTIVE: To examine the differences in clinical treatment and outcomes between African American and White women in a nationally representative cohort of patients with TNBC and further examine the contributions of sociodemographic, clinical, and neighborhood factors to TNBC outcome disparities. DESIGN, SETTING, AND PARTICIPANTS: This population-based, retrospective cohort study included 23 123 women who received a diagnosis of nonmetastatic TNBC between January 1, 2010, and December 31, 2015, followed up through December 31, 2016, and identified from the

Surveillance, Epidemiology, and End Results data set. The study was conducted from July 2019 to November 2020. The analyses were performed from July 2019 to June 2020. EXPOSURES: Race and ethnicity, including non-Hispanic African American and non-Hispanic White race. MAIN OUTCOMES AND MEASURES: Using logistic regression analysis and competing risk regression analysis, we estimated odds ratios (ORs) of receipt of treatment and hazard ratios (HRs) of breast cancer mortality in African American patients compared with White patients. RESULTS: Of 23 213 participants, 5881 (25.3%) were African American women and 17 332 (74.7%) were White women. Compared with White patients, African American patients had lower odds of receiving surgery (OR, 0.69; 95% CI, 0.60-0.79) and chemotherapy (OR, 0.89; 95% CI, 0.81-0.99) after adjustment for sociodemographic, clinicopathologic, and county-level factors. During a 43-month follow-up, 3276 patients (14.2%) died of breast cancer. The HR of breast cancer mortality was 1.28 (95% CI, 1.18-1.38) for African American individuals after adjustment for sociodemographic and county-level factors. Further adjustment for clinicopathological and treatment factors reduced the HR to 1.16 (95% CI, 1.06-1.25). This association was observed in patients living in socioeconomically less deprived counties (HR, 1.26; 95% CI, 1.14-1.39), urban patients (HR, 1.21; 95% CI, 1.11-1.32), patients having stage II (HR, 1.19; 95% CI, 1.02-1.39) or III (HR, 1.15; 95% CI, 1.01-1.31) tumors that were treated with chemotherapy, and patients younger than 65 years (HR, 1.24; 95% CI, 1.12-1.37). CONCLUSIONS AND RELEVANCE: In this retrospective cohort study, African American women with nonmetastatic TNBC had a significantly higher risk of breast cancer mortality compared with their White counterparts, which was partially explained by their disparities in receipt of surgery and chemotherapy.

Cho, H. M., et al. (2021). "Gamma-glutamyltransferase and the risk of head and neck cancer mortality." J Oral Pathol Med **50**(8): 803-811.

BACKGROUND: The purpose of this study was to determine the association between baseline serum gamma-glutamyltransferase levels and the mortality risk of head and neck cancers. METHODS: A total of 481 414 Korean participants aged 40-79 years at enrollment were examined. The hazard ratios for head and neck cancer mortality were analyzed using Cox proportional hazards models, which were adjusted for potential confounding factors. RESULTS: In the overall study population, high gamma-glutamyltransferase levels were significantly associated with head and neck cancers mortality in a dose-response linear relation ($p < 0.001$). After excluding participants (n = 125) who died of head and neck cancers within five years of enrollment, the main results remained similar to those of the analysis of all 313 head and neck cancers deaths in the study population. CONCLUSION: These findings indicate that serum gamma-glutamyltransferase activity is positively associated with an increased mortality risk in head and neck cancers in a dose-dependent manner.

Cho, M. H., et al. (2021). "Association of Aspirin, Metformin, and Statin Use with Gastric Cancer Incidence and Mortality: A Nationwide Cohort Study." Cancer Prev Res (Phila) **14**(1): 95-104.

Anticancer effects of aspirin, metformin, and statins against gastric cancer, one of the most common cancers in the world, have been reported. This retrospective cohort study aimed to investigate independent associations of aspirin, metformin, and statin use with gastric cancer incidence and mortality after adjustment for concomitant use of other drugs, using pooled cohort data extracted from the Korean National Health Insurance claim database. Follow-up started on January 1, 2004 and ended at the date of gastric cancer diagnosis, death, or December 31, 2013. Exposures to drugs were defined as cumulative duration of use for aspirin and cumulative defined daily dose for metformin and statin, and were entered as time-dependent variables in Cox analysis models to avoid immortal time bias. Use of aspirin for longer than 182.5 and 547.5 days during 2-year interval was associated with reduced risks of gastric cancer incidence and mortality, respectively. Patients with diabetes were at higher risk of gastric cancer incidence and mortality than nondiabetic people, regardless of metformin treatment. However, metformin use among patients with diabetes was associated with a reduction in gastric cancer mortality in a dose-response manner. Statin use was also associated with a reduction of gastric cancer mortality in the general population, but not with gastric cancer incidence. In conclusion, long-term use of aspirin was independently associated with reduced incidence and mortality of gastric cancer in the general population, but metformin or statin use was only associated with a reduction of gastric cancer mortality in patients with diabetes and in the general population, respectively. PREVENTION RELEVANCE: Long-term use of aspirin was independently associated with reduced incidence and mortality of gastric cancer in the general population. Metformin or statin use, however, was only associated with a reduction of gastric cancer mortality in diabetic patients and in the general population in a dose-response manner, respectively.

Choi, E., et al. (2021). "Effectiveness of the Korean National Cancer Screening Program in reducing breast cancer mortality." NPJ Breast Cancer **7**(1): 83.

High incidences of breast cancer (BC) are reported in Asian women in their forties, and it is not clear whether mammographic screening reduces mortality among them. This study evaluated the effect of BC screening on mortality in Korea. We conducted a nationwide prospective cohort study of women invited to the Korean National Cancer Screening Program (KNCSP) between 2002 and 2003 (N = 8,300,682), with data linkage to the Korea Central Cancer Registry and death certificates through 2014 and 2015, respectively. Exposure to mammographic screening was defined using a modified never/ever approach. The primary study outcome was adjusted mortality rate ratio (MRR) for BC among screened and non-screened women estimated by Poisson regression. An adjusted MRR for all cause-death other than BC was examined to account for selection bias in the cohort. BC incidence rates for screened and non-screened women were 84.41 and 82.88 per 100,000 women-years, respectively. BC mortality rates for screened and non-screened women were 5.81 and 13.43 per 100,000 women-years, respectively, with an adjusted MRR for BC of 0.43 (95% CI, 0.41-0.44). The adjusted MRR for all-cause death excluding BC was 0.52 (95% CI, 0.52-0.52). The greatest reduction in BC mortality was noted for women aged 45-54 years, and there was no observable reduction in mortality after the age of 70 years. In conclusion, the KNCSP has been effective in reducing BC mortality among Korean women aged 40-69 years.

Choi, H., et al. (2021). "Increasing Mortality in Korean Patients With Breast Cancer: High Mortality Rate in Elderly Breast Cancer Population Due to Suboptimal Treatment and Other Diseases." Cancer Control **28**: 10732748211037914.

BACKGROUND: The incidence of breast cancer in Asia, including Korea, has rapidly increased. Each country has shown different clinical features. This study presents a comprehensive understanding of breast cancer in different age groups in Korea and determines potential measures for improving patient survival. METHODS: Patients diagnosed with invasive breast cancer stages I to III with available clinicopathologic and follow-up data were included in the study. Kaplan-Meier survival graphs were generated for each group and compared using log-rank test. The hazard ratio for each risk factor was calculated using the Cox regression model and the 95% confidence interval. RESULTS: The final cohort included 833 patients with a mean age of 51.3+/-11.3 years (range, 22-89 years), and 191 (22.9%) of them were aged >60 years. Patients aged >/=60 years had worse overall survival (OS) and distant disease-free survival than those aged <60 years. Although no difference was observed in the tumor biology, elderly patients showed significant differences in practice patterns: they tended to undergo mastectomy (40.2% vs 62.8%, P<0.001), did not receive the standard chemotherapy (88.4% vs 69.3%, P < 0.001), and had a higher risk of developing second primary cancer or diseases other than breast cancer (1.2% vs 6.8%, P < 0.001), which significantly correlated with poor survival in elderly patients. CONCLUSION: Less-than-the-standard treatment of care or development of a second primary disease resulted in poor prognosis in elderly patients in Korea. A multi-institutional and multinational study is warranted to elucidate the clinical features of breast cancer in Asian patients.

Choi, H., et al. (2021). "Association of Adipopenia at Preoperative PET/CT with Mortality in Stage I Non-Small Cell Lung Cancer." Radiology **301**(3): 645-653.

Background Body mass index (BMI) and sarcopenia status are well-established prognostic factors in patients with lung cancer. However, the relationship between the amount of adipose tissue and survival remains unclear. Purpose To investigate the association between baseline adipopenia and outcomes in patients with early-stage non-small cell lung cancer (NSCLC). Materials and Methods Consecutive patients who underwent surgical resection for stage I NSCLC between 2011 and 2015 at a single tertiary care center were retrospectively identified. The primary outcome was the 5-year overall survival (OS) rate, and secondary outcomes were the 5-year disease-free survival (DFS) rate and the major postoperative complication rate. The abdominal total fat volume at the waist and the skeletal muscle area at the L3 level were obtained from preoperative PET/CT data and were normalized by the height squared to calculate the fat volume index (FVI) and skeletal muscle index. Adipopenia was defined as the sex-specific lowest quartile of the FVI for the study sample, and sarcopenia was determined using the skeletal muscle index reference value (men, <55 cm(2)/m(2); women, <39 cm(2)/m(2)). The association between body composition and outcomes was evaluated using Cox regression analysis. Results A total of 440 patients (median age, 65 years [interquartile range, 58-72 years]; 243 men) were evaluated. Most underweight patients (<20 kg/m(2)) had adipopenia (97%, 36 of 37 patients), but overweight patients (25-30 kg/m(2), n = 138) and obese patients (>30 kg/m(2), n = 14) did not have adipopenia (3%, four of 152 patients). In the group with a normal BMI (20-25 kg/m(2)), 28% (70 of 251 patients) had adipopenia and 67% (168 of 251 patients) had sarcopenia. After adjusting for age, sex, smoking history, surgical procedure, stage, histologic

type, BMI, and sarcopenia, adipopenia was associated with reduced 5-year OS (hazard ratio [HR] = 2.2; 95% CI: 1.1, 3.8; P = .02) and 5-year non-cancer-specific OS rates (HR = 3.2; 95% CI: 1.2, 8.7; P = .02). There was no association between adipopenia and postoperative complications (P = .45) or between adipopenia and the 5-year DFS rate (P = .18). Conclusion Baseline adipopenia was associated with a reduced 5-year overall survival rate in patients with early-stage non-small cell lung cancer and may indicate risk for non-cancer-related death. (c) RSNA, 2021 Online supplemental material is available for this article.

Choi, J., et al. (2021). "Effects of Screenings in Reducing Colorectal Cancer Incidence and Mortality Differ by Polygenic Risk Scores." Clin Transl Gastroenterol **12**(5): e00344.

INTRODUCTION: Colorectal cancer (CRC) screening reduces CRC incidence and mortality. However, it is unclear whether the reduction in CRC risk may differ by genetic susceptibility. METHODS: We evaluated this question in a cohort of 304,740 participants of European descent aged 50 years and older. Genetic susceptibility was measured using a polygenic risk score (PRS) constructed with risk variants identified in genomewide association studies. Cox models were used to estimate hazard ratios and 95% confidence intervals of CRC risk. RESULTS: Over a median follow-up of 7.0 years, 2,261 incident CRC cases and 528 CRC deaths were identified. CRC screening was associated with a significantly reduced CRC incidence among individuals with a high (hazard ratio, 0.80; 95% confidence interval, 0.71-0.92) and intermediate PRS (0.84, 0.71-0.98) but not among those with a low PRS (1.03, 0.86-1.25; Pinteraction, 0.005). A similar but more evident difference was observed for mortality (Pinteraction, 0.046), with more than 30% reduced mortality observed in the high PRS group (0.69, 0.52-0.91). Among the younger group (age 50-60 years), CRC screenings were associated with a slightly (but nonsignificantly) elevated incidence and mortality in the low PRS group but a reduced risk in the high PRS group (Pinteraction, 0.043 [incidence]; 0.092 [mortality]). No significant interaction was observed in the older group (age > 60 years). DISCUSSION: Individuals with a higher genetic risk benefited more substantially from CRC screenings than those with a lower risk. Our findings suggest that PRS may be used to develop personalized CRC screening to maximize its effect on CRC prevention.

Choi, J. K., et al. (2021). "Association between Moving to a High-Volume Hospital in the Capital Area and the Mortality among Patients with Cancer: A Large Population-Based Cohort Study." Int J Environ Res Public Health **18**(7).

This study aimed to identify the association between moving to a high-volume hospital and the mortality of patients with cancer living in the district. The study population comprised participants diagnosed with cancer within the past nine years (2004-2012). The final sample included 8197 patients with cancer, 3939 were males (48.1%), and 4258 were females (51.9%). A Cox proportional hazard model was used to estimate the hazard ratio (HR) for death. Confounding variables including sex, age, type of social security, income level, disability, and utilization volume were incorporated into the model. Among patients with cancer living in the district, 2874 (35.1%) used healthcare services in Seoul. About 10% (n = 834) of patients died during the follow-up period. The HR for death in females (HR: 0.68, 95% CI: 0.58-0.81) was lower than that in males. Additionally, the HR for the death of patients using healthcare services in Seoul (HR: 1.30, 95% CI: 1.11-1.53) was higher than those patients who did not use healthcare services in Seoul. Among patients utilizing services in the province, wealthier patients' survival probability was significantly higher than that of others. The cause of income differences should be identified, and accessibility to medical use of low-income families should be enhanced to prevent mortality of patients from cancer disparities.

Choi, M., et al. (2021). "Association of Insulin, Metformin, and Statin with Mortality in Breast Cancer Patients." Cancer Res Treat **53**(1): 65-76.

PURPOSE: This study investigated the association of insulin, metformin, and statin use with survival and whether the association was modified by the hormone receptor status of the tumor in patients with breast cancer. MATERIALS AND METHODS: We studied 7,452 patients who had undergone surgery for breast cancer at Seoul National University Hospital from 2008 to 2015 using the nationwide claims database. Exposure was defined as a recorded prescription of each drug within 12 months before the diagnosis of breast cancer. RESULTS: Patients with prior insulin or statin use were more likely to be older than 50 years at diagnosis and had a higher comorbidity index than those without it ($p < 0.01$ for both). The hazard ratio (HR) for death with insulin use was 5.7 ($p < 0.01$), and the effect was attenuated with both insulin and metformin exposure with an HR of 1.2 ($p=0.60$). In the subgroup analyses, a heightened risk of death with insulin was further prominent with an HR of 17.9 ($p < 0.01$) and was offset by co-administration of metformin with an HR of 1.3 ($p=0.67$) in patients with estrogen receptor (ER)-negative breast cancer. Statin use was associated with increased overall mortality

only in patients with ER-positive breast cancer with HR for death of 1.5 (p=0.05). CONCLUSION: Insulin or statin use before the diagnosis of breast cancer was associated with an increase in all-cause mortality. Subsequent analyses suggested that metformin or statin use may have been protective in patients with ER-negative disease, which warrants further studies.

Christopherson, K. M., et al. (2021). "A Machine Learning Model Approach to Risk-Stratify Patients With Gastrointestinal Cancer for Hospitalization and Mortality Outcomes." Int J Radiat Oncol Biol Phys **111**(1): 135-142.

PURPOSE: Patients with gastrointestinal (GI) cancer frequently experience unplanned hospitalizations, but predictive tools to identify high-risk patients are lacking. We developed a machine learning model to identify high-risk patients. METHODS AND MATERIALS: In the study, 1341 consecutive patients undergoing GI (abdominal or pelvic) radiation treatment (RT) from March 2016 to July 2018 (derivation) and July 2018 to January 2019 (validation) were assessed for unplanned hospitalizations within 30 days of finishing RT. In the derivation cohort of 663 abdominal and 427 pelvic RT patients, a machine learning approach derived random forest, gradient boosted decision tree, and logistic regression models to predict 30-day unplanned hospitalizations. Model performance was assessed using area under the receiver operating characteristic curve (AUC) and prospectively validated in 161 abdominal and 90 pelvic RT patients using Mann-Whitney rank-sum test. Highest quintile of risk for hospitalization was defined as "high-risk" and the remainder "low-risk." Hospitalizations for high- versus low-risk patients were compared using Pearson's chi(2) test and survival using Kaplan-Meier log-rank test. RESULTS: Overall, 13% and 11% of patients receiving abdominal and pelvic RT experienced 30-day unplanned hospitalization. In the derivation phase, gradient boosted decision tree cross-validation yielded AUC = 0.823 (abdominal patients) and random forest yielded AUC = 0.776 (pelvic patients). In the validation phase, these models yielded AUC = 0.749 and 0.764, respectively (P < .001 and P = .002). Validation models discriminated high- versus low-risk patients: in abdominal RT patients, frequency of hospitalization was 39% versus 9% in high- versus low-risk groups (P < .001) and 6-month survival was 67% versus 92% (P = .001). In pelvic RT patients, frequency of hospitalization was 33% versus 8% (P = .002) and survival was 86% versus 92% (P = .15) in high- versus low-risk patients. CONCLUSIONS: In patients with GI cancer undergoing RT as part of multimodality treatment, machine learning models for 30-day unplanned hospitalization discriminated high- versus low-risk patients. Future applications will test utility of models to prompt interventions to decrease hospitalizations and adverse outcomes.

Chronister, B. N. C., et al. (2021). "Dietary Acid Load, Serum Polychlorinated Biphenyl Levels, and Mortality Following Breast Cancer in the Long Island Breast Cancer Study Project." Int J Environ Res Public Health **19**(1).

Dietary acid load (DAL) may be associated with all-cause mortality (ACM) and breast cancer-specific mortality (BCM), and these associations may be modified by serum polychlorinated biphenyl (PCB) levels. Participants included 519 women diagnosed with first primary in situ or invasive breast cancer in 1996/1997 with available lipid-corrected PCB data. After a median of 17 years, there were 217 deaths (73 BCM). Potential renal acid load (PRAL) and net endogenous acid production (NEAP) scores calculated from a baseline food frequency questionnaire estimated DAL. Cox regression estimated covariate-adjusted hazard ratios (HRs) and 95% confidence intervals (CIs) for associations between PRAL and NEAP with mortality. We evaluated effect measure modification by total serum PCB levels (>median vs. </=median). PRAL quartile 4 versus quartile 1 was associated with an ACM HR of 1.31 (95%CI = 0.90-1.92). In the upper median of PCBs, ACM HRs were 1.43 (95%CI = 0.96-2.11) and 1.40 (95%CI = 0.94-2.07) for PRAL and NEAP upper medians, respectively. In the lower median of PCBs, the upper median of NEAP was inversely associated with BCM (HR = 0.40, 95%CI = 0.19-0.85). DAL may be associated with increased risk of all-cause mortality following breast cancer among women with high total serum PCB levels, but inversely associated with breast cancer mortality among women with low PCB levels.

Chu, J., et al. (2022). "[Spatio-temporal trend of female breast cancer mortality in Shandong Province from 1970 to 2013]." Zhonghua Yu Fang Yi Xue Za Zhi **56**(5): 609-613.

The mortality of female breast cancer in Shandong Province has increased since the 1970. The differential decomposition analysis found that the slight decline in the crude mortality of breast cancer among women was entirely due to non-demographic factors during the 1970-1990, and the significant increase in the crude mortality was due to a combination of demographic and non-demographic factors since the 1990. The contribution rate of demographic factor has gradually increased from 53.5% in 2004-2005 to 59.5% in 2011-2013, while that of non-demographic factor has decreased from 46.5% to 40.5%. The women aged 45-64 years old were the major population of female breast cancer deaths, accounting for 40%-60% of total

breast cancer deaths in different times, and then the mortality in female aged 55-64 years old increased rapidly, with increases of 52.12%, 115.19% and 29.01% in 2011-2013 over the 1970-1974, 1990-1992 and 2004-2005, respectively (Z=-7.342,P<0.001). Compared with 1970-1974, the age-standardized mortality rate of rural women increased by 41.86% in 2011-2013 (Z=-17.933, P<0.001), and that of urban women increased by 18.62% in 2011-2013 (Z=-25.642, P<0.001). The age-standardized mortality rate of breast cancer in urban women was higher than that in rural women in different times (all P<0.05). The spatial scan analysis found that eastern Shandong Province was found to be a sustained high-risk area for death, and other high-risk areas were transferred from north to southwest of Shandong between 1970 and 2013.

Clarke, M. A., et al. (2022). "Racial and Ethnic Differences in Hysterectomy-Corrected Uterine Corpus Cancer Mortality by Stage and Histologic Subtype." JAMA Oncol **8**(6): 895-903.

IMPORTANCE: Uterine cancer incidence has been increasing, particularly rates of aggressive, nonendometrioid subtypes, which are disproportionately higher among non-Hispanic Black women. The association of subtype-specific trends with uterine cancer mortality and with the role of tumor subtype and stage at diagnosis with racial disparities in uterine cancer deaths at the population-based level are not known. OBJECTIVE: To estimate histologic subtype- and stage-specific uterine cancer mortality rates by race and ethnicity, corrected for hysterectomy. DESIGN, SETTING, AND PARTICIPANTS: This cohort study used the US Surveillance, Epidemiology, and End Results-18 Incidence-Based Mortality database, representing approximately 26% of the US population and including deaths that occurred from 2000 to 2017. Hysterectomy correction was based on hysterectomy prevalence data from the Behavioral Risk Factor Surveillance System. Uncorrected and corrected rates associated with uterine corpus cancer cases diagnosed between 2000 and 2017 and uterine corpus cancer deaths occurring between 2010 and 2017 were age-adjusted to the 2000 US standard population and are expressed per 100 000 person-years, and annual percent changes in rates were calculated using log-linear regression. Data analysis was performed from March 10 to May 20, 2021. EXPOSURES: Tumor histologic subtype, cancer stage at diagnosis, and race and ethnicity. RESULTS: Among 208 587 women diagnosed with uterine cancer during 2000-2017 (15 983 [7.7%] were Asian; 20 302 [9.7%] Black; 23 096 [11.1%] Hispanic; and 149 206 [71.5%] White individuals), there were 16 797 uterine cancer deaths between 2010 and 2017, corresponding to a hysterectomy-corrected mortality rate of 15.7 per 100 000 person-years. Hysterectomy-corrected rates were highest among Black women, overall, by histologic subtype and stage at diagnosis. Among all women, uterine corpus cancer mortality rates increased significantly by 1.8% (95% CI, 1.5%-2.9%) per year from 2010 to 2017, as did rates of nonendometrioid carcinomas (2.7%; 95% CI, 1.8%-3.6%), with increases occurring in Asian (3.4%; 95% CI, 0.3%-6.6%), Black (3.5%; 95% CI, 2.2%-4.9%), Hispanic (6.7%; 95% CI, 1.9%-11.8%), and White women (1.5%; 95% CI, 0.6%-2.4%). In contrast, endometrioid carcinoma mortality rates remained stable. CONCLUSIONS AND RELEVANCE: The findings of this cohort study suggest a significant increase of nonendometrioid uterine carcinoma mortality rates, aligning with recent incidence trends. The factors associated with these trends are not well understood and require more investigation of possible mechanisms. Despite stable incidence rates, endometrioid cancer mortality rates have not decreased over the past decade at the population level, suggesting limited progress in treatment for these cancers. The substantial disparities in uterine corpus cancer mortality rates among non-Hispanic Black women cannot be fully explained by subtype distribution and stage at diagnosis.

Cleries, R., et al. (2022). "No Excess Mortality up to 10 Years in Early Stages of Breast Cancer in Women Adherent to Oral Endocrine Therapy: A Probabilistic Graphical Modeling Approach." Int J Environ Res Public Health **19**(6).

Breast cancer (BC) is globally the most frequent cancer in women. Adherence to endocrine therapy (ET) in hormone-receptor-positive BC patients is active and voluntary for the first five years after diagnosis. This study examines the impact of adherence to ET on 10-year excess mortality (EM) in patients diagnosed with Stages I to III BC (N = 2297). Since sample size is an issue for estimating age- and stage-specific survival indicators, we developed a method, ComSynSurData, for generating a large synthetic dataset (SynD) through probabilistic graphical modeling of the original cohort. We derived population-based survival indicators using a Bayesian relative survival model fitted to the SynD. Our modeling showed that hormone-receptor-positive BC patients diagnosed beyond 49 years of age at Stage I or beyond 59 years at Stage II do not have 10-year EM if they follow the prescribed ET regimen. This result calls for developing interventions to promote adherence to ET in patients with hormone receptor-positive BC and in turn improving cancer survival. The presented methodology here demonstrates the potential use of probabilistic graphical modeling for generating reliable synthetic datasets for validating population-based survival indicators when sample size is an issue.

Clift, A. K., et al. (2022). "Development and validation of clinical prediction models for breast cancer incidence and mortality: a protocol for a dual cohort study." BMJ Open **12**(3): e050828.

INTRODUCTION: Breast cancer is the most common cancer and the leading cause of cancer-related death in women worldwide. Risk prediction models may be useful to guide risk-reducing interventions (such as pharmacological agents) in women at increased risk or inform screening strategies for early detection methods such as screening. METHODS AND ANALYSIS: The study will use data for women aged 20-90 years between 2000 and 2020 from QResearch linked at the individual level to hospital episodes, cancer registry and death registry data. It will evaluate a set of modelling approaches to predict the risk of developing breast cancer within the next 10 years, the 'combined' risk of developing a breast cancer and then dying from it within 10 years, and the risk of breast cancer mortality within 10 years of diagnosis. Cox proportional hazards, competing risks, random survival forest, deep learning and XGBoost models will be explored. Models will be developed on the entire dataset, with 'apparent' performance reported, and internal-external cross-validation used to assess performance and geographical and temporal transportability (two 10-year time periods). Random effects meta-analysis will pool discrimination and calibration metric estimates from individual geographical units obtained from internal-external cross-validation. We will then externally validate the models in an independent dataset. Evaluation of performance heterogeneity will be conducted throughout, such as exploring performance across ethnic groups. ETHICS AND DISSEMINATION: Ethics approval was granted by the QResearch scientific committee (reference number REC 18/EM/0400: OX129). The results will be written up for submission to peer-reviewed journals.

Cohen, C. M., et al. (2022). "Racial and Ethnic Disparities in Cervical Cancer Incidence, Survival, and Mortality by Histologic Subtype." J Clin Oncol: JCO2201424.

PURPOSE: We conducted an integrated population-based analysis of histologic subtype-specific cervical cancer incidence, survival, and incidence-based mortality by race and ethnicity, with correction for hysterectomy prevalence. METHODS: Using the SEER 21 and 18 registries, we selected primary cases of malignant cervical cancer diagnosed among women >/= 15 years. We evaluated age-adjusted incidence rates among cases diagnosed between 2000 and 2018 (SEER21) and incidence-based mortality rates among deaths from 2005 to 2018 (SEER18), per 100,000 person-years. Rates were stratified by histologic subtype and race/ethnicity (incidence and mortality), and stage, age at diagnosis, and county-level measures of social determinants of health (incidence only). Incidence and mortality rates were corrected for hysterectomy using data from the Behavioral Risk Factor Surveillance System. We estimated 5-year relative survival by histologic subtype and stratified by stage at diagnosis. RESULTS: Incidence rates of cervical squamous cell carcinoma were highest in Black and Hispanic women, while incidence rates of cervical adenocarcinoma (ADC) were highest among Hispanic and White women, particularly for localized ADC. County-level income and education variables were inversely associated with squamous cell carcinoma incidence rates in all racial and ethnic groups but had less influence on ADC incidence rates. Black women had the highest overall mortality rates and lowest 5-year relative survival, irrespective of subtype and stage. Disparities in survival were particularly pronounced for Black women with regional and distant ADC, compared with other racial/ethnic groups. CONCLUSION: Although Black women are less likely to be diagnosed with ADC compared with all other racial/ethnic groups, they experience the highest mortality rates for this subtype, likely attributed to the poor survival observed for Black women with regional and distant ADC.

Collin, L. J., et al. (2022). "Time to Surgical Treatment and Facility Characteristics as Potential Drivers of Racial Disparities in Breast Cancer Mortality." Ann Surg Oncol **29**(8): 4728-4738.

BACKGROUND: Black women are more likely to die of breast cancer than White women. This study evaluated the contribution of time to primary surgical management and surgical facility characteristics to racial disparities in breast cancer mortality among both Black and White women. METHODS: The study identified 2224 Black and 3787 White women with a diagnosis with stages I to III breast cancer (2010-2014). Outcomes included time to surgical treatment (> 30 days from diagnosis) and breast cancer mortality. Odds ratios (ORs) and 95% confidence intervals (CIs) associating surgical facility characteristics with surgical delay were computed, and Cox proportional hazards regression was used to compute hazard ratios (HRs) and 95% CIs associating delay and facility characteristics with breast cancer mortality. RESULTS: Black women were two times more likely to have a surgical delay (OR, 2.15; 95% CI, 1.92-2.41) than White women. Racial disparity in surgical delay was least pronounced among women treated at a non-profit facility (OR, 1.95; 95% CI, 1.70-2.25). The estimated mortality rate for Black women was two times that for White women (HR, 2.00; 95%

CI, 1.83-2.46). Racial disparities in breast cancer mortality were least pronounced among women who experienced no surgical delay (HR, 1.81; 95% CI, 1.28-2.56), received surgery at a government facility (HR, 1.31; 95% CI, 0.76-2.27), or underwent treatment at a Commission on Cancer-accredited facility (HR, 1.82; 95% CI, 1.38-2.40). CONCLUSIONS: Black women were more likely to experience a surgical delay and breast cancer death. Persistent racial disparities in breast cancer mortality were observed across facility characteristics except for government facilities.

Collin, L. J., et al. (2020). "A balancing act: racial disparities in cardiovascular disease mortality among women diagnosed with breast cancer." Ann Cancer Epidemiol **4**.

BACKGROUND: The cardiotoxic effects of breast cancer therapies are well documented in clinical trials. However, clinical trials often underrepresent those at highest risk for cardiovascular disease (CVD)related outcomes and have limited generalizability to the larger breast cancer population. In addition, racial differences in treatment-associated CVD mortality have yet to be explored. In this study, we sought to quantify the relationship between breast cancer therapies and CVD mortality, and explore whether this effect differed between non-Hispanic black (NHB) and white (NHW) women. METHODS: Using data from the Georgia Cancer Registry, we identified women diagnosed with a first primary invasive breast cancer [2010-2014], residing in the metropolitan Atlanta area (n=3,580 NHB; n=4,923 NHW), and followed them for mortality through December 31, 2018. Exposures of interest included therapies with potential cardiotoxic effects including chemotherapy and hormone therapy, which are routinely collected by the GCR. Individual agents are not captured within the GCR, therefore trastuzumab was identified using natural language processing of textual descriptions. We used propensity score weighted Cox proportional hazards regression to calculate hazard ratios (HRs) and 95% confidence intervals (CIs) for the association between each treatment modality and CVD mortality among the overall cohort and by race. RESULTS: In the overall cohort, similar hazards of CVD mortality were found among women treated with chemotherapy (HR =1.10, 95% CI: 0.62, 1.96) and hormone therapy (HR =0.94, 95% CI: 0.59, 1.50), compared to women who did not receive the respective treatments. In contrast, women treated with trastuzumab had a higher hazard of CVD mortality compared to women not treated with trastuzumab (HR =2.05, 95% CI: 0.76, 5.52). In race-specific models, hormone therapy was associated with a higher hazard of CVD mortality among NHB women (HR =2.18, 95% CI: 0.78, 6.12), but not NHW women (HR =0.66, 95% CI: 0.39, 1.13). Similar, albeit attenuated, associations were found for chemotherapy. We were unable to investigate race-specific effects of trastuzumab due to low prevalence and insufficient number of events. CONCLUSIONS: In our study, we observed more pronounced associations of chemotherapy and hormone therapy with CVD mortality among NHB women, for whom we know have greater CVD-related comorbidities at breast cancer diagnosis. Patients may benefit from treatment plans that find a balance between curative breast cancer treatment and prevention of CVD-related events and mortality. CVD-related outcomes may be most relevant for women with hormone receptor positive disease due to shared risk factors (e.g., obesity, tobacco use, physical activity) and longer survival.

Collin, L. J., et al. (2022). "Preexisting stress-related diagnoses and mortality: A Danish cancer cohort study." Cancer **128**(6): 1312-1320.

BACKGROUND: This study evaluated the association between preexisting stress-related diagnoses and mortality in a Danish population-based cancer cohort. METHODS: This study included Danish patients with cancer diagnosed in 1995-2011 who had a stress-related diagnosis before their cancer diagnosis. Cancer patients without a prior stress-related diagnosis were matched 5:1 to the stress disorder cohort by cancer site, age group, calendar period, and sex. The 5-year cumulative incidence of cancer-specific and all-cause mortality was computed by stress-related diagnosis category. Hazard ratios and 95% confidence intervals (CIs) associating stress-related diagnoses with mortality were computed by follow-up time, stress-related diagnosis category, stage, comorbidity status, and cancer type. RESULTS: This study identified 4437 cancer patients with a preexisting stress-related diagnosis and 22,060 matched cancer cohort members. The 5-year cumulative risk of cancer-specific mortality was 33% (95% CI, 32%-35%) for those with a preexisting stress-related diagnosis and 29% (95% CI, 28%-29%) for those without a prior stress-related diagnosis. Cancer patients with a preexisting stress-related diagnosis had a 1.3 times higher cancer-specific mortality rate than the comparison cohort members (95% CI, 1.2-1.5). This increase persisted across categories of stress-related diagnosis. The association varied by stage and cancer type, with more pronounced associations found among those with a late stage at diagnosis and hematological malignancies. CONCLUSIONS: Cancer patients with preexisting stress-related diagnoses had increased rates of cancer-specific and all-cause mortality. The results suggest that psychiatric comorbidities may be an important consideration for cancer prognosis, and cancer

treatment informed by a patient's history may improve outcomes.

Collin, L. J., et al. (2021). "Receipt of Guideline-Concordant Care Does Not Explain Breast Cancer Mortality Disparities by Race in Metropolitan Atlanta." J Natl Compr Canc Netw.

BACKGROUND: Racial disparities in breast cancer mortality in the United States are well documented. Non-Hispanic Black (NHB) women are more likely to die of their disease than their non-Hispanic White (NHW) counterparts. The disparity is most pronounced among women diagnosed with prognostically favorable tumors, which may result in part from variations in their receipt of guideline care. In this study, we sought to estimate the effect of guideline-concordant care (GCC) on prognosis, and to evaluate whether receipt of GCC modified racial disparities in breast cancer mortality. PATIENTS AND METHODS: Using the Georgia Cancer Registry, we identified 2,784 NHB and 4,262 NHW women diagnosed with a stage I-III first primary breast cancer in the metropolitan Atlanta area, Georgia, between 2010 and 2014. Women were included if they received surgery and information on their breast tumor characteristics was available; all others were excluded. Receipt of recommended therapies (chemotherapy, radiotherapy, endocrine therapy, and anti-HER2 therapy) as indicated was considered GCC. We used Cox proportional hazards models to estimate the impact of receiving GCC on breast cancer mortality overall and by race, with multivariable adjusted hazard ratios (HRs). RESULTS: We found that NHB and NHW women were almost equally likely to receive GCC (65% vs 63%, respectively). Failure to receive GCC was associated with an increase in the hazard of breast cancer mortality (HR, 1.74; 95% CI, 1.37-2.20). However, racial disparities in breast cancer mortality persisted despite whether GCC was received (HRGCC: 2.17 [95% CI, 1.61-2.92]; HRnon-GCC: 1.81 [95% CI, 1.28-2.91]). CONCLUSIONS: Although receipt of GCC is important for breast cancer outcomes, racial disparities in breast cancer mortality did not diminish with receipt of GCC; differences in mortality between Black and White patients persisted across the strata of GCC.

Colonna, M., et al. (2022). "Health status of prevalent cancer cases as measured by mortality dynamics (cancer vs. noncancer): Application to five major cancers sites." Cancer **128**(20): 3663-3673.

BACKGROUND: Cancer prevalence is heterogeneous because it includes individuals who are undergoing initial treatment and those who are in remission, experiencing relapse, or cured. The proposed statistical approach describes the health status of this group by estimating the probabilities of death among prevalent cases. The application concerns colorectal, lung, breast, and prostate cancers and melanoma in France in 2017. METHODS: Excess mortality was used to estimate the probabilities of death from cancer and other causes. RESULTS: For the studied cancers, most deaths from cancer occurred during the first 5 years after diagnosis. The probability of death from cancer decreased with increasing time since diagnosis except for breast cancer, for which it remained relatively stable. The time beyond which the probability of death from cancer became lower than that from other causes depended on age and cancer site: for colorectal cancer, it was 6 years after diagnosis for women (7 years for men) aged 75-84 and 20 years for women (18 years for men) aged 45-54 years, whereas cancer was the major cause of death for women younger than 75 years whatever the time since diagnosis for breast and for all patients younger than 75 years for lung cancer. In contrast, deaths from other causes were more frequent in all the patients older than 75 years. Apart from breast cancer in women younger than 55 years and lung cancer in women older than 55 years and men older than 65 years, the probability of death from cancer among prevalent cases fell below 1%, with varying times since diagnosis. CONCLUSIONS: The authors' approach can be used to better describe the burden of cancer by estimating outcomes in prevalent cases.

de Azambuja, E., et al. (2020). "Impact of solid cancer on in-hospital mortality overall and among different subgroups of patients with COVID-19: a nationwide, population-based analysis." ESMO Open **5**(5): e000947.

BACKGROUND: Cancer seems to have an independent adverse prognostic effect on COVID-19-related mortality, but uncertainty exists regarding its effect across different patient subgroups. We report a population-based analysis of patients hospitalised with COVID-19 with prior or current solid cancer versus those without cancer. METHODS: We analysed data of adult patients registered until 24 May 2020 in the Belgian nationwide database of Sciensano. The primary objective was in-hospital mortality within 30 days of COVID-19 diagnosis among patients with solid cancer versus patients without cancer. Severe event occurrence, a composite of intensive care unit admission, invasive ventilation and/or death, was a secondary objective. These endpoints were analysed across different patient subgroups. Multivariable logistic regression models were used to analyse the association between cancer and clinical characteristics (baseline analysis) and the effect of cancer on in-hospital mortality and on severe event occurrence, adjusting for clinical characteristics (in-hospital

analysis). RESULTS: A total of 13 594 patients (of whom 1187 with solid cancer (8.7%)) were evaluable for the baseline analysis and 10 486 (892 with solid cancer (8.5%)) for the in-hospital analysis. Patients with cancer were older and presented with less symptoms/signs and lung imaging alterations. The 30-day in-hospital mortality was higher in patients with solid cancer compared with patients without cancer (31.7% vs 20.0%, respectively; adjusted OR (aOR) 1.34; 95% CI 1.13 to 1.58). The aOR was 3.84 (95% CI 1.94 to 7.59) among younger patients (<60 years) and 2.27 (95% CI 1.41 to 3.64) among patients without other comorbidities. Severe event occurrence was similar in both groups (36.7% vs 28.8%; aOR 1.10; 95% CI 0.95 to 1.29). CONCLUSIONS: This population-based analysis demonstrates that solid cancer is an independent adverse prognostic factor for in-hospital mortality among patients with COVID-19. This adverse effect was more pronounced among younger patients and those without other comorbidities. Patients with solid cancer should be prioritised in vaccination campaigns and in tailored containment measurements.

de Boer, A. Z., et al. (2021). "Prediction of Other-Cause Mortality in Older Patients with Breast Cancer Using Comorbidity." Cancers (Basel) **13**(7).

Background: Individualized treatment in older patients with breast cancer can be improved by including comorbidity and other-cause mortality in prediction tools, as the other-cause mortality risk strongly increases with age. However, no optimal comorbidity score is established for this purpose. Therefore, this study aimed to compare the predictive value of the Charlson comorbidity index for other-cause mortality with the use of a simple comorbidity count and to assess the impact of frequently occurring comorbidities. Methods: Surgically treated patients with stages I-III breast cancer aged >/=70 years diagnosed between 2003 and 2009 were selected from the Netherlands Cancer Registry. Competing risk analysis was performed to associate 5-year other-cause mortality with the Charlson index, comorbidity count, and specific comorbidities. Discrimination and calibration were assessed. Results: Overall, 7511 patients were included. Twenty-nine percent had no comorbidities, and 59% had a Charlson score of 0. After five years, in 1974, patients had died (26%), of which 1450 patients without a distant recurrence (19%). Besides comorbidities included in the Charlson index, the psychiatric disease was strongly associated with other-cause mortality (sHR 2.44 (95%-CI 1.70-3.50)). The c-statistics of the Charlson index and comorbidity count were similar (0.65 (95%-CI 0.64-0.65) and 0.64 (95%-CI 0.64-0.65)). Conclusions: The predictive value of the Charlson index for 5-year other-cause mortality was similar to using comorbidity count. As it is easier to use in clinical practice, our findings indicate that comorbidity count can aid in improving individualizing treatment in older patients with breast cancer. Future studies should elicit whether geriatric parameters could improve prediction.

de Boer, A. Z., et al. (2022). "Breast cancer mortality of older patients with and without recurrence analysed by novel multi-state models." Eur J Cancer **174**: 212-220.

INTRODUCTION: In older patients with breast cancer, the risk of dying from other causes than breast cancer strongly increases after the age of 70. The aim of this study was to assess contributions of breast cancer mortality versus other-cause mortality after locoregional or distant recurrence in a population-based cohort of older patients analysed by multi-state models. METHODS: Surgically treated patients >/=70 years diagnosed with stage I-III breast cancer in 2003-2009 were selected from the Netherlands Cancer Registry. A novel multi-state model with locoregional and distant recurrence that incorporates relative survival was fitted. Other-cause and breast cancer mortality were indicated as population and excess mortality. RESULTS: Overall, 18,419 patients were included. Ten-year cumulative incidences of locoregional and distant recurrence were 2.8% (95%CI 2.6-3.1%) and 12.5% (95%CI 11.9-13.1%). Other-cause mortality increased from 23.9% (95%CI 23.7-24.2%) in patients 70-74 years to 73.8% (95%CI 72.2-75.4%) in those >/=80 years. Ten-year probabilities of locoregional or distant recurrence with subsequent breast cancer death were 0.4-1.3% and 10.2-14.6%, respectively. For patients with a distant recurrence in the first two years after diagnosis, breast cancer death probabilities were 95.3% (95%CI 94.2-96.4%), 93.1% (95%CI 91.6-94.6%), and 88.6% (95%CI 86.5-90.8%) in patients 70-74, 75-79, and >/=80 years. CONCLUSION: In older patients without recurrence, prognosis is driven by other-cause mortality. Although locoregional recurrence is a predictor for worse outcome, given its low incidence it contributes little to breast cancer mortality after diagnosis. For patients who develop a distant recurrence, breast cancer remains the dominant cause of death, even at old age.

De Giorgi, A., et al. (2021). "Do Sex-Related Differences of Comorbidity Burden and/or In-Hospital Mortality Exist in Cancer Patients? A Retrospective Study in an Internal Medicine Setting." Life (Basel) **11**(3).

Cancer represents important comorbidity, and data on outcomes are usually derived from selected oncologic units. Our aim was to evaluate possible sex-related differences and factors associated with in-

hospital mortality (IHM) in a consecutive cohort of elderly patients with cancer admitted to internal medicine. We included all patients admitted to our department with a diagnosis of cancer during 2018. Based on the International Classification of Diseases, 9th Revision, Clinical Modification, demography, comorbidity burden, and diagnostic procedures were evaluated, with IHM as our outcome. We evaluated 955 subjects with cancer (23.9% of total hospital admissions), 42.9% were males, and the mean age was 76.4 +/- 11.4 years. Metastatic cancer was diagnosed in 18.2%. The deceased group had a higher modified Elixhauser Index (17.6 +/- 7.7 vs. 14 +/- 7.3, $p < 0.001$), prevalence of cachexia (17.9% vs. 7.2%, $p < 0.001$), and presence of metastasis (27.8% vs. 16.3%, $p = 0.001$) than survivors. Females had a higher age (77.4 +/- 11.4 vs. 75.5 +/- 11.4, $p = 0.013$), and lower comorbidity (10.2 +/- 5.9 vs. 12.0 +/- 5.6, $p < 0.001$) than males. IHM was not significantly different among sex groups, but it was independently associated with cachexia and metastasis only in women. Comorbidities are highly prevalent in patients with cancer admitted to the internal medicine setting and are associated with an increased risk of all-cause mortality, especially in female elderly patients with advanced disease.

de Haan-Du, J., et al. (2022). "The value of glycemic control prior to cancer diagnosis on all-cause mortality among patients with type 2 diabetes in Dutch primary care." Cancer Epidemiol Biomarkers Prev.

BACKGROUND: Poor glycemic control prior to cancer diagnosis for patients with pre-existing type 2 diabetes (T2DM) may predict a worse cancer diagnosis. We investigated the association between pre-diagnosis glycemic control and all-cause mortality in patients with T2DM who develop cancer. METHODS: This prospective cohort study linked data from three sources covering 1989-2019: a T2DM benchmarking database, the Netherlands Cancer Registry, and the Personal Records Database. We included patients with T2DM and incident primary breast, colorectal, or prostate cancer (stage 0-III), with target glycemic control defined according to Dutch guidelines. Analysis involved estimating the association between glycemic control and all-cause mortality with Cox proportional hazard models, accounting for individual expected survival relative to the general population and relevant disease (e.g., diabetes duration and medications) and individual (e.g., age and gender) characteristics. RESULTS: Of the 71,648 linked cases, 620 had breast cancer, 774 had colorectal cancer, and 438 had prostate cancer, with follow-up data available for 6.4 (4.2-8.4), 5.6 (2.7-7.6), and 6.3 (4.5-8.2) years, respectively. Compared to patients with pre-diagnosis glycemic control at target, the hazard ratios and 95% confidence intervals for mortality among those with pre-diagnosis glycemic control not at target were 1.40 (1.00-1.96) for breast cancer, 1.45 (1.12-1.88) for colorectal cancer, and 1.39 (0.98-1.98) for prostate cancer. CONCLUSIONS: Among patients with T2DM in Dutch primary care, poor glycemic control before diagnosis with breast and colorectal cancer can increase mortality compared to good control. IMPACT: Glycemic control prior to cancer diagnosis is of prognostic value.

de la Cour, C. D., et al. (2022). "Non-aspirin NSAIDs and head and neck cancer mortality in a Danish nationwide cohort study." Cancer Epidemiol **77**: 102121.

BACKGROUND: Evidence suggests that non-aspirin non-steroidal anti-inflammatory drugs (NSAIDs) have antineoplastic properties of potential importance for survival of head and neck cancer. METHODS: We conducted a nationwide cohort study including all individuals with primary head and neck squamous cell carcinoma in Denmark during 2000-2016 at age 30-84 years, with no history of cancer (except non-melanoma skin cancer), and alive at 1 year after diagnosis. Nationwide registries provided information on drug use, causes of death and potential confounders, and additional clinical information was obtained for a subpopulation. We conducted Cox proportional hazards regression to estimate multivariable-adjusted hazard ratios (HRs) with 95% confidence intervals (CIs) for the association between post-diagnosis non-aspirin NSAID use (defined as >/=1 filled prescription within first year after diagnosis) and cancer-specific mortality. RESULTS: Among 10,770 head and neck cancer 1-year survivors, the HR for cancer-specific mortality with non-aspirin NSAID use was 1.68 at 1 year after diagnosis, but declined and stabilized around 1.15 (95% CI 1.02-1.29) at 2 years after diagnosis. Among 2-year survivors, the HRs for cancer-specific mortality with non-aspirin NSAID use remained slightly increased in analyses stratified by age, sex, stage, and pre-diagnosis non-aspirin NSAID use. Similar results were seen in the subpopulation (n = 1029) with additional clinical information, and among 5-year survivors with additional non-aspirin NSAID exposure assessment. CONCLUSION: In this nationwide cohort of patients with head and neck cancer, use of non-aspirin NSAIDs was associated with a slightly increased mortality risk, warranting further evaluation.

de la Cour, C. D., et al. (2022). "Low-dose aspirin use and mortality risk in patients with head and neck cancer: A nationwide cohort study of 10 770 patients." Int J Cancer **150**(6): 969-975.

Several recent observational studies have linked low-dose aspirin use to improved survival in

patients with head and neck cancer. However, studies of patterns of aspirin use and risk of cancer-specific mortality are lacking. This nationwide cohort study included all patients in the Danish Cancer Registry with a primary diagnosis of head and neck squamous cell cancer (HNSCC) during 2000 to 2016, aged 30 to 84 years, without prior cancer (except nonmelanoma skin cancer) and alive 1 year after diagnosis. Nationwide registries provided information on filled prescriptions, mortality and potential confounding factors. For a subpopulation, a clinical database provided additional information, including human papillomavirus (HPV) tumor status. We used Cox proportional hazards regression models to estimate adjusted hazard ratios (HRs) with 95% confidence intervals (CIs) for the association between postdiagnostic low-dose aspirin use (>/=1 prescription within first year after diagnosis) and risk of cancer-specific mortality. We identified 10 770 patients with HNSCC during a median follow-up of 3.9 years. Of these, 1799 (16.7%) were low-dose aspirin users. Postdiagnostic use of low-dose aspirin was associated with a HR of 0.97 (95% CI 0.82-1.15) for cancer-specific mortality. Similar neutral associations were found according to patterns of aspirin use. No apparent trends emerged according to age, sex, topography or stage. A tendency towards a decreased cancer-specific mortality risk with low-dose aspirin use was observed among HPV-positive patients; however, the statistical precision was low. In conclusion, we did not observe an association between postdiagnostic low-dose aspirin use and cancer-specific mortality in a nationwide cohort of patients with HNSCC.

De la Cruz Ku, G., et al. (2022). "Hepatocellular carcinoma as predominant cancer subgroup accounting for sex differences in post-hepatectomy liver failure, morbidity and mortality." HPB (Oxford) **24**(9): 1453-1463.

BACKGROUND: Experimental evidence suggests sex dependent differences in liver regeneration. Limited evidence is available examining sex differences in post-hepatectomy liver failure (PHLF) and postoperative outcomes. Our aim was to assess the influence of sex on the outcomes after liver resection. METHODS: The hepatectomy targeted National Surgical Quality Improvement Program (NSQIP) database was assessed for associations between sex and outcomes. RESULTS: A total of 13,401 patients underwent elective hepatic resection between 2014-2017. PHLF was highest among male patients with hepatocellular carcinoma (HCC) (OR = 2.81,95%CI:1.40-5.62). Male sex was independently associated with increased PHLF (OR = 1.47,95%CI:1.15-1.88), major complications (OR = 1.25,95%CI:1.08-1.45), mortality (OR = 1.61,95%CI:1.03-2.50), and if only major resections were assessed (OR = 1.38,95%CI:1.03-1.84). Diagnosis specific subgroup analyses revealed that effects of sex were predominantly HCC associated. CONCLUSIONS: This is the largest series investigating the effects of gender on outcomes after hepatic resection. We documented that women undergoing liver resection have significantly lower risk of PHLF. This difference seemed influenced by the striking increase of PHLF in male HCC patients. These hypothesis suggest that sex might play a role in preoperative risk stratification.

de la Cruz-Ku, G., et al. (2020). "Neutrophil-to-lymphocyte ratio predicts early mortality in females with metastatic triple-negative breast cancer." PLoS One **15**(12): e0243447.

BACKGROUND: The aim of this study was to determine the utility of the neutrophil-to-lymphocyte ratio (NLR) as a biomarker for predicting early-mortality (<2 years) among females with metastatic triple-negative breast cancer (mTNBC). METHODS: We reviewed 118 medical records of females with mTNBC. The cut-off value for the NLR (<2.5 and >/=2.5) was determined with receiver operating characteristic curves (area under the curve: 0.73; 95% CI: 0.62-0.85). Survival curves were estimated using the Kaplan-Meier method and compared with the Log-rank test. Multivariate Cox regression was used to identify the risk of mortality at two years. Moreover, we performed sensitivity analyses with different cut-off values and a subgroup analysis in females that only received chemotherapy. RESULTS: The median follow-up was 24 months. Females with NLR >/=2.5 had a poor overall survival compared to females with NLR <2.5 (6% vs. 28%, p<0.001) at two years. This outcome remained when we stratified for females that only received chemotherapy (8% vs. 36%, p = 0.001). Multivariate analyses identified NLR >/=2.5 as a poor prognostic risk factor for mortality in the entire population (HR: 2.12, 95% CI: 1.32-3.39) and among females that received chemotherapy (HR: 2.68, 95% CI: 1.46-4.92). CONCLUSION: The NLR is an accessible and reliable biomarker that predicts early mortality among females with mTNBC. Our results suggest that females with high NLR values have poor prognosis despite receiving standard chemotherapy. Health providers should evaluate the possibility to enroll these patients in novel immunotherapy trials.

de Los, A. J. P. P., et al. (2022). "Influence of type 2 diabetes mellitus on mortality in women with breast cancer: A matched case-control study." J Diabetes Complications **36**(8): 108249.

AIMS: The study assessed the association between the presence of type2 diabetes mellitus

(T2DM) and mortality in women with breast cancer (BC). METHODS: A matched pair case-control study was conducted at the State Cancer Center, which is located in Xalapa, Veracruz, Mexico. It was matched by age (+/-3 years) within a cohort of 1442 patients with BC. Descriptive statistics were performed. Analysis through paired odds ratio (OR and multivariate analyses were used to calculate the association between BC mortality and the variables studied. RESULTS: 166 cases and 166 controls with confirmed diagnosis of BC were studied, with a mean age of 52.9 +/- 11.9 years. The T2DM was associated with an increased mortality of women with BC (OR = 1.75 95 %CI 1.06-2.89). Similarly, metastasis (OR = 14.17 95 %CI 6.19-32.342), advanced clinical stage (OR = 3.04 95 %CI 1.45 - 6.38), and the molecular subtypes Her2 (OR = 2.0 95 %CI 1.02-3.92), and triple negative (OR = 3.54 95 %CI 1.72-7.32). There was no difference in mean glucose between cases and controls (208.9 +/- 132 vs 194.4 +/- 90.4 mg/dL, respectively). CONCLUSION: T2DM was found to be a relevant risk factor for BC mortality in this Mexican population. Thus, it is important to consider the presence and evolution of DM in the prevention programs, diagnostic algorithms and treatments established for BC.

de Morais Fernandes, F. C. G., et al. (2021). "Incidence and mortality from thyroid cancer in Latin America." Trop Med Int Health **26**(7): 800-809.

OBJECTIVE: To describe trends in thyroid cancer incidence and mortality in Latin America. METHODS: Ecological study of time series, with incidence data from the International Agency for Research on Cancer for the 1990-2012 period and mortality data of 16 countries obtained from WHO for the 1995-2013 period. The trends of incidence rates were analysed by the Joinpoint regression. Average annual percentage change and 95% confidence intervals were calculated for incidence and mortality. RESULTS: Incidence and mortality from thyroid cancer in Latin America were higher in women, with the highest incidence rate in women in Quito (Ecuador) aged 40-59 years: 42.2 new cases per 100 000 inhabitants, and mortality of 4.8/100 000 in women over 60. Thyroid cancer incidence increased in women of all age groups in Cali (Colombia), Costa Rica and Quito (Ecuador); and in men in Costa Rica. Incidence rates were stable above the age of 60 years in Cali, in Goiania (Brazil), Quito (Ecuador) and Valdivia (Chile) in men, and in women in Goiania (Brazil) and Valdivia (Chile). Mortality among women increased in Ecuador (AAPC = 3.28 CI 95% 1.36; 5.24), Guatemala (AAPC = 6.14 CI 95% 2.81; 9.58) and Mexico (AAPC = 0.67 CI 95% 0.16; 1.18). CONCLUSIONS: Thyroid cancer incidence in Latin America is high and rising in women. Mortality remains stable in most countries of Latin America.

de Nes, L. C. F., et al. (2022). "Postoperative mortality risk assessment in colorectal cancer: development and validation of a clinical prediction model using data from the Dutch ColoRectal Audit." BJS Open **6**(2).

BACKGROUND: As the outcome of modern colorectal cancer (CRC) surgery has significantly improved over the years, however, renewed and adequate risk stratification for mortality is important to identify high-risk patients. This population-based study was conducted to analyse postoperative outcomes in patients with CRC and to create a risk model for 30-day mortality. METHODS: Data from the Dutch Colorectal Audit were used to assess differences in postoperative outcomes (30-day mortality, hospital stay, blood transfusion, postoperative complications) in patients with CRC treated from 2009 to 2017. Time trends were analysed. Clinical variables were retrieved (including stage, age, sex, BMI, ASA grade, tumour location, timing, surgical approach) and a prediction model with multivariable regression was computed for 30-day mortality using data from 2009 to 2014. The predictive performance of the model was tested among a validation cohort of patients treated between 2015 and 2017. RESULTS: The prediction model was obtained using data from 51 484 patients and the validation cohort consisted of 32 926 patients. Trends of decreased length of postoperative hospital stay and blood transfusions were found over the years. In stage I-III, postoperative complications declined from 34.3 per cent to 29.0 per cent ($P < 0.001$) over time, whereas in stage IV complications increased from 35.6 per cent to 39.5 per cent ($P = 0.010$). Mortality decreased in stage I-III from 3.0 per cent to 1.4 per cent ($P < 0.001$) and in stage IV from 7.6 per cent to 2.9 per cent ($P < 0.001$). Eight factors, including stage, age, sex, BMI, ASA grade, tumour location, timing, and surgical approach were included in a 30-day mortality prediction model. The results on the validation cohort documented a concordance C statistic of 0.82 (95 per cent c.i. 0.80 to 0.83) for the prediction model, indicating good discriminative ability. CONCLUSION: Postoperative outcome improved in all stages of CRC surgery in the Netherlands. The developed model accurately predicts postoperative mortality risk and is clinically valuable for decision-making.

de Oliveira, G. S., et al. (2022). "Trends in cervical cancer mortality rate in women aged 20 years and older in Brazil from 2005 to 2019." Women Health **62**(6): 532-543.

The objective of this study was to analyze the trend of the age standardized mortality rate (ASMR) for cervical cancer in Brazil between 2005 and 2019

and investigate its association with the Socio-demographic Index (SDI), an indicator of development status strongly correlated with health outcomes. We conducted an ecological time-series study using data from the Mortality Information System of the Ministry of Health. Trend analyses were performed using Prais-Winsten regression. The association between the SDI and ASMR was evaluated using simple linear regression. Between 2005 and 2019, 105,472 deaths from cervical cancer were recorded. The ASMR was 10.18 deaths/100,000 women. The North region presented the highest magnitude (20.23 deaths/100,000 women) and the Southeast region the lowest (7.83 deaths/100,000 women). We observed a decreasing trend of the ASMR for cervical cancer in the country. The Northeast, Central-West and Southeast regions showed a decreasing trend; South stationary trend and the North region showed an increasing trend. Most of the states showed a stationary or decreasing trend. It was found that the SDI was inversely associated with the ASMR and Annual Percent Change (APC). In conclusion, we observed a decreasing trend of ASMR for cervical cancer and inverse association with SDI in Brazil.

De Rocchi, D., et al. (2021). "Mortality temporal trends and cancer incidence profiles of residents in the petrochemical industrially contaminated town of Gela (Sicily, Italy)." Ann Ist Super Sanita **57**(2): 174-182.

OBJECTIVE: In 2000, a vast area in Gela (Sicily, Italy) was defined as a national priority contaminated site due to pollution from a petrochemical complex. This study is aimed at addressing the influence of the petrochemical complex on the health profile of residents in Gela. METHODS: Trend analysis by gender was performed for mortality for all diseases and malignant cancers, in the period 1980-2014 for residents in the municipality of Gela, by directly standardized rates and Joinpoint regressions, using, as a reference population, people resident in the Sicily region. SMRs were computed for 5-year periods in the same timespan. Since the beginning of the period analyzed, the share of population of Gela represents 1.5% of total residents in Sicily. Cancer incidence was analyzed for the period 2007-2012 applying a hierarchical Bayesian model to estimate Standardized Incidence Ratios (SIR). Ranks of these ratios were computed to highlight the most incident diseases affecting the population. Malignant neoplasms of lung, stomach and colon were selected because of a priori interest, as they are associated, in etiological terms, with the main contaminants found in the area. Malignant neoplasms of liver, pancreas and larynx were selected as "control diseases" since they share the same main risk factors (smoke and alcohol consumption) of neoplasms of a priori interest, but are not associated with the priority index contaminants identified in Gela. RESULTS: Mortality rates for all causes combined in both genders in Gela decreased over time, but they were higher than those of the whole Sicilian population. The trend of mortality rates due to all malignant cancers increased in men, especially from 1980 to 1987. This result was confirmed by the Joinpoint regression (annual percentage change (APC) 9.8). SMRs analysis showed significant excesses in mortality due to all diseases for both genders compared to the reference population. Other excesses were observed for mortality due to malignant cancers in men and for circulatory diseases in women. The trend for cancers in women in Gela increased from the mid-nineties but less than in men. SIR estimates were higher than 1 for all the diseases analyzed and in both sexes, and their ranks highlighted that cancer sites of a priori interest hold higher positions than "control diseases", although credibility intervals overlapped. CONCLUSIONS: Results highlight that the health profile of residents in Gela is worse than the one of the reference population. Moreover, cancer incidence is in excess in all the sites analyzed and mortality due to all cancers combined has a trend compatible with a cumulative impact due to petrochemical contamination.

Defossez, G., et al. (2021). "Cancer incidence and mortality trends in France over 1990-2018 for solid tumors: the sex gap is narrowing." BMC Cancer **21**(1): 726.

OBJECTIVE: To analyze trends in cancer incidence and mortality (France, 1990-2018), with a focus on men-women disparities. METHODS: Incidence data stemmed from cancer registries (FRANCIM) and mortality data from national statistics (CepiDc). Incidence and mortality rates were modelled using bidimensional penalized splines of age and year (at diagnosis and at death, respectively). Trends in age-standardized rates were summarized by the average annual percent changes (AAPC) for all-cancers combined, 19 solid tumors, and 8 subsites. Sex gaps were indicated using male-to-female rate ratios (relative difference) and male-to-female rate differences (absolute difference) in 1990 and 2018, for incidence and mortality, respectively. RESULTS: For all-cancers, the sex gap narrowed over 1990-2018 in incidence (1.6 to 1.2) and mortality (2.3 to 1.7). The largest decreases of the male-to-female incidence rate ratio were for cancers of the lung (9.5 to 2.2), lip - oral cavity - pharynx (10.9 to 3.1), esophagus (12.6 to 4.5) and larynx (17.1 to 7.1). Mixed trends emerged in lung and oesophageal cancers, probably explained by differing risk factors for the two main histological subtypes. Sex incidence gaps narrowed due to increasing trends in men and women for skin melanoma (0.7 to 1, due to initially higher rates in

women), cancers of the liver (7.4 to 4.4) and pancreas (2.0 to 1.4). Sex incidence gaps narrowed for colon-rectum (1.7 to 1.4), urinary bladder (6.9 to 6.1) and stomach (2.7 to 2.4) driven by decreasing trends among men. Other cancers showed similar increasing incidence trends in both sexes leading to stable sex gaps: thyroid gland (0.3 to 0.3), kidney (2.2 to 2.4) and central nervous system (1.4 to 1.5). CONCLUSION: In France in 2018, while men still had higher risks of developing or dying from most cancers, the sex gap was narrowing. Efforts should focus on avoiding risk factors (e.g., smoking) and developing etiological studies to understand currently unexplained increasing trends.

Degeling, K., et al. (2021). "An inverse stage-shift model to estimate the excess mortality and health economic impact of delayed access to cancer services due to the COVID-19 pandemic." Asia Pac J Clin Oncol **17**(4): 359-367.

AIM: Decreased cancer incidence and reported changes to clinical management indicate that the COVID-19 pandemic has delayed cancer diagnosis and treatment. This study aimed to develop and apply a flexible model to estimate the impact of delayed diagnosis and treatment on survival outcomes and healthcare costs based on a shift in the disease stage at treatment initiation. METHODS: A model was developed and made publicly available to estimate population-level health economic outcomes by extrapolating and weighing stage-specific outcomes by the distribution of stages at treatment initiation. It was applied to estimate the impact of 3- and 6-month delays based on Australian data for stage I breast cancer, colorectal cancer, and lung cancer patients, and for T1 melanoma. Two approaches were explored to estimate stage shifts following a delay: (a) based on the relation between time to treatment initiation and overall survival (breast, colorectal, and lung cancer), and (b) based on the tumor growth rate (melanoma). RESULTS: Using a conservative once-off 3-month delay and considering only shifts from stage I/T1 to stage II/T2, 88 excess deaths and $12 million excess healthcare costs were predicted in Australia over 5 years for all patients diagnosed in 2020. For a 6-month delay, excess mortality and healthcare costs were 349 deaths and $46 million over 5 years. CONCLUSIONS: The health and economic impacts of delays in treatment initiation cause an imminent policy concern. More accurate individual patient data on shifts in stage of disease during and after the COVID-19 pandemic are critical for further analyses.

Degett, T. H., et al. (2021). "Prediction of the postoperative 90-day mortality after acute colorectal cancer surgery: development and temporal validation of the ACORCA model." Int J Colorectal Dis **36**(9): 1873-1883.

PURPOSE: The aim of this study was to develop and validate a model to predict 90-day mortality after acute colorectal cancer surgery. METHODS: The model was developed in all patients undergoing acute colorectal cancer surgery in 2014-2016 and validated in a patient group operated in 2017 in Denmark. The outcome was 90-day mortality. Tested predictor variables were age, sex, performance status, BMI, smoking, alcohol, education level, cohabitation status, tumour localization and primary surgical procedure. Variables were selected according to the smallest Akaike information criterion. The model was shrunken by bootstrapping. Discrimination was evaluated with a receiver operated characteristic curve, calibration with a calibration slope and the accuracy with a Brier score. RESULTS: A total of 1450 patients were included for development of the model and 451 patients for validation. The 90-day mortality rate was 19% and 20%, respectively. Age, performance status, alcohol, smoking and primary surgical procedure were the final variables included in the model. Discrimination (AUC = 0.79), calibration (slope = 1.04, intercept = 0.04) and accuracy (brier score = 0.13) were good in the developed model. In the temporal validation, discrimination (AUC = 0.80) and accuracy (brier score = 0.13) were good, and calibration was acceptable (slope = 1.19, intercept = 0.52). CONCLUSION: We developed prediction model for 90-day mortality after acute colorectal cancer surgery that may be a promising tool for surgeons to identify patients at risk of postoperative mortality.

Del Pozo Cruz, B., et al. (2022). "Prospective Associations of Daily Step Counts and Intensity With Cancer and Cardiovascular Disease Incidence and Mortality and All-Cause Mortality." JAMA Intern Med **182**(11): 1139-1148.

IMPORTANCE: Recommendations for the number of steps per day may be easier to enact for some people than the current time- and intensity-based physical activity guidelines, but the evidence to support steps-based goals is limited. OBJECTIVE: To describe the associations of step count and intensity with all-cause mortality and cancer and cardiovascular disease (CVD) incidence and mortality. DESIGN, SETTING, AND PARTICIPANTS: This population-based prospective cohort study used data from the UK Biobank for 2013 to 2015 (median follow-up, 7 years) and included adults 40 to 79 years old in England, Scotland, and Wales. Participants were invited by email to partake in an accelerometer study. Registry-based morbidity and mortality were ascertained through October 2021. Data analyses were performed

during March 2022. EXPOSURES: Baseline wrist accelerometer-measured daily step count and established cadence-based step intensity measures (steps/min): incidental steps, (<40 steps/min), purposeful steps (>/=40 steps/min); and peak-30 cadence (average steps/min for the 30 highest, but not necessarily consecutive, min/d). MAIN OUTCOMES AND MEASURES: All-cause mortality and primary and secondary CVD or cancer mortality and incidence diagnosis. For cancer, analyses were restricted to a composite cancer outcome of 13 sites that have a known association with reduced physical activity. Cox restricted cubic spline regression models were used to assess the dose-response associations. The linear mean rate of change (MRC) in the log-relative hazard ratio for each outcome per 2000 daily step increments were also estimated. RESULTS: The study population of 78 500 individuals (mean [SD] age, 61 [8] years; 43 418 [55%] females; 75 874 [97%] White individuals) was followed for a median of 7 years during which 1325 participants died of cancer and 664 of CVD (total deaths 2179). There were 10 245 incident CVD events and 2813 cancer incident events during the observation period. More daily steps were associated with a lower risk of all-cause (MRC, -0.08; 95% CI, -0.11 to -0.06), CVD (MRC, -0.10; 95% CI, -0.15 to -0.06), and cancer mortality (MRC, 95% CI, -0.11; -0.15 to -0.06) for up to approximately 10 000 steps. Similarly, accruing more daily steps was associated with lower incident disease. Peak-30 cadence was consistently associated with lower risks across all outcomes, beyond the benefit of total daily steps. CONCLUSIONS AND RELEVANCE: The findings of this population-based prospective cohort study of 78 500 individuals suggest that up to 10 000 steps per day may be associated with a lower risk of mortality and cancer and CVD incidence. Steps performed at a higher cadence may be associated with additional risk reduction, particularly for incident disease.

Deng, J., et al. (2022). "Risk, Incidence, and Mortality of Breast Cancer in Primary Sjogren's Syndrome: A Systematic Review and Meta-Analysis." Front Immunol **13**: 904682.

BACKGROUND: Primary Sjogren's syndrome (pSS) and breast cancer are a highly prevalent autoimmune disease and malignancy, respectively, both occurring predominantly in females. Whether there is a link between these two diseases is uncertain. We conducted a systematic review and meta-analysis to investigate the risk, incidence, and mortality of breast cancer in patients with pSS. METHODS: We systematically searched Embase, PubMed, and Web of Science on January 31, 2022 to identify the study that assessed risk, incidence, or mortality of breast cancer in pSS. The fixed or random-effects models were applied to pool the effect estimates based on heterogeneity measured by Cochran's Q-test and Higgins' I(2). RESULTS: Ten studies involving 725,805 participants and 64,836 pSS patients were included in our analysis. The pooled result showed that, overall, pSS was not associated with the risk (SIR=0.92, 95%CI: 0.66-1.29, P=0.646) and mortality (HR = 0.78, 95%CI: 0.26-2.34, P = 0.664) of breast cancer; however, when stratified by geographic region, we found that patients with pSS in Asian countries (SIR=1.32, 95%CI: 1.10-1.58, P=0.003) and Argentina (SIR=3.76, 95%CI: 1.04-9.45, P=0.019) had an elevated risk of breast cancer, while pSS in Europe was associated with a reduced risk (SIR=0.61, 95%CI: 0.51-0.73, P<0.001). The pooled result from 28,635 female pSS patients indicated that the incidence of breast cancer was 2.15 (95% CI: 1.33-3.50) per 1000 person/years. CONCLUSION: This study suggests that there may be geographical differences in the association between pSS and breast cancer risk; patients with pSS in European countries are associated with a lower risk of breast cancer, while Asia and Argentina are the opposite. Future research is needed to further characterize the effect of pSS on breast cancer risk and the pathophysiological mechanisms underlying this association to unravel the complex relationship between the two.

Deng, X., et al. (2022). "Trends in Incidence, Mortality, and Survival of Penile Cancer in the United States: A Population-Based Study." Front Oncol **12**: 891623.

PURPOSE: The aim of this study is to investigate the trends in incidence and mortality, and explore any change in survival of penile cancer in the United States. METHODS: We obtained data from the Surveillance, Epidemiology, and End Results (SEER) database (2000-2018) utilizing the SEER Stat software. The joinpoint regression was used to analyze the secular trend of incidence and incidence-based mortality (IBM) stratified by age, race, and summary stage. The 5-year relative survival rate was also calculated. RESULT: The age-adjusted rates of penile cancer patients were 0.38 (0.37-0.39) and 0.21 (0.2-0.21) for overall incidence and IBM, respectively. The 5-year relative survival rates were 67.7%, 66.99%, and 65.67% for the calendar periods of 2000-2004, 2005-2009, and 2010-2014, respectively. No significant changes in incidence by era were observed from 2000 to 2018 [annual percentage change (APC) = 0.5%, p = 0.064]. The IBM rate of penile cancer showed an initial significant increase from 2000 to 2002 (APC = 78.6%, 95% CI, -1.7-224.6) followed by a deceleration rate of 4.6% (95% CI, 3.9-5.3) during 2002 to 2018. No significant improvement in 5-year relative survival was observed. The trends by age, race, and summary stage

in incidence and IBM were significantly different. CONCLUSION: This study, using population-level data from the SEER database, showed an increasing trend in IBM and no significant improvement in the 5-year relative survival rate. Meanwhile, the incidence of penile cancer exhibited a relatively stable trend during the study period. These results might be due to the lack of significant progress in the treatment and management of penile cancer patients in the United States in recent decades. More efforts, like increasing awareness among the general population and doctors, and centralized management, might be needed in the future to improve the survival of this rare disease.

Deng, Z., et al. (2022). "Mortality after second malignancy in breast cancer survivors compared to a first primary cancer: a nationwide longitudinal cohort study." NPJ Breast Cancer **8**(1): 82.

Limited information exists about survival outcomes after second primary cancers (SPCs) among breast cancer survivors. Studies suggest that mortality after certain SPCs may be higher than mortality after first primary cancers (FPCs) of the same type. A cohort study was conducted among 63,424 US women using the Surveillance, Epidemiology, and End Results 18 database (2000-2016) to compare mortality after a SPC among breast cancer survivors to mortality among women after a FPC using Cox proportional hazard regression. Propensity scores were used to match survivors with SPCs to women with FPCs 1:1 based on cancer type and prognostic factors. During a median follow-up of 42 months, 11,532 cancer deaths occurred after SPCs among survivors compared to 9305 deaths after FPCs. Cumulative cancer mortality was 44.7% for survivors with SPCs and 35.2% for women with FPCs. Survivors with SPCs had higher risk of cancer death (hazard ratio (HR): 1.27, 95% CI: 1.23-1.30) and death overall (HR: 1.18, 95% CI: 1.15-1.21) than women with FPCs. Increased risk of cancer death after SPCs compared to FPCs was observed for cancer in breast, lung, colon and/or rectum, uterus, lymphoma, melanoma, thyroid, and leukemia. Estrogen receptor status and treatment of the prior breast cancer as well as time between prior breast cancer and SPC significantly modified the mortality difference between women with SPC and FPC. A more tailored approach to early detection and treatment could improve outcomes from second cancer in breast cancer survivors.

Deravi, N., et al. (2022). "Three-year weight change and risk of all-cause, cardiovascular, and cancer mortality among Iranian adults: over a decade of follow-up in the Tehran Lipid and Glucose Study." BMC Public Health **22**(1): 1762.

BACKGROUND: We investigated the impact of weight change on mortality in a population-based cohort setting. METHODS: We conducted two weight measurements for 5436 participants aged >/= 30 years with an approximate 3-year interval. Based on their weight change, we categorized participants to: > 5% weight loss, 3-5% weight loss, stable weight (+/- < 3%), 3-5% weight gain, > 5% weight gain. We followed participants for mortality annually up to March 20th 2018. We applied the multivariable Cox proportional hazard models to estimate hazard ratios (HRs) and 95% confidence intervals (CIs) of weight change categories for all-cause, cardiovascular (CV), and cancer mortality, considering stable weight as reference. The Cox models was adjusted for age, sex, educational level, body mass index, smoking status, hypertension, hypercholesterolemia, diabetes, and cardiovascular disease (CVD) at baseline. RESULTS: During a median follow-up of 14.4 years, 629 deaths (247 CV and 126 cancer deaths) have occurred. Over 5% weight loss and gain were associated with increased risk of all-cause mortality in multivariable analysis with HRs of 1.47 [95% CI: 1.17-1.85] and 1.27 [1.02-1.57], respectively; however, a 3-5% loss or gain did not alter the risk of all-cause mortality significantly. These significant risks for wight change > 5% were not modified by the presence of diabetes, obesity, and smoking status; however, the unfavorable impact of weight change on mortality events was more prominent in those older than > 65 years (P-value for interaction: 0.042). After excluding those with history of CVD, diabetes, and cancer during the weight measurements period, these associations significantly attenuated (HR: 1.29 [0.89-1.87] for > 5% weight loss and 1.12 [0.84-1.50] for > 5% weight gain). Additionally, a > 5% weight loss was also associated with about 60% higher risk for CV mortality (HR: 1.62 [1.15-2.28]), and a 3-5% weight loss was associated with about 95% higher risk of cancer mortality (HR: 1.95 [1.13-3.38]). CONCLUSIONS: Our findings showed a U-shaped association across weight change categories for all-cause mortality risk with over 5% weight gain and loss causing higher risk. Moreover, weight loss can have adverse impact on CV and cancer mortality events.

Desai, A., et al. (2021). "Mortality in hospitalized patients with cancer and coronavirus disease 2019: A systematic review and meta-analysis of cohort studies." Cancer **127**(9): 1459-1468.

BACKGROUND: Heterogeneous evidence exists on the effect of coronavirus disease 2019 (COVID-19) on the clinical outcomes of patients with cancer. METHODS: A systematic review was performed using the Medline, Embase, and CENTRAL databases and the World Health Organization Novel

Coronavirus website to identify studies that reported mortality and characteristics of patients with cancer who were diagnosed with COVID-19. The primary study outcome was mortality, defined as all-cause mortality or in-hospital mortality within 30 days of initial COVID-19 diagnosis. The pooled proportion of mortality was estimated using a random-effects model, and study-level moderators of heterogeneity were assessed through subgroup analysis and metaregression. RESULTS: Among 2922 patients from 13 primarily inpatient studies of individuals with COVID-19 and cancer, the pooled 30-day mortality rate was 30% (95% CI, 25%-35%). The overall pooled 30-day mortality rate among 624 patients from 5 studies that included a mixture of inpatient and outpatient populations was 15% (95% CI, 9%-22%). Among the hospitalized studies, the heterogeneity (I(2) statistic) of the meta-analysis remained high (I(2) , 82%). Cancer subtype (hematologic vs solid), older age, male sex, and recent active cancer therapy each partially explained the heterogeneity of mortality reporting. In multivariable metaregression, male sex, along with an interaction between the median patient age and recent active cancer therapy, explained most of the between-study heterogeneity (R(2) , 96%). CONCLUSIONS: Pooled mortality estimates for hospitalized patients with cancer and COVID-19 remain high at 30%, with significant heterogeneity across studies. Dedicated community-based studies are needed in the future to help assess overall COVID-19 mortality among the broader population of patients with cancer.

Dess, R. T., et al. (2020). "Development and Validation of a Clinical Prognostic Stage Group System for Nonmetastatic Prostate Cancer Using Disease-Specific Mortality Results From the International Staging Collaboration for Cancer of the Prostate." JAMA Oncol **6**(12): 1912-1920.

IMPORTANCE: In 2016, the American Joint Committee on Cancer (AJCC) established criteria to evaluate prediction models for staging. No localized prostate cancer models were endorsed by the Precision Medicine Core committee, and 8th edition staging was based on expert consensus. OBJECTIVE: To develop and validate a pretreatment clinical prognostic stage group system for nonmetastatic prostate cancer. DESIGN, SETTING, AND PARTICIPANTS: This multinational cohort study included 7 centers from the United States, Canada, and Europe, the Shared Equal Access Regional Cancer Hospital (SEARCH) Veterans Affairs Medical Centers collaborative (5 centers), and the Cancer of the Prostate Strategic Urologic Research Endeavor (CaPSURE) registry (43 centers) (the STAR-CAP cohort). Patients with cT1-4N0-1M0 prostate adenocarcinoma treated from January 1, 1992, to December 31, 2013 (follow-up completed December 31, 2017). The STAR-CAP cohort was randomly divided into training and validation data sets; statisticians were blinded to the validation data until the model was locked. A Surveillance, Epidemiology, and End Results (SEER) cohort was used as a second validation set. Analysis was performed from January 1, 2018, to November 30, 2019. EXPOSURES: Curative intent radical prostatectomy (RP) or radiotherapy with or without androgen deprivation therapy. MAIN OUTCOMES AND MEASURES: Prostate cancer-specific mortality (PCSM). Based on a competing-risk regression model, a points-based Score staging system was developed. Model discrimination (C index), calibration, and overall performance were assessed in the validation cohorts. RESULTS: Of 19 684 patients included in the analysis (median age, 64.0 [interquartile range (IQR), 59.0-70.0] years), 12 421 were treated with RP and 7263 with radiotherapy. Median follow-up was 71.8 (IQR, 34.3-124.3) months; 4078 (20.7%) were followed up for at least 10 years. Age, T category, N category, Gleason grade, pretreatment serum prostate-specific antigen level, and the percentage of positive core biopsy results among biopsies performed were included as variables. In the validation set, predicted 10-year PCSM for the 9 Score groups ranged from 0.3% to 40.0%. The 10-year C index (0.796; 95% CI, 0.760-0.828) exceeded that of the AJCC 8th edition (0.757; 95% CI, 0.719-0.792), which was improved across age, race, and treatment modality and within the SEER validation cohort. The Score system performed similarly to individualized random survival forest and interaction models and outperformed National Comprehensive Cancer Network (NCCN) and Cancer of the Prostate Risk Assessment (CAPRA) risk grouping 3- and 4-tier classification systems (10-year C index for NCCN 3-tier, 0.729; for NCCN 4-tier, 0.746; for Score, 0.794) as well as CAPRA (10-year C index for CAPRA, 0.760; for Score, 0.782). CONCLUSIONS AND RELEVANCE: Using a large, diverse international cohort treated with standard curative treatment options, a proposed AJCC-compliant clinical prognostic stage group system for prostate cancer has been developed. This system may allow consistency of reporting and interpretation of results and clinical trial design.

Deuker, M., et al. (2021). "Bladder cancer stage and mortality: urban vs. rural residency." Cancer Causes Control **32**(2): 139-145.

OBJECTIVE: Relative to urban populations, rural patients may have more limited access to care, which may undermine timely bladder cancer (BCa) diagnosis and even survival. METHODS: We tested the effect of residency status (rural areas [RA < 2500 inhabitants] vs. urban clusters [UC >/= 2500

inhabitants] vs. urbanized areas [UA, >/=50,000 inhabitants]) on BCa stage at presentation, as well as on cancer-specific mortality (CSM) and other cause mortality (OCM), according to the US Census Bureau definition. Multivariate competing risks regression (CRR) models were fitted after matching of RA or UC with UA in stage-stratified analyses. RESULTS: Of 222,330 patients, 3496 (1.6%) resided in RA, 25,462 (11.5%) in UC and 193,372 (87%) in UA. Age, tumor stage, radical cystectomy rates or chemotherapy use were comparable between RA, UC and UA (all p > 0.05). At 10 years, RA was associated with highest OCM followed by UC and UA (30.9% vs. 27.7% vs. 25.6%, p < 0.01). Similarly, CSM was also marginally higher in RA or UC vs. UA (20.0% vs. 20.1% vs. 18.8%, p = 0.01). In stage-stratified, fully matched CRR analyses, increased OCM and CSM only applied to stage T1 BCa patients. CONCLUSION: We did not observe meaningful differences in access to treatment or stage distribution, according to residency status. However, RA and to a lesser extent UC residency status, were associated with higher OCM and marginally higher CSM in T1N0M0 patients. This observation should be further validated or refuted in additional epidemiological investigations.

Dezube, A. R., et al. (2022). "Pre-COVID-19 National Mortality Trends in Open and Video-Assisted Lobectomy for Non-Small Cell Lung Cancer." J Surg Res **274**: 213-223.

INTRODUCTION: In the current era of episode-based hospital reimbursements, it is important to determine the impact of hospital size on contemporary national trends in surgical technique and outcomes of lobectomy. METHODS: Patients aged >18 y undergoing open and video-assisted thoracoscopic surgery (VATS) lobectomy from 2008 to 2014 were identified using insurance claims data from the National Inpatient Sample. The impact of hospital size on surgical approach and outcomes for both open and VATS lobectomy were analyzed. RESULTS: Over the 7-y period, 202,668 lobectomies were performed nationally, including 71,638 VATS and 131,030 open. Although the overall number of lobectomies decreased (30,058 in 2008 versus 27,340 in 2014, P < 0.01), the proportion of VATS lobectomies increased (24.0% versus 46.9%), and open lobectomies decreased (76.0% versus 53.0%, all P < 0.01). When stratified by hospital size, small hospitals had a significant increase in the proportion of open lobectomies (6.4%-12.2%; P = 0.01) and trend toward increased number of VATS lobectomies (2.7%-12.2%). Annual mortality rates for VATS (range: 1.0%-1.9%) and open (range: 1.9%-2.4%) lobectomy did not significantly differ over time (all P > 0.05) but did decrease among small hospitals (4.1%-1.3% and 5.1%-1.1% for VATS and open, respectively; both P < 0.05). After adjusting for confounders, hospital bed size was not a predictor of in-hospital mortality. CONCLUSIONS: Utilization of VATS lobectomies has increased over time, more so among small hospitals. Mortality rates for open lobectomy remain consistently higher than VATS lobectomy (range 0.4%-1.4%) but did not significantly differ over time. This data can help benchmark hospital performance in the future.

Dhir, A. A. and S. P. Sawant (2021). "Cardiac morbidity & mortality in patients with breast cancer: A review." Indian J Med Res **154**(2): 199-209.

Cardiovascular disease (CVD) and breast cancer cause substantial morbidity and mortality in women and are major public health concerns. Breast cancer survivors are at a greater risk for CVD-related mortality compared to women without breast cancer. Breast cancer and cardiovascular diseases share a number of common risk factors. Breast cancer treatments like anthracycline based chemotherapy, novel targeted therapy and radiation therapy can cause cardiotoxicity. With improvements in breast cancer prevention and treatment, there is a significant improvement in survival and this shifts focus from disease control to long term effects of treatment and quality of life. Assessing CVD and minimizing complications from cancer therapy are important treatment goals.

Dhungel, B., et al. (2022). "Occupation- and industry-specific cancer mortality among Japanese women from 1980 to 2015." BMC Public Health **22**(1): 2003.

BACKGROUND: The number of women in Japan who continue working after childbirth is on the rise. Over the past few years, Japan's cancer mortality rate has increased. About 50% of all cancer deaths among Japanese women aged 25-64 are caused by lung, gastric, pancreatic and colorectal cancers. This study aims to examine the difference in mortality risk for key cancers among women and explore the effect of the economic crisis in the mid-1990s separately for occupational and industrial categories. METHODS: Data from 1980 to 2015 were gathered from the Japanese Population Census and National Vital Statistics conducted in the same year. A Poisson regression analysis was used to estimate mortality risk and mortality trends for lung, gastric, pancreatic and colorectal cancer among Japanese working women aged 25-64 years. RESULTS: Across most industrial and occupational groups, the trends in age-standardised cancer mortality rate for women have declined. Workers in management, security and transportation have a higher cancer mortality risk than sales workers. The risk of death from all four cancers is higher for workers in the mining and electricity industries than for

wholesale and retail workers. CONCLUSION: To improve the health and well-being of employed Japanese women, it is crucial to monitor cancer mortality trends. Using these population-level quantitative risk estimates, industry- and occupation-specific prevention programmes can be developed to target women at higher cancer risk and enable the early detection and treatment of cancer.

Di Donato, V., et al. (2021). "Modified fragility index and surgical complexity score are able to predict postoperative morbidity and mortality after cytoreductive surgery for advanced ovarian cancer." Gynecol Oncol **161**(1): 4-10.

OBJECTIVE: The aim of this study was to assess the impact of surgical complexity on postoperative complications and mortality, according to patient's frailty (mFI) following surgery for ovarian cancer. METHODS: Patients undergoing cytoreductive surgery for ovarian cancer from 2008 to 2018 were identified from our database. A surgical complexity score from 1 to 3 was used to assess the extent of surgery (simple to complex, respectively). mFI with 11 variables, based on mapping the Canadian Study of Health and Aging Frailty Index to the NSQIP comorbidities was evaluated. Data were analyzed using Fisher exact test, independent sample t-test, and logistic regression. RESULTS: Of 263 patients identified, 33% reported at least one postoperative complication and 6% had severe complications. BMI >/= 30 ($p = 0.04$) increased mFI ($p = 0.04$) and high-complexity surgery ($p < 0.001$) were independent predictors of severe complications (G3-G5). Patients with high frailty index score (mFI >/= 3) who underwent intermediate or high-complexity surgery were at higher risk of severe complications ranging from 29.4% to 50. CONCLUSIONS: The combined evaluation of mFI and surgical complexity expected may identify patients at higher risk for severe morbidity allowing to stratify patients who are less likely to tolerate a surgical extensive treatment.

Di, J., et al. (2021). "Current status and development trends of morbidity and mortality in gastric cancer patients in Xining, 2009-2016." Am J Transl Res **13**(11): 12431-12439.

OBJECTIVE: The incidence of gastric cancer is declining in parts of Asia including China. This study was designed to investigate the incidence and mortality trend of gastric cancer in different regions and ethnic groups in Xining of Qinghai-Tibet Plateau. METHODS: Data of gastric cancer from January 2009 to December 2016 were collected from Disease Control Center in Xining for repeated cross-sectional study. PRIMARY OUTCOME MEASURES: Gastric cancer. PARTICIPANTS: Xining resident population with pathological diagnosis of gastric cancer. MAIN OUTCOME MEASURE: Age, gender composition ratio, morbidity, mortality and trends. RESULTS: There were 4822 new cases of gastric cancer from 2009 to 2016, including 3583 males and 1239 females; 2290 cases were in villages and 2532 in towns. Male incidence rate (38.37/100,000) was higher than female (13.35/100,000). The incidence in rural areas (39.29/100,000) was higher than in urban areas (20.59/100,000). During 2009-2016, there were 2109 gastric cancer deaths in Xining, 1543 in males and 566 in females. There were 1185 cases in villages and 924 in cities. Male mortality (16.64/100,000) was higher than female (6.42/100,000). The mortality rate in rural areas (20.40/100,000) was higher than in urban areas (7.62/100,000). CONCLUSION: Overall morbidity and mortality rates of gastric cancer are on the rise in Xining. Male morbidity and mortality rates are higher than female ones, and rural areas are higher than urban areas.

Di Maso, M., et al. (2020). "Adherence to the Mediterranean Diet and Mortality after Breast Cancer." Nutrients **12**(12).

Adherence to Mediterranean diet has been consistently associated with a reduced mortality in the general population, but evidence for women with breast cancer is scanty. METHODS: A cohort of 1453 women with breast cancer diagnosed between 1991 and 1994 in northern Italy was followed-up for vital status for 15 years after diagnosis. The pre-diagnostic habitual diet was assessed through a structured questionnaire and adherence to the Mediterranean diet was evaluated through the Mediterranean Diet Score. Hazard ratios (HR) of death with confidence intervals (CI) were estimated using Cox model, adjusting for potential confounders. RESULTS: Compared to women who scarcely adhere to the Mediterranean diet ($n = 332$, 22.8%), those highly adherent ($n = 500$, 34.4%) reported higher intakes of carbohydrates, mono-unsaturated and poly-unsaturated fatty acids, vitamins, folate, and carotenoids, and lower intakes of cholesterol and animal proteins. Adherence to the Mediterranean diet was associated with a better prognosis: 15-year overall survival of 63.1% for high and 53.6% for low adherence, respectively ($p = 0.013$). HR for all-cause mortality was 0.72 (95% CI: 0.57-0.92) and HR for breast cancer mortality was 0.65 (95% CI: 0.43-0.98) for women 55 years and older. No significant association emerged for breast cancer mortality in the total cohort. CONCLUSIONS: Although dietary habits may have changed after breast cancer diagnosis, these findings indicate that women who ate according to the Mediterranean dietary pattern prior to their diagnosis may have greater chance of a

favorable prognosis after breast cancer diagnosis compared to those who did not.

Diaz, K. M. and S. C. Gilchrist (2021). "Possible Reverse Causation and Confounding in Study of the Association of Sedentary Behavior With Cancer Mortality-Reply." JAMA Oncol **7**(1): 139-140.

Didkowska, J., et al. (2022). "Cancer incidence and mortality in Poland in 2019." Sci Rep **12**(1): 10875.

The purpose of this paper is to offer the most important epidemiological indicators of malignant neoplasms in Poland for the year 2019. In 2019, the Polish National Cancer Registry received information on almost 171.2 thousand new cancer cases and 100.3 thousand cancer deaths. The most common male cancers were prostate (20.6%), lung (16.1%), colon (6.8%), bladder (6.4%), and rectal (4.2%) cancers. Age-standardized incidence rates were at 118 per 100,000 for prostate, 89 for lung, 40 for colon, 38 for bladder, and 23 for the rectum. The most prevalent female cancers encompassed breast (22.9%), lung (9.9%), corpus uteri (7.0%), colon (5.9%), and ovary (4.3%). Age-standardized incidence rate was at 95 per 100,000 for breast cancer, 40 for lung 40, 29 for corpus uteri, 24 for colon, and 18 for ovarian cancer. The five leading causes of male cancer deaths were cancer of the lung (27.4%), prostate (10.3%), colon (8.0%), bladder (5.8%), and stomach (5.7%). Age-standardized mortality rates were 100 per 100,000 for lung, 46 for prostate, 32 for colon, 24 for urinary bladder, and 22 for stomach cancer. Most female deaths due to cancer were caused by lung (17.9%), breast (15.1%), colon (7.7%), ovary (6.0%), pancreas (5.7%), and corpus uteri (4.0%) cancers. Age-standardized mortality rates were 39 per 100,000 for lung, 33 for breast, 17 for colon, 13 for ovarian, 13 for pancreatic, and 9 for corpus uteri cancer.

Dieci, M. V., et al. (2022). "Clinical profile and mortality of Sars-Cov-2 infection in cancer patients across two pandemic time periods (Feb 2020-Sep 2020; Sep 2020-May 2021) in the Veneto Oncology Network: The ROVID study." Eur J Cancer **167**: 81-91.

INTRODUCTION: We analyzed a cohort of patients with cancer and Sars-Cov-2 infection from the Veneto Oncology Network registry across two pandemic time periods. MATERIALS AND METHODS: 761 patients with cancer and SARS-CoV-2 infection were included. RESULTS: 198 patients were diagnosed during the first pandemic time period (TP1; February 2020 September 2020), 494 during TP2 before the vaccination campaign (TP2/pre-vaccination; September 2020-21 February 2021) and 69 in TP2/post-vaccination (22 February 2021-15 May 2021). TP2 vs TP1 patients were younger ($p = 0.004$), showed more frequently a good performance status ($p < 0.001$) and <2 comorbidities ($p = 0.002$), were more likely to be on active anticancer therapy ($p = 0.006$). Significantly fewer patients in TP2 (3-4%) vs TP1 (22%) had an in-hospital potential source of infection ($p < 0.001$). TP2 patients were more frequently asymptomatic ($p = 0.003$). Significantly fewer patients from TP2 were hospitalized ($p < 0.001$) or admitted to intensive care unit ($p = 0.006$). All-cause mortality decreased from 30.3% in TP1, to 8.9% and 8.7% in the two TP2 periods ($p < 0.001$), reflected by a significant reduction in Sars-Cov-2-related mortality (15.2%, 7.5% and 5.8% in the three consecutive time periods, $p = 0.004$). CONCLUSIONS: Differences in clinical characteristics and features of Sars-Cov-2 infection between TP1 and TP2 reflect the effects of protective measures and increased testing capacity. The lower mortality in TP2 is in line with a less frail population. However, the vast majority of death events in TP2 were related to COVID-19, reinforcing the priority to protect cancer patients.

Dieli-Conwright, C. M., et al. (2022). "Cardiometabolic risk factors, physical activity, and postmenopausal breast cancer mortality: results from the Women's Health Initiative." BMC Womens Health **22**(1): 32.

BACKGROUND: Higher physical activity levels are associated with lower breast cancer-specific mortality. In addition, the metabolic syndrome is associated with higher breast cancer-specific mortality. Whether the physical activity association with breast cancer mortality is modified by number of metabolic syndrome components (cardiometabolic risk factors) in postmenopausal women with early-stage breast cancer remains unknown. METHODS: Cardiovascular risk factors included high waist circumference, hypertension, high cholesterol, and diabetes. Breast cancers were verified by medical record review. Mortality finding were enhanced by serial National Death Index queries. Cox proportional hazards regression models were used to estimate associations between baseline physical activity and subsequent breast cancer-specific and overall mortality following breast cancer diagnosis in Women's Health Initiative participants. These associations were examined after stratifying by cardiometabolic risk factor group. RESULTS: Among 161,308 Women's Health Initiative (WHI) participants, 8543 breast cancers occurred after 9.5 years (median) follow-up in women, additionally with information on cardiometabolic risk factors and physical activity at entry. In multi-variable analyses, as measured from cancer diagnosis, higher physical activity levels were associated with lower all-cause mortality risk (hazard ratio [HR] 0.86, 95% confidence

interval [CI] 0.78-0.95, trend P < 0.001) but not with breast cancer-specific mortality (HR 0.85, 95% CI 0.70 to 1.04, trend P = 0.09). The physical activity and all-cause mortality association was not significantly modified by cardiometabolic risk factor number. CONCLUSIONS: Among women with early-stage breast cancer, although higher antecedent physical activity was associated with lower risk of all-cause mortality, the association did not differ by cardiometabolic risk factor number.

Diers, J., et al. (2021). "Mortality and complication management after surgery for colorectal cancer depending on the DKG minimum amounts for hospital volume." Eur J Surg Oncol **47**(4): 850-857.

BACKGROUND: The German Cancer Society ("Deutsche Krebsgesellschaft"; DKG) certifies on a volunteer base colorectal cancer centers based on, among other things, minimum operative amounts (at least 30 oncological colon cancer resections and 20 oncological rectal cancer resections per year). In this work, nationwide hospital mortality and death after documented complications ('Failure to Rescue' = FtR) were evaluated depending on the fulfillment of the minimum amounts. METHODS: This is a retrospective analysis of the nationwide hospital billing data (DRG data, 2012-2017). Categorization is based on the DKG minimum quantities (fully, partially or not fulfilled). RESULTS: Of 287,227 patients analyzed, 56.5% were operated in centers that met the DKG minimum amounts. The overall hospital mortality rate was 5.0%. In centers which met the minimum quantities, it was significantly lower (4.3%) than in hospitals which partially (5.7%) or not (6.2%) met the minimum quantities. The risk-adjusted hospital mortality rate for patients in hospitals who meet the minimum amount was 20% lower (OR 0.80; 95% CI [0.74-0.87], p < 0.001). For complications, both surgical and non-surgical, there was an unadjusted and adjusted lower FtR in hospitals that met the minimum amounts (e.g. anastomotic leak: 11.2% vs. 15.6%, p < 0.001; pulmonary artery embolism 21.3% vs. 28.2%, p = 0.001). CONCLUSION: There is a 1/3 lower mortality and FtR rate after surgery for a colon or rectal cancer in centers fulfilling the DKG minimum amounts. The presented data implicate that there is an urgent need for a nationwide centralization program.

Diers, J., et al. (2021). "Hospital volume following major surgery for gastric cancer determines in-hospital mortality rate and failure to rescue: a nation-wide study based on German billing data (2009-2017)." Gastric Cancer **24**(4): 959-969.

BACKGROUND: For many cancer resections, a hospital volume-outcome relationship exists. The data regarding gastric cancer resection-especially in the western hemisphere-are ambiguous. This study analyzes the impact of gastric cancer surgery caseload per hospital on postoperative mortality and failure to rescue in Germany. METHODS: All patients diagnosed with gastric cancer from 2009 to 2017 who underwent gastric resection were identified from nation-wide administrative data. Hospitals were grouped into five equal caseload quintiles (I-V in ascending caseload order). Postoperative deaths and failure to rescue were determined. RESULTS: Forty-six thousand one hundred eighty-seven patients were identified. There was a significant shift from partial resections in low-volume hospitals to more extended resections in high-volume centers. The overall in-house mortality rate was 6.2%. The crude in-hospital mortality rate ranged from 7.9% in quintile I to 4.4% in quintile V, with a significant trend between volume categories (p < 0.001). In the multivariable logistic regression analysis, quintile V hospitals (average of 29 interventions/year) had a risk-adjusted odds ratio of 0.50 (95% CI 0.39-0.65), compared to the baseline in-house mortality rate in quintile I (on average 1.5 interventions/year) (p < 0.001). In an analysis only evaluating hospitals with more than 30 resections per year mortality dropped below 4%. The overall postoperative complication rate was comparable between different volume quintiles, but failure to rescue (FtR) decreased significantly with increasing caseload. CONCLUSION: Patients who had gastric cancer surgery in hospitals with higher volume had better outcomes and a reduced failure to rescue rates for severe complications.

Dillon, J., et al. (2021). "Mortality in Older Patients with Breast Cancer Undergoing Breast Surgery: How Low is "Low Risk"?" Ann Surg Oncol **28**(10): 5758-5767.

BACKGROUND: Breast surgery carries a low risk of postoperative mortality. For older patients with multiple comorbidities, even low-risk procedures can confer some increased perioperative risk. We sought to identify factors associated with postoperative mortality in breast cancer patients >/=70 years to create a nomogram for predicting risk of death within 90 days. METHODS: Patients diagnosed with nonmetastatic invasive breast cancer (2010-2016) were selected from the National Cancer Database. Unadjusted OS was estimated using the Kaplan-Meier method. Multivariate logistic regression was used to estimate the association of age and surgery with 90-day mortality and to build a predictive nomogram. RESULTS: Among surgical patients >/=70 years, unadjusted 90-day mortality increased with increasing age (70-74 = 0.4% vs. >/=85 = 1.6%), comorbidity score (0 = 0.5% vs. >/=3 = 2.7%), and disease stage (I = 0.4% vs. III = 2.7%; all p < 0.001). After adjustment,

death within 90 days of surgery was associated with higher age (>/=85 vs. 70-74: odds ratio [OR] 3.16, 95% confidence interval [CI] 2.74-3.65), comorbidity score (>/=3 vs. 0: OR 4.79, 95% CI 3.89-5.89), and disease stage (III vs. I: OR 4.30, 95% CI 3.69-5.00). Based on these findings, seven variables (age, gender, comorbidity score, facility type, facility location, clinical stage, and surgery type) were selected to build a nomogram; estimates of risk of death within 90 days ranged from <1 to >30%. CONCLUSIONS: Breast operations remain relatively low-risk procedures for older patients with breast cancer, but select factors can be used to estimate the risk of postoperative mortality to guide surgical decision-making among older women.

Ding, D., et al. (2022). "Physical activity, diet quality and all-cause cardiovascular disease and cancer mortality: a prospective study of 346 627 UK Biobank participants." Br J Sports Med.

OBJECTIVES: To examine independent and interactive associations of physical activity and diet with all-cause, cardiovascular disease (CVD) and physical activity, diet and adiposity-related (PDAR) cancer mortality. METHODS: This population-based prospective cohort study (n=346 627) is based on the UK Biobank data with linkage to the National Health Service death records to 30 April 2020. A left-truncated Cox proportional hazards model was fitted to examine the associations between exposures (self-reported total moderate-to-vigorous intensity physical activity (MVPA), vigorous-intensity physical activity (VPA) and a diet quality index (score ranged 0-3)) and outcomes (all-cause, CVD and PDAR cancer mortality). RESULTS: During a median follow-up of 11.2 years, 13 869 participants died from all causes, 2650 from CVD and 4522 from PDAR cancers. Compared with quartile 1 (Q1, 0-210 min/week), Q2-Q4 of MVPA were associated with lower risks of all-cause (HR ranged from 0.87 (95% CI: 0.83 to 0.91) to 0.91 (95% CI: 0.87 to 0.96)), CVD (HR ranged from 0.85 (95% CI: 0.76 to 0.95) to 0.90 (95% CI: 0.81 to 1.00)) and PDAR cancer mortality (HR ranged from 0.86 (95% CI: 0.79 to 0.93) to 0.94 (95% CI: 0.86 to 1.02)). Compared with no VPA, any VPA was associated with lower risk for all-cause and CVD mortality (HR ranged from 0.85 (95% CI: 0.80 to 0.89) to 0.88 (95% CI: 0.84 to 0.93) and from 0.75 (95% CI: 0.68 to 0.83) to 0.90 (95% CI: 0.80 to 1.02), respectively). Although not reaching statistical significance for all-cause and CVD mortality, being in the best dietary category (diet quality index=2-3) was associated with a reduction in PDAR cancer mortality (HR=0.86, 95% CI: 0.78 to 0.93). No additive or multiplicative interactions between physical activity categories and dietary quality was found. When comparing across physical activity and diet combinations, the lowest risk combinations consistently included the higher levels of physical activity and the highest diet quality score. CONCLUSIONS: Adhering to both quality diet and sufficient physical activity is important for optimally reducing the risk of mortality from all causes, CVD and PDAR cancers.

Divakar, P. and L. Davies (2022). "Trends in Incidence and Mortality of Larynx Cancer in the US." JAMA Otolaryngol Head Neck Surg.

IMPORTANCE: Larynx cancer is associated with considerable morbidity for patients and has a high mortality rate. Historical analyses showed that the incidence of larynx cancer was decreasing but the mortality was not similarly improving. OBJECTIVE: To assess whether incidence and mortality trends in larynx cancer in the US have improved. DESIGN, SETTING, AND PARTICIPANTS: This cohort study used population-based data from the Surveillance, Epidemiology, and End Results Program database for patients older than 18 years who were diagnosed with laryngeal cancer between January 1, 1986, and December 31, 2018. Data were analyzed from May 1, 2021, to May 31, 2022. MAIN OUTCOMES AND MEASURES: The main outcomes were incidence and mortality of larynx cancer by sex, subsite, and patterns of surgical treatment. RESULTS: Among 40 850 US patients with larynx cancer diagnosed from 1986 to 2018 (80.4% male), the incidence of larynx cancer decreased 55% from 5.00 per 100 000 people (95% CI, 4.70-5.32 per 100 000 people) to 2.26 per 100 000 people (95% CI, 2.11-2.42 per 100 000 people). During the same period, mortality decreased only 43% from 1.59 per 100 000 people (95% CI, 1.53-1.64 per 100 000 people) to 0.89 per 100 000 people (95% CI, 0.86-0.92 per 100 000 people). This corresponds to a 25% relative increase in case-fatality rate. Examination by stage showed a decrease in the incidence of localized disease at diagnosis of 40% from 2.65 per 100 000 people (95% CI, 2.44-2.89 per 100 000 people) to 1.60 per 100 000 people (95% CI, 1.45-1.76 per 100 000 people) from 1986 to 2002 and of 45% from 2.15 per 100 000 people (95% CI, 1.98-2.34 per 100 000 people) to 1.19 per 100 000 people (95% CI, 1.08-1.31 per 100 000 people) from 2005 to 2018. Distribution of larynx cancer by subsite remained stable, with most cases affecting the glottis. The proportion of patients receiving surgery as their first course of treatment decreased regardless of stage at presentation. CONCLUSIONS AND RELEVANCE: In this cohort study, between 1986 and 2018, the incidence of larynx cancer decreased in the US, primarily because of the decrease in the incidence of localized disease. Mortality did not decrease similarly, resulting in an increased case-fatality rate overall.

Encouraging earlier referrals for cancer concern, focusing resources where larynx cancer rates remain highest, renewing attention to research on new biologic causes of different tumor biologic characteristics, and conducting trials to directly compare treatments may help reverse this trend.

Dixon, S. B., et al. (2021). "Cardiac biomarkers and association with subsequent cardiomyopathy and mortality among adult survivors of childhood cancer: A report from the St. Jude Lifetime Cohort." Cancer **127**(3): 458-466.

BACKGROUND: Survivors of childhood cancer exposed to cardiotoxic therapies are at significant cardiovascular risk. The utility of cardiac biomarkers for identifying the risk of future cardiomyopathy and mortality is unknown. METHODS: N-terminal pro-B-type natriuretic peptide (NT-proBNP) and cardiac troponin T (cTnT) were assessed in 1213 adults 10 or more years from a childhood cancer diagnosis; 786 were exposed to anthracycline chemotherapy and/or chest-directed radiation therapy (RT). NT-proBNP values above age- and sex-specific 97.5th percentiles were considered abnormal. Generalized linear models estimated cross-sectional associations between abnormal NT-proBNP and anthracycline or chest RT doses as risk ratios with 95% confidence intervals (CIs). A Poisson distribution estimated rates and a Cox proportional hazards model estimated hazard ratios (HRs) for future cardiac events and death. RESULTS: At a median age of 35.5 years (interquartile range, 29.8-42.5 years), NT-proBNP and cTnT were abnormal in 22.5% and 0.4%, respectively. Exposure to chest RT and exposure to anthracycline chemotherapy were each associated with a dose-dependent increased risk for abnormal NT-proBNP (P for trend <.0001). Among exposed survivors with no history of Common Terminology Criteria for Adverse Events-graded cardiomyopathy and with normal systolic function, survivors with abnormal NT-proBNP had higher rates per 1000 person-years of cardiac mortality (2.93 vs 0.96; P < .0001) and future cardiomyopathy (32.10 vs 15.98; P < .0001) and an increased risk of future cardiomyopathy (HR, 2.28; 95% CI, 1.28-4.08) according to a multivariable assessment. CONCLUSIONS: Abnormal NT-proBNP values were prevalent and, among survivors who were exposed to cardiotoxic therapy but did not have a history of cardiomyopathy or current systolic dysfunction, identified those at increased risk for future cardiomyopathy. Further longitudinal studies are needed to confirm this novel finding.

D'Journo, X. B., et al. (2021). "Risk Prediction Model of 90-Day Mortality After Esophagectomy for Cancer." JAMA Surg **156**(9): 836-845.

IMPORTANCE: Ninety-day mortality rates after esophagectomy are an indicator of the quality of surgical oncologic management. Accurate risk prediction based on large data sets may aid patients and surgeons in making informed decisions. OBJECTIVE: To develop and validate a risk prediction model of death within 90 days after esophagectomy for cancer using the International Esodata Study Group (IESG) database, the largest existing prospective, multicenter cohort reporting standardized postoperative outcomes. DESIGN, SETTING, AND PARTICIPANTS: In this diagnostic/prognostic study, we performed a retrospective analysis of patients from 39 institutions in 19 countries between January 1, 2015, and December 31, 2019. Patients with esophageal cancer were randomly assigned to development and validation cohorts. A scoring system that predicted death within 90 days based on logistic regression beta coefficients was conducted. A final prognostic score was determined and categorized into homogeneous risk groups that predicted death within 90 days. Calibration and discrimination tests were assessed between cohorts. EXPOSURES: Esophageal resection for cancer of the esophagus and gastroesophageal junction. MAIN OUTCOMES AND MEASURES: All-cause postoperative 90-day mortality. RESULTS: A total of 8403 patients (mean [SD] age, 63.6 [9.0] years; 6641 [79.0%] male) were included. The 30-day mortality rate was 2.0% (n = 164), and the 90-day mortality rate was 4.2% (n = 353). Development (n = 4172) and validation (n = 4231) cohorts were randomly assigned. The multiple logistic regression model identified 10 weighted point variables factored into the prognostic score: age, sex, body mass index, performance status, myocardial infarction, connective tissue disease, peripheral vascular disease, liver disease, neoadjuvant treatment, and hospital volume. The prognostic scores were categorized into 5 risk groups: very low risk (score, >/=1; 90-day mortality, 1.8%), low risk (score, 0; 90-day mortality, 3.0%), medium risk (score, -1 to -2; 90-day mortality, 5.8%), high risk (score, -3 to -4: 90-day mortality, 8.9%), and very high risk (score, </=-5; 90-day mortality, 18.2%). The model was supported by nonsignificance in the Hosmer-Lemeshow test. The discrimination (area under the receiver operating characteristic curve) was 0.68 (95% CI, 0.64-0.72) in the development cohort and 0.64 (95% CI, 0.60-0.69) in the validation cohort. CONCLUSIONS AND RELEVANCE: In this study, on the basis of preoperative variables, the IESG risk prediction model allowed stratification of an individual patient's risk of death within 90 days after esophagectomy. These data suggest that this model can help in the decision-making process when esophageal cancer surgery is being considered and in informed consent.

Dobiesz, B. A., et al. (2022). "Colorectal cancer mortality in women: trend analysis in Brazil and its regions and states." Rev Bras Enferm **75**(2): e20210751.

OBJECTIVES: to analyze colorectal cancer mortality trends in women in Brazil and its regions and states. METHODS: ecological, time-series study with trend analysis of deaths caused by colorectal cancer in women in Brazil and its regions and states between 2008 and 2019. Polynomial regression was used to treat the data. RESULTS: 48,225 deaths of women caused by colorectal cancer were examined. There was an increasing mortality trend in Brazilian women, with regional differences that resulted from socioeconomic, political, and cultural inequalities. The South Region stood out with the highest rate (7.32) in 2008, which increased to 8.65 in 2019, followed by the Southeast Region, whose rates were 6.72 and 9.05 in 2008 and 2019, respectively. CONCLUSIONS: colorectal cancer mortality increased, which indicates the need to expand public policies oriented toward screening and early diagnosis of colorectal cancer in women.

Dociak-Salazar, E., et al. (2022). "Gait speed as a predictor of mortality in older men with cancer: A longitudinal study in Peru." Heliyon **8**(2): e08862.

BACKGROUND: Given the increase in incidence and mortality from cancer in recent years in Latin America and Peru, it is necessary to identify frailty older adults at higher risk of disability, hospitalizations and mortality. However, its measure is complex and requires time. For this reason, it has been proposed that frailty can be evaluated by a single measure, as gait speed. We aimed to evaluate the role of gait speed as a predictor of mortality in older men with cancer in Peru. METHODS: A prospective cohort study was carried out that included military veterans (aged 60 years and older) with an oncological diagnosis evaluated at the Centro Medico Naval in Peru during the period 2013-2015. Slow gait speed was defined as <0.8 m/s. All-cause mortality was recorded during a 2-year follow-up. Sociodemographic characteristics, medical and personal history, and functional assessment measures were collected. We performed Cox regression analysis to calculate hazard ratios with their respective 95% confidence intervals. RESULTS: 922 older men were analyzed from 2013 to 2015, 56.9% (n = 525) of whom were >70 years of age. 41.3% (n = 381) had slow gait speed with a mortality incidence of 22.9% (n = 211) at the end of follow-up. The most frequent types of cancer in the participants who died were of the lung and airways (26.1%), liver and bile ducts (23.2%), and lymphomas and leukemias (16.6%). In the adjusted Cox regression analysis, we found that slow gait speed was a risk factor for mortality in older men with cancer (adjusted hazard ratio = 1.55; 95% confidence interval: 1.21-2.23). CONCLUSIONS: Slow gait speed was associated with an increased risk of mortality in older men with cancer. Gait speed could represent a simple, useful, inexpensive, rapidly applicable marker of frailty for the identification of older men at higher risk of mortality. Gait speed could be useful in low- and middle-income countries, and in rural areas with limited access to health services.

Dodiyi-Manuel, A., et al. (2022). "Cancer Related Mortality in Port Harcourt, Southern Nigeria." West Afr J Med **39**(3): 237-240.

BACKGROUND: Globally, cancer is a leading cause of death and source of resistance to increasing life expectancy. In 2019, the World Health Organisation estimated cancer as the first or second leading cause of death before the age of 70 in 112 countries and third or fourth in 23 other countries. Despite the fact that cancer has been recognized as a public health problem, there is paucity of data on cancer mortality in Nigeria. The aim of this study is to determine the pattern of cancer mortality at the University of Port Harcourt Teaching Hospital. MATERIALS AND METHODS: This is a 5 year retrospective study of all cancer related deaths at the University of Port Harcourt Teaching Hospital from 1st January, 2014 to 31st December, 2018. Relevant data were extracted and analyzed using Statistical Package for Social Sciences version 24. RESULTS: There were 4449 deaths during the period under review, of which 293 were cancer related deaths, giving a mortality rate of 6.59%. There were 114 males and 179 females giving a male to female ratio of 1:1.6. Cancer of the breast was the most common cause of cancer death and accounted for 61 (20.8%) deaths within the study period. CONCLUSION: Cancer is a major cause of mortality in Nigeria. Cancer of the breast is the leading cause of cancer mortality in females and overall while cancer of the prostate remains the commonest in men.

Domanchuk, T. I., et al. (2021). "Comparative Analysis of Incidence and Mortality from Gastric Cancer among the Population of Europe and Ukraine." Wiad Lek **74**(3 cz 2): 596-602.

OBJECTIVE: The aim: To study the incidence and mortality from gastric cancer in Europe and Ukraine. PATIENTS AND METHODS: Materials and methods: Using statistical and medico-epidemiological methods, the analysis of the database of the National Cancer Registry of Gastric Cancer and Global cancer statistics 2018. RESULTS: Results: Gastric cancer remains an important cancer worldwide and is responsible for over 1,000,000 new cases in 2018 and an estimated 783,000 deaths, making it the fifth most frequently diagnosed cancer and the third

leading cause of cancer death. Among men, it is the most commonly diagnosed cancer and the leading cause of cancer death in several countries of Europe, including Ukraine. Incidence rates are markedly elevated in Central/Eastern Europe, whereas the rates in Northern Europe are generally low. In the dynamics of the last decade, the primary incidence of gastric cancer has shown a tendency to decrease, as in Ukraine, from 25.5 per 100 thousand population in 2010 to 19.5 similar cases in 2019, which is -23.5% visibility) and in the Chernivtsi region (on -22.3% visibility). In Ukraine, as well as in Europe, the incidence and mortality of gastric cancer in men is 2 times higher than in women. CONCLUSION: Conclusions: Incidence and mortality rates have declined in Europe in the past decades. Trends in the ten-year dynamics of reducing the incidence and mortality of gastric cancer in Ukraine prove the effectiveness and feasibility of introducing preventive measures at the state level in the future.

Dominguez-Rojas, J. A., et al. (2022). "Association of Cancer Diagnosis and Therapeutic Stage With Mortality in Pediatric Patients With COVID-19, Prospective Multicenter Cohort Study From Latin America." Front Pediatr **10**: 885633.

BACKGROUND: Children with cancer are at risk of critical disease and mortality from COVID-19 infection. In this study, we describe the clinical characteristics of pediatric patients with cancer and COVID-19 from multiple Latin American centers and risk factors associated with mortality in this population. METHODS: This study is a multicenter, prospective cohort study conducted at 12 hospitals from 6 Latin American countries (Argentina, Bolivia, Colombia, Ecuador, Honduras and Peru) from April to November 2021. Patients younger than 14 years of age that had an oncological diagnosis and COVID-19 or multisystemic inflammatory syndrome in children (MIS-C) who were treated in the inpatient setting were included. The primary exposure was the diagnosis and treatment status, and the primary outcome was mortality. We defined "new diagnosis" as patients with no previous diagnosis of cancer, "established diagnosis" as patients with cancer and ongoing treatment and "relapse" as patients with cancer and ongoing treatment that had a prior cancer-free period. A frequentist analysis was performed including a multivariate logistic regression for mortality. RESULTS: Two hundred and ten patients were included in the study; 30 (14%) died during the study period and 67% of patients who died were admitted to critical care. Demographics were similar in survivors and non-survivors. Patients with low weight for age (<-2SD) had higher mortality (28 vs. 3%, p = 0.019). There was statistically significant difference of mortality between patients with new diagnosis (36.7%), established diagnosis (1.4%) and relapse (60%), (p <0.001). Most patients had hematological cancers (69%) and they had higher mortality (18%) compared to solid tumors (6%, p= 0.032). Patients with concomitant bacterial infections had higher mortality (40%, p = 0.001). MIS-C, respiratory distress, cardiovascular symptoms, altered mental status and acute kidney injury on admission were associated with higher mortality. Acidosis, hypoxemia, lymphocytosis, severe neutropenia, anemia and thrombocytopenia on admission were also associated with mortality. A multivariate logistic regression showed risk factors associated with mortality: concomitant bacterial infection OR 3 95%CI (1.1-8.5), respiratory symptoms OR 5.7 95%CI (1.7-19.4), cardiovascular OR 5.2 95%CI (1.2-14.2), new cancer diagnosis OR 12 95%CI (1.3-102) and relapse OR 25 95%CI (2.9-214). CONCLUSION: Our study shows that pediatric patients with new onset diagnosis of cancer and patients with relapse have higher odds of all-cause mortality in the setting of COVID-19. This information would help develop an early identification of patients with cancer and COVID-19 with higher risk of mortality.

Dong, W., et al. (2022). "Variation in and Factors Associated With US County-Level Cancer Mortality, 2008-2019." JAMA Netw Open **5**(9): e2230925.

IMPORTANCE: The association between cancer mortality and risk factors may vary by geography. However, conventional methodological approaches rarely account for this variation. OBJECTIVE: To identify geographic variations in the association between risk factors and cancer mortality. DESIGN, SETTING, AND PARTICIPANTS: This geospatial cross-sectional study used county-level data from the National Center for Health Statistics for individuals who died of cancer from 2008 to 2019. Risk factor data were obtained from County Health Rankings & Roadmaps, Health Resources and Services Administration, and Centers for Disease Control and Prevention. Analyses were conducted from October 2021 to July 2022. MAIN OUTCOMES AND MEASURES: Conventional random forest models were applied nationwide and by US region, and the geographical random forest model (accounting for local variation of association) was applied to assess associations between a wide range of risk factors and cancer mortality. RESULTS: The study included 7 179 201 individuals (median age, 70-74 years; 3 409 508 women [47.5%]) who died from cancer in 3108 contiguous US counties during 2008 to 2019. The mean (SD) county-level cancer mortality rate was 177.0 (26.4) deaths per 100 000 people. On the basis of the variable importance measure, the random forest models identified multiple risk factors associated with

cancer mortality, including smoking, receipt of Supplemental Nutrition Assistance Program (SNAP) benefits, and obesity. The geographical random forest model further identified risk factors that varied at the county level. For example, receipt of SNAP benefits was a high-importance factor in the Appalachian region, North and South Dakota, and Northern California; smoking was of high importance in Kentucky and Tennessee; and female-headed households were high-importance factors in North and South Dakota. Geographic areas with certain high-importance risk factors did not consistently have a corresponding high prevalence of the same risk factors. CONCLUSIONS AND RELEVANCE: In this cross-sectional study, the associations between cancer mortality and risk factors varied by geography in a way that did not correspond strictly to risk factor prevalence. The degree to which other place-specific characteristics, observed and unobserved, modify risk factor effects should be further explored, and this work suggests that risk factor importance may be a preferable paradigm for selecting cancer control interventions compared with risk factor prevalence.

Dongchen, X., et al. (2022). "Risk of mortality and other adverse outcomes from myocardial infarction in cancer survivors: a meta-analysis." Int J Clin Oncol.

BACKGROUND AND PURPOSE: Myocardial infarction (MI) is an acute cardiovascular disease that can increase prognosis risks such as arrhythmia, heart failure, shock, etc. Studies have found that even well-controlled coexistence of cancer could affect the quality of life in MI patients. However, the prognostic impact of cancer on MI patients is controversial. This meta-analysis aimed to assess the influence of cancer on the risk of future all-cause mortality, cardiovascular mortality, and major adverse cardiovascular and cerebrovascular events (MACCE) in MI patients. METHODS: The Embase, PubMed, and Cochrane libraries were searched for cohort studies and case-control from inception to May 2022. The quality of the included pieces of literature was assessed using the Newcastle-Ottawa Quality Assessment Scale (NOS). All statistical analyses were performed using Stata statistical software versions 14.0 and 16.0. Sensitivity analysis assessed the robustness of the results, and funnel plots and Egger's tests evaluated the publication bias. RESULTS: A total of 10 studies were included, covering 7,210,530 participants. Summary analyses show that compared with non-cancer patients, cancer increased the risk of long-term all-cause mortality in MI patients (HR 1.58, 95% CI 1.36-1.84, I(2) = 94.2%). However, no significant difference was observed in the risk of cardiovascular mortality (HR 1.18, 95% CI 0.91-1.54, I(2) = 52.4%) or MACCE (HR 1.26, 95% CI 0.94-1.70, I(2) = 99.2%). In subgroup analysis, cancer was associated with the risk of recurrent MI (HR 1.18, 95% CI 1.03-1.34, I(2) = 88.8%), and major bleeding (HR 2.01, 95% CI 1.60-2.52, I(2) = 93.1%), with no significant difference in the risk of stroke (HR 1.11, 95% CI 0.97-1.27, I(2) = 85.1%). CONCLUSION: This meta-analysis shows that cancer increases the risk of all-cause mortality, recurrent MI, and major bleeding in MI patients but is not associated with the risk of cardiovascular death. Therefore, comprehensive multidisciplinary management and monitoring of potential future adverse events in MI patients with cancer are needed. SYSTEMATIC REVIEW REGISTRATION: The meta-analysis was registered in the International Register of Prospective Systematic Reviews (NO. CRD42022332775).

Donkers, H., et al. (2021). "The impact of socioeconomic deprivation on mortality in cervical cancer patients in Cornwall (England)." Eur J Cancer Care (Engl) **30**(5): e13463.

OBJECTIVES: To assess the association between risk factors, including socioeconomic deprivation, and mortality, recurrence and chemo- or radiation toxicity in cervical cancer patients. METHODS: Retrospective study of cervical cancer patients diagnosed between January 2007 and July 2018. Patient characteristics and mortality data, including recurrence, were assessed, together with socioeconomic deprivation measures evaluated using the English Indices of Multiple Deprivation. Markov multi-state models were used to model mortality and recurrence, and logistic regression models were used to model chemo- or radiation toxicity. RESULTS: Included were 243 women with a median age of 49 years. A total of 57 patients died (23%), of which 41 due to cervical cancer, and 21 (9%) had recurrent disease. Hazard ratios (HR) showed no evidence of association between socioeconomic deprivation and cancer-specific hazard of mortality from diagnosis or recurrence, hazard of mortality due to other causes or hazard of cancer recurrence. Furthermore, there was no evidence of association between socioeconomic deprivation and chemo- or radiation toxicity (bowel, bladder or vaginal stenosis). CONCLUSIONS: No associations were found between socioeconomic deprivation and cancer mortality or recurrence in cervical cancer patients in the population of Cornwall. In addition, no association was found between socioeconomic deprivation and chemo- or radiation toxicity.

Dorantes-Acosta, E., et al. (2022). "Mortality in children with cancer and SARS-CoV-2 in Latin America: A systematic review." Front Pediatr **10**: 928612.

The new COVID-19 disease is caused by a novel coronavirus (SARS-CoV-2), that probably originated in Wuhan, China, and has currently infected 505,817,953 people and caused 6,213,876 deaths in the world. On the American continent, 152,265,980 cases and 2,717,108 deaths have been reported to WHO (World Health Organization). The Latin America and the Caribbean (LAC) region presents an epidemiological challenge due to its population's heterogeneity and socioeconomic inequality. A particularly vulnerable population is that of children with cancer, and their mortality from COVID-19 has been reported to be 3.6% globally. This work aimed to study the lethality of SARS-CoV-2 infection in children with cancer in the Latin American region. Our objective was to systematically review published scientific literature and search hospital databases in Latin America to explore mortality in this region. A median of mortality of 9.8% was found in the articles analyzed. In addition, we collected five databases from Latin American hospitals. We concluded that there was an underestimation in the mortality registry of this group of patients in the analyzed region. Therefore, although the causes are unknown, it is necessary to strengthen the case-reporting system to determine the reality in complex and particular areas such as Latin America.

Duffy, S. W., et al. (2021). "Beneficial Effect of Consecutive Screening Mammography Examinations on Mortality from Breast Cancer: A Prospective Study." Radiology **299**(3): 541-547.

Background Previously, the risk of death from breast cancer was analyzed for women participating versus those not participating in the last screening examination before breast cancer diagnosis. Consecutive attendance patterns may further refine estimates. Purpose To estimate the effect of participation in successive mammographic screening examinations on breast cancer mortality. Materials and Methods Participation data for Swedish women eligible for screening mammography in nine counties from 1992 to 2016 were linked with data from registries and regional cancer centers for breast cancer diagnosis, cause, and date of death (Uppsala University ethics committee registration number: 2017/147). Incidence-based breast cancer mortality was calculated by whether the women had participated in the most recent screening examination prior to diagnosis only (intermittent participants), the penultimate screening examination only (lapsed participants), both examinations (serial participants), or neither examination (serial nonparticipants). Rates were analyzed with Poisson regression. We also analyzed incidence of breast cancers proving fatal within 10 years. Results Data were available for a total average population of 549 091 women (average age, 58.9 years +/- 6.7 [standard deviation]). The numbers of participants in the four groups were as follows: serial participants, 392 135; intermittent participants, 41 746; lapsed participants, 30 945; and serial nonparticipants, 84 265. Serial participants had a 49% lower risk of breast cancer mortality (relative risk [RR], 0.51; 95% CI: 0.48, 0.55; P < .001) and a 50% lower risk of death from breast cancer within 10 years of diagnosis (RR, 0.50; 95% CI: 0.46, 0.55; P < .001) than serial nonparticipants. Lapsed and intermittent participants had a smaller reduction. Serial participants had significantly lower risk of both outcomes than lapsed or intermittent participants. Analyses correcting for potential biases made little difference to the results. Conclusion Women participating in the last two breast cancer screening examinations prior to breast cancer diagnosis had the largest reduction in breast cancer death. Missing either one of the last two examinations conferred a significantly higher risk. Published under a CC BY 4.0 license. Online supplemental material is available for this article. See also the editorial by Stephen A. Feig in this issue.

Duggan, C., et al. (2021). "National health system characteristics, breast cancer stage at diagnosis, and breast cancer mortality: a population-based analysis." Lancet Oncol **22**(11): 1632-1642.

BACKGROUND: In some countries, breast cancer age-standardised mortality rates have decreased by 2-4% per year since the 1990s, but others have yet to achieve this outcome. In this study, we aimed to characterise the associations between national health system characteristics and breast cancer age-standardised mortality rate, and the degree of breast cancer downstaging correlating with national age-standardised mortality rate reductions. METHODS: In this population-based study, national age-standardised mortality rate estimates for women aged 69 years or younger obtained from GLOBOCAN 2020 were correlated with a broad panel of standardised national health system data as reported in the WHO Cancer Country Profiles 2020. These health system characteristics include health expenditure, the Universal Health Coverage Service Coverage Index (UHC Index), dedicated funding for early detection programmes, breast cancer early detection guidelines, referral systems, cancer plans, number of dedicated public and private cancer centres per 10 000 patients with cancer, and pathology services. We tested for differences between continuous variables using the non-parametric Kruskal-Wallis test, and for categorical variables using the Pearson chi(2) test. Simple and multiple linear regression analyses were fitted to identify associations between health system characteristics and age-standardised breast cancer

mortality rates. Data on TNM stage at diagnosis were obtained from national or subnational cancer registries, supplemented by a literature review of PubMed from 2010 to 2020. Mortality trends from 1950 to 2016 were assessed using the WHO Cancer Mortality Database. The threshold for significance was set at a p value of 0.05 or less. FINDINGS: 148 countries had complete health system data. The following variables were significantly higher in high-income countries than in low-income countries in unadjusted analyses: health expenditure (p=0.0002), UHC Index (p<0.0001), dedicated funding for early detection programmes (p=0.0020), breast cancer early detection guidelines (p<0.0001), breast cancer referral systems (p=0.0030), national cancer plans (p=0.014), cervical cancer early detection programmes (p=0.0010), number of dedicated public (p<0.0001) and private (p=0.027) cancer centres per 10 000 patients with cancer, and pathology services (p<0.0001). In adjusted multivariable regression analyses in 141 countries, two health system characteristics were significantly associated with lower age-standardised mortality rates: higher UHC Index levels (beta=-0.12, 95% CI -0.16 to -0.08) and increasing numbers of public cancer centres (beta=-0.23, -0.36 to -0.10). These findings indicate that each unit increase in the UHC Index was associated with a 0.12-unit decline in age-standardised mortality rates, and each additional public cancer centre per 10 000 patients with cancer was associated with a 0.23-unit decline in age-standardised mortality rate. Among 35 countries with available breast cancer TNM staging data, all 20 that achieved sustained mean reductions in age-standardised mortality rate of 2% or more per year for at least 3 consecutive years since 1990 had at least 60% of patients with invasive breast cancer presenting as stage I or II disease. Some countries achieved this reduction without most women having access to population-based mammographic screening. INTERPRETATION: Countries with low breast cancer mortality rates are characterised by increased levels of coverage of essential health services and higher numbers of public cancer centres. Among countries achieving sustained mortality reductions, the majority of breast cancers are diagnosed at an early stage, reinforcing the value of clinical early diagnosis programmes for improving breast cancer outcomes. FUNDING: None.

Dulskas, A., et al. (2021). "Trends in Incidence and Mortality of Primary Liver Cancer in Lithuania 1998-2015." Int J Environ Res Public Health **18**(3).

Background: Recently, reports have suggested that rates of liver cancer have increased during the last decades in developed countries; increasing hepatocellular carcinoma and cholangiocarcinoma rates were reported. The aim of this study was to examine time trends in incidence and mortality rates of liver cancer for the period of 1998-2015 in Lithuania by sex, age, and histology. Methods: We examined the incidence of liver cancer from 1998 to 2015 using data from the Lithuanian Cancer Registry. Age-standardized incidence rates were calculated by sex, age, and histology. Trends were analyzed using the Joinpoint Regression Program to estimate the annual percent change. Results: A total of 3086 primary liver cancer cases were diagnosed, and 2923 patients died from liver cancer. The total number of liver cancer cases changed from 132 in 1998 to 239 in 2015. Liver cancer incidence rates changed during the study period from 5.02/100,000 in 1998 to 10.54/100,000 in 2015 in men and from 2.43/100,000 in 1998 to 6.25/100,000 in 2015 in women. Annual percentage changes (APCs) in the age-standardized rates over this period were 4.5% for incidence and 3.6% for mortality. Hepatocellular cancer incidence rates were stable from 1998 to 2005 (APC -5.9, p = 0.1) and later increased by 6.7% per year (p < 0.001). Intrahepatic ductal carcinoma incidence increased by 8.9% per year throughout the study period. The rise in incidence was observed in all age groups; however, in age groups < 50 and between 70 and 79 years, observed changes were not statistically significant. For mortality, the significant point of trend change was detected in 2001, where after stable mortality, rates started to increase by 2.4% per year. Conclusions: Primary liver cancer incidence and mortality increased in both sexes in Lithuania. The rise om incidence was observed in both sexes and main histology groups. The increasing incidence trend may be related to the prevalence of main risk factors (alcohol consumption, hepatitis B and C infections. and diabetes).

Dupont-Lucas, C., et al. (2022). "Increased risk of cancer and mortality in a large French population-based paediatric-onset inflammatory bowel disease retrospective cohort." J Crohns Colitis.

BACKGROUND AND AIMS: Paediatric-onset IBD (pIBD) is associated with an increased risk of cancer and mortality in adulthood. The aims of this study were to measure the incidence of cancer and mortality in patients with pIBD and identify factors associated with mortality and cancer. METHODS: All patients diagnosed with Crohn's disease (CD) or ulcerative colitis (UC) before the age of 17 years between 1988 and 2011 in the EPIMAD registry, were retrospectively followed until 2013 for cancer and 2015 for mortality. Standardized incidence (SIR) and mortality ratios (SMR) were estimated compared to the general population. Cox regression was used to compare effect of exposures on cancer and mortality among IBD patients. RESULTS: We included 1,344 patients (52% males, 75% CD), totalising 12,957

patient-years for cancer incidence and 18,817 patient-years for mortality. There were 14 cases of cancer (median age 27.8 years) and 15 deaths (median age 28.8 years). The incidence of cancer and of mortality were increased compared to the general population: all-cancer SIR = 2.7 (95%CI: 1.5-4.8), SMR = 1.7 (95%CI: 1.0-2.8). Colorectal cancer had the highest SIR and SMR: SIR=41.2 (95%CI: 17.2-99.0), SMR=70.4 (95%CI 22.7-218.2). Cancer was associated with (HR, 95%CI): active smoking at diagnosis (5.5, 1.8-16.5), p=0.002, any exposure to anti-TNF (6.1, 1.7-22.3), p=0.0065 and exposure to combination therapy (7.4, 1.8-29.7), p=0.0047. Mortality was associated with extraintestinal manifestations (HR 4.9 (95% CI: 1.7-13.8), p=0.003). CONCLUSIONS: In this large population-based cohort, patients with pIBD had an increased risk of both cancer (2.7-fold) and mortality (1.7-fold), particularly for colorectal cancer.

Duran-Romero, A. J., et al. (2022). "Trends in mortality rates for oral and oropharyngeal cancer in Spain, 1979-2018." Oral Dis **28**(2): 336-344.

OBJECTIVE: To analyse mortality rate trends in Spain for oral cavity and oropharyngeal cancer (OCOPC) from 1979 to 2018, evaluating differences between oral cavity cancer (OCC) and oropharyngeal cancer (OPC). MATERIALS AND METHODS: Death certificates and mid-year population data were collected from the Spanish National Statistics Institute. Age-standardized mortality rates were calculated using the direct method. Joinpoint regressions were used to identify significant changes in mortality trends. Independent effects of age, period and cohort (APC) were estimated. RESULTS: A total of 52,057 deaths were registered from OCOPC, 38,988 from OCC and 13,069 from OPC between 1979 and 2018. While OCC mortality rates declined, OCOPC rates increased slightly and OPC significantly. OCC and OPC mortality reached their highest values between 1979 and 1992, when OCC rates began to decrease in males and OPC levelled off until 2018. Lip cancer suffered the highest drop. APC models showed a mortality increase in males and females from 40 to 45 and 50 to 55 years of age, respectively. CONCLUSIONS: Favourable OCC mortality trends was plausibly influenced by decreased tobacco/alcohol consumption, while OPC rise was probably associated with increased human papillomavirus infection. The importance of closely monitoring these cancers by age group, sex and location, and continuing with preventive measures against known risk factors, is highlighted.

Durham, D. D., et al. (2021). "Do competing causes of mortality contribute to overdiagnosis in lung cancer screening?" Lung Cancer **153**: 21-24.

Overdiagnosed cancers are those that are screen-detected but never would have been symptomatic during patients' lifetimes. Indolent cancers are overdiagnosed cancers. Non-indolent cancers can be overdiagnosed when patients die of causes other than the screen-detected cancer and would have, in the absence of screening, been asymptomatic and undiagnosed at the time of death. This is termed competing cause of mortality (CCM) overdiagnosis. Deaths soon after screen detection may represent CCM overdiagnosis. We examined time from screen-detection to death among the 35 participants in the National Lung Screening Trial (NLST) low-dose computed tomography arm with screen-detected lung cancer and died of non-lung-cancer causes. Seven participants died within 6 months, and 20 died more than 24 months after diagnosis. Deaths due to non-lung cancer causes soon after screen detection were uncommon, arguing against widespread CCM overdiagnosis in the NLST. However, CCM overdiagnosis is likely more frequent in community-based screening given the higher prevalence of comorbidities.

Dursun, F., et al. (2022). "Absolute Prostate Specific Antigen after 6 Months of Androgen Deprivation Therapy Is a Predictor of Overall and Cancer-Specific Mortality in Men with Hormone-Sensitive Prostate Cancer." J Urol **208**(2): 317-324.

PURPOSE: We sought to determine if absolute prostate specific antigen (PSA) value after 6 months of androgen deprivation therapy (ADT) is predictive of subsequent survival in patients with prostate adenocarcinoma. MATERIALS AND METHODS: We performed a retrospective review of men receiving care within the Veterans Health Administration who initiated ADT for prostate adenocarcinoma. We used low- (</=0.2 ng/ml), intermediate- (>0.2 to 4 ng/ml) and high-risk (>4 ng/ml) absolute PSA values after 6-9 months of ADT, previously described in Southwest Oncology Group trial 9346. The primary endpoints were all-cause mortality and prostate cancer-specific mortality (PCSM). Kaplan-Meier survival curves for each PSA category were estimated and log-rank test was conducted. We employed Cox regression analysis adjusted for covariates and inverse propensity score weights associated with PSA categories to estimate the PSA category association with PCSM and all-cause mortality. RESULTS: We identified 9,170 patients in our cohort. Following ADT induction, 3,508 patients had low, 3,419 had intermediate and 2,243 had high PSA values. Two- and 5-year survival rates for low, intermediate and high PSA groups were 93.9% and 85.2% vs 88.6% and 71.2% vs 63.6% and 38.6%, respectively (p <0.0001). Patients in the high and

intermediate PSA categories had a 15-fold and 3-fold higher risk of PCSM compared to those with PSA <0.2 ng/ml (p <0.0001). CONCLUSIONS: Absolute PSA in hormone-sensitive prostate cancer after 6-9 months of ADT is a predictor of overall mortality and PCSM. This measure can rapidly assess the efficacy of new interventions in phase 2 clinical trials.

Duvvuri, A., et al. (2021). "Risk of Colorectal Cancer and Cancer Related Mortality After Detection of Low-risk or High-risk Adenomas, Compared With No Adenoma, at Index Colonoscopy: A Systematic Review and Meta-analysis." Gastroenterology **160**(6): 1986-1996 e1983.

BACKGROUND & AIMS: The risk of metachronous colorectal cancer (CRC) among patients with no adenomas, low-risk adenomas (LRAs), or high-risk adenomas (HRAs), detected at index colonoscopy, is unclear. We performed a systematic review and meta-analysis to compare incidence rates of metachronous CRC and CRC-related mortality after a baseline colonoscopy for each group. METHODS: We searched the PubMed, Embase, Google Scholar, and Cochrane databases for studies that reported the incidence of CRC and adenoma characteristics after colonoscopy. The primary outcome was odds of metachronous CRC and CRC-related mortality per 10,000 person-years of follow-up after baseline colonoscopy for all the groups. RESULTS: Our final analysis included 12 studies with 510,019 patients (mean age, 59.2 +/- 2.6 years; 55% male; mean duration of follow up, 8.5 +/- 3.3 years). The incidence of CRC per 10,000 person-years was marginally higher for patients with LRAs compared to those with no adenomas (4.5 vs 3.4; odds ratio [OR], 1.26; 95% CI, 1.06-1.51; I(2)=0), but significantly higher for patients with HRAs compared to those with no adenoma (13.8 vs 3.4; odds ratio [OR], 2.92; 95% CI, 2.31-3.69; I(2)=0) and patients with HRAs compared to LRAs (13.81 vs 4.5; OR, 2.35; 95% CI, 1.72-3.20; I(2)=55%). However, the CRC-related mortality per 10,000 person-years did not differ significantly for patients with LRAs compared to no adenomas (OR, 1.15; 95% CI, 0.76-1.74; I(2)=0) but was significantly higher in persons with HRAs compared with LRAs (OR, 2.48; 95% CI, 1.30-4.75; I(2)=38%) and no adenomas (OR, 2.69; 95% CI, 1.87-3.87; I(2)=0). CONCLUSIONS: The results of this systematic review and meta-analysis demonstrate that the risk of metachronous CRC and mortality is significantly higher for patients with HRAs, but this risk is very low in patients with LRAs, comparable to patients with no adenomas. Follow-up of patients with LRAs detected at index colonoscopy should be the same as for persons with no adenomas.

Dyba, T., et al. (2021). "The European cancer burden in 2020: Incidence and mortality estimates for 40 countries and 25 major cancers." Eur J Cancer **157**: 308-347.

INTRODUCTION: Europe is an important focus for compiling accurate and up-to-date world cancer statistics owing to its large share of the world's total cancer burden. This article presents incidence and mortality estimates for 25 major cancers across 40 individual countries within European areas and the European Union (EU-27) for the year 2020. METHODS: The estimated national incidence and mortality rates are based on statistical methodology previously applied and verified using the most recently collected incidence data from 151 population-based cancer registries, mortality data and 2020 population estimates. RESULTS: Estimates reveal 4 million new cases of cancer (excluding non-melanoma skin cancer) and 1.9 million cancer-related deaths. The most common cancers are: breast in women (530,000 cases), colorectum (520,000), lung (480,000) and prostate (470,000). These four cancers account for half the overall cancer burden in Europe. The most common causes of cancer deaths are: lung (380,000), colorectal (250,000), breast (140,000) and pancreatic (130,000) cancers. In EU-27, the estimated new cancer cases are approximately 1.4 million in males and 1.2 million in females, with over 710,000 estimated cancer deaths in males and 560,000 in females. CONCLUSION: The 2020 estimates provide a basis for establishing priorities in cancer-control measures across Europe. The long-established role of cancer registries in cancer surveillance and the evaluation of cancer control measures remain fundamental in formulating and adapting national cancer plans and pan-European health policies. Given the estimates are built on recorded data prior to the onset of coronavirus disease 2019 (COVID-19), they do not take into account the impact of the pandemic.

Dzaye, O., et al. (2021). "Coronary artery calcium is associated with long-term mortality from lung cancer: Results from the Coronary Artery Calcium Consortium." Atherosclerosis **339**: 48-54.

BACKGROUND AND AIMS: Coronary artery calcium (CAC) scores have been shown to be associated with CVD and cancer mortality. The use of CAC scores for overall and lung cancer mortality risk prediction for patients in the Coronary Artery Calcium Consortium was analyzed. METHODS: We included 55,943 patients aged 44-84 years without known heart disease from the CAC Consortium. There were 1,088 cancer deaths, among which 231 were lung cancer, identified by death certificates with a mean follow-up of 12.2 +/- 3.9 years. Fine-and-Gray competing-risk regression was used for overall and lung cancer-

specific mortality, accounting for the competing risk of CVD death and after adjustment for CVD risk factors. Subdistribution hazard ratios (SHR) were reported. RESULTS: The mean age of all patients was 57.1 +/- 8.6 years, 34.9% were women, and 89.6% were white. Overall, CAC was strongly associated with cancer mortality. Lung cancer mortality increased with increasing CAC scores, with rates per 1000-person years of 0.2 (95% CI: 0.1-0.3) for CAC = 0 and 0.8 (95% CI: 0.6-1.0) for CAC >/=400. Compared with CAC = 0, hazards were increased for those with CAC >/=400 for lung cancer mortality [SHR: 1.7 (95% CI: 1.2-2.6)], which was driven by women [SHR: 2.3 (95% CI: 1.1-4.8)], but not significantly increased for men. Risks were higher in those with positive smoking history [SHR: 2.2 (95% CI: 1.2-4.2)], with associations driven by women [SHR: 4.0 (95% CI: 1.4-11.5)]. CONCLUSIONS: CAC scores were associated with increased risks for lung cancer mortality, with strongest associations for current and former smokers, especially in women. Used in conjunction with other clinical variables, our data pinpoint a potential synergistic use of CAC scanning beyond CVD risk assessment for identification of high-risk lung cancer screening candidates.

Fallara, G., et al. (2021). "A drug comorbidity index to predict mortality in men with castration resistant prostate cancer." PLoS One **16**(7): e0255239.

BACKGROUND: The Charlson Comorbidity Index is a poor predictor of mortality in men with castration resistant prostate cancer (CRPC). To improve this prediction, we created a comorbidity index based on filled prescriptions intended to be used in registry-based studies. MATERIALS AND METHODS: In a population-based cohort of men with CPRC a drug comorbidity index (DCI-CRPC) was calculated based on prescriptions filled during a 365-day period before the date of CRPC diagnosis to predict mortality. Five risk categories for men with CRPC were defined based on PSA kinetics. Mortality rates were described by Kaplan-Meier curves. The predictive ability of the DCI-CRPC was compared in univariable models to that of the original DCI, derived from men in the general population, and to that of the Charlson Comorbidity Index. RESULTS: In 1,885 men with CRPC the median overall survival ranged from 3.0 years (95% confidence interval [CI] 2.8 to 3.4) in the first tertile of the DCI-CRPC, to 1.0 year (95% CI 0.9 to 1.1) in the third tertile of the DCI-CRPC. The index had higher discriminative ability (C-index 0.667) than the Charlson Comorbidity Index (C-index 0.508). The discriminative ability of the DCI-CRPC was highest in the subgroup with least aggressive cancer (C-index 0.651) and lowest in men with most aggressive cancer (C-index 0.618). The performance of the DCI-CRPC was comparable to that of the original DCI. CONCLUSION: Our newly created comorbidity index using filled prescriptions predicted death in men with CRPC better than the Charlson Comorbidity Index.

Fan, H. L., et al. (2022). "Liver transplantation with simultaneous splenectomy increases risk of cancer development and mortality in hepatocellular carcinoma patients." World J Gastrointest Surg **14**(9): 930-939.

BACKGROUND: Splenectomy has previously been found to increase the risk of cancer development, including lung, non-melanoma skin cancer, leukemia, lymphoma, Hodgkin's lymphoma, and ovarian cancer. The risk of cancer development in liver transplantation (LT) with simultaneous splenectomy remains unclear. AIM: To compare hepatocellular carcinoma (HCC) recurrence and de novo malignancy between patients undergoing LT with and without simultaneous splenectomy. METHODS: We retrospectively analyzed the outcomes of 120 patients with HCC within the University of California San Francisco criteria who received LT with (n = 35) and without (n = 85) simultaneous splenectomy in the Tri-Service General Hospital. Univariate and multivariate Cox regression analyses for cancer-free survival and mortality were established. The comparison of the group survival status and group cancer-free status was done by generating Kaplan-Meier survival curves and log-rank tests. RESULTS: The splenectomy group had more hepatitis C virus infection, lower platelet count, higher -fetoprotein level, and longer operating time. Splenectomy and age were both positive independent factors for prediction of cancer development [hazard ratio (HR): 2.560 and 1.057, respectively, $P < 0.05$]. Splenectomy and hypertension were positive independent factors for prediction of mortality. (HR: 2.791 and 2.813 respectively, $P < 0.05$). The splenectomy group had a significantly worse cancer-free survival (CFS) and overall survival (OS) curve compared to the non-splenectomy group (5-year CFS rates: 53.4% vs 76.5%, $P = 0.003$; 5-year OS rate: 68.1 vs 89.3, $P = 0.002$). CONCLUSION: Our study suggests that simultaneous splenectomy should be avoided as much as possible in HCC patients who have undergone LT.

Fan, Y., et al. (2022). "Intake of Soy, Soy Isoflavones and Soy Protein and Risk of Cancer Incidence and Mortality." Front Nutr **9**: 847421.

BACKGROUND AND AIMS: Associations between soy intake and risk of cancer have been evaluated in prospective observational studies with inconsistent results. Whether the potential anticancer effects offered by soy were attributed to soy isoflavones and soy protein still needs to be elucidated.

This study aimed to comprehensively quantify the association of soy, soy isoflavones and soy protein intake with risk of cancer incidence and cancer mortality by conducting a meta-analysis of all available studies. METHODS: PubMed, Embase, Web of Science, and Cochrane Library databases were searched up to 16 September 2021. Prospective cohort studies that examined the effect of soy, soy isoflavones and soy protein on cancer incidence and cancer mortality were identified. Random-effects models were used to pool the multivariable-adjusted relative risks (RRs) and corresponding 95% confidence intervals (CIs). The potential dose-response relations were explored by using generalized least-squares trend estimation. RESULTS: Eighty one prospective cohort studies were included in the meta-analysis. A higher intake of soy was significantly associated with a 10% reduced risk of cancer incidence (RR, 0.90; 95% CI, 0.83-0.96). Each additional 25 g/d soy intake decreased the risk of cancer incidence by 4%. Intake of soy isoflavones was inversely associated with risk of cancer incidence (RR, 0.94; 95% CI, 0.89-0.99), whereas no significant association was observed for soy protein. The risk of cancer incidence was reduced by 4% with each 10 mg/d increment of soy isoflavones intake. Similar inverse associations were also found for soy in relation to site-specific cancers, particularly lung cancer (RR, 0.67; 95%CI, 0.52-0.86) and prostate cancer (RR, 0.88; 95%CI, 0.78-0.99). However, high intake of soy, soy isoflavones and soy protein were not associated with cancer mortality. CONCLUSIONS: Higher intake of soy and soy isoflavones were inversely associated with risk of cancer incidence, which suggested that the beneficial role of soy against cancer might be primarily attributed to soy isoflavones. These findings support recommendations to include soy as part of a healthy dietary pattern for the prevention of cancer.

Fang, T., et al. (2022). "Proposed Models for Prediction of Mortality in Stage-I and Stage-II Gastric Cancer and 5 Years after Radical Gastrectomy." J Oncol **2022**: 4510000.

The current American Joint Committee on Cancer (AJCC) staging system provides limited information for patients with early death from stage-I and stage-II gastric cancer (GC) and death at >5 years after radical gastrectomy. The aim of this study was to construct nomogram models to predict the mortality risk of these patients. In this study, clinical and pathological data on patients who underwent curative gastrectomy at Harbin Medical University Cancer Hospital between 2000 and 2014 were retrospectively collected. Receiver operating characteristic analysis was used to screen for sensitive serum immune biomarkers to predict the risk of mortality death >5 years after radical gastrectomy (Group A) and risk of early death in stage-I and stage-II GC (Group B). The prediction model was constructed by combining serum immune markers with clinicopathological features by R Studio. We found that serum fibrinogen (F), systemic immune inflammation (SII), and pTNM stage were independent risk factors for prognosis in Group A ($P < 0.05$). F, SII, age, Borrmann type, and scope of gastrectomy were independent risk factors for prognosis in Group B ($P < 0.05$). The area under the curve of the predictive model in Groups A and B was 0.726 and 0.848, respectively. In conclusion, the predictive models of F and SII combined with clinicopathological features can predict high mortality risk in patients with stage-I and stage-II GC and >5 years after radical gastrectomy, which will contribute to the supplement of the traditional AJCC system and to individual survival prediction.

Farhadi, K., et al. (2022). "Trends in lip, oral cavity, and pharyngeal cancer mortality in the United States, 1999-2019." J Oral Pathol Med **51**(9): 763-770.

BACKGROUND: Changes in the epidemiology of lip, oral cavity, and pharyngeal (LOCP) cancers have been reported in the United States. This study aimed to examine recent trends in LOCP cancer mortality in the United States from 1999 to 2019. METHODS: National mortality data were extracted from CDC WONDER, 1999-2019. International Classification of Diseases Codes, 10th Revision-C00-C14, were used to identify decedents of malignant neoplasms of the lip, oral cavity, and pharynx. LOCP cancer mortality trends were assessed by fitting a Joinpoint regression model overall, and by race/ethnicity, sex, age, and US Census Region. Annual Percentage Changes (APC) were derived to estimate variations in mortality trends over time. RESULTS: The age-adjusted mortality rate (AAMR) for LOCP cancers was 2.5 per 100 000 (95% CI: 2.5-2.5), equivalent to 180 532 deaths during 1999-2019. Overall mortality trends have stabilized since 2009 (APC = 0.3; 95% CI: -0.1, 0.7), but an examination by subtype revealed rising mortality trends from cancers of the lip and oral cavity (APC = 1.2; 95% CI: 0.7, 1.6) and pharynx (APC = 3.2; 95% CI: 1.7, 4.8), and declining trends in malignancies of other and ill-defined areas of the lip, oral cavity, and pharynx (APC = -2.7; 95% CI: -3.4, -2.0). Trend variations were also noted by sex, age, US Census Region, and race/ethnicity. CONCLUSIONS: There are differential trends in mortality from LOCP cancers in the United States. Investigating the biological, individual, and contextual factors related to LOCP cancers would guide effective public health intervention efforts.

Farhadi, K., et al. (2022). "Trends in nasopharyngeal cancer mortality in the United States, 1999-2020." Community Dent Oral Epidemiol.

OBJECTIVES: The incidence of nasopharyngeal cancer (NPC) has been declining in the United States (US) in recent years. However, little is known about the latest trends in NPC mortality in the US population. This study aimed to examine the trends in NPC mortality rate by age, sex, race and ethnicity and US Census Region from 1999 to 2020. METHODS: Mortality data were extracted from the Centers for Disease Control and Prevention's Wide-ranging Online Data for Epidemiologic Research (WONDER) database. Decedents whose cause of death was NPC were identified using the International Classification of Diseases Codes, 10th Revision: C11.0-C11.9. Trends in age adjusted mortality rates (AAMR) from NPC were assessed using a joinpoint regression model. Annual Percentage Changes (APC) and Average Annual Percentage Changes were examined overall and by age, sex, race and ethnicity and census region. RESULTS: From 1999 through 2020, a total of 14 534 NPC deaths were recorded in the US (AAMR = 0.2 per 100 000; 95% CI: 0.2, 0.2). Overall trends remained stationary throughout the study period. Since 2006, recent trends declined by 6.1% per year (95% CI: -8.4, -3.7) among Non-Hispanic Whites, and by 2.7% per year among Non-Hispanic Blacks, Asians/Pacific Islanders and Hispanics. Trends either stabilized or declined by sex, age and US Census Region. Similar results were obtained when the analysis was restricted to decedents aged 65 years and above. CONCLUSIONS: Stationary or declining trends in NPC mortality could be due to the falling incidence of the disease and/or advances in medical diagnosis and treatment. Considering the enigmatic nature of NPC, future studies should explore the genetic and sociodemographic factors associated with the trends reported in this study.

Farias, A. J., et al. (2022). "Lung Cancer Mortality Racial/Ethnic Disparities in Patient Experiences with Care: a SEER-CAHPS Study." J Racial Ethn Health Disparities.

BACKGROUND: To determine whether there are racial/ethnic disparities in patient experiences with care among lung cancer survivors, whether they are associated with mortality. METHODS: A retrospective cohort study of lung cancer survivors > 65 years old who completed a CAHPS survey > 6 months after the date of diagnosis. We used data from the SEER-Consumer Assessment of Healthcare Providers Systems (SEER-CAHPS(R)) database from 2000 to 2013 to assess racial/ethnic differences in patient experiences with care multivariable Cox proportional hazards models to assess the association between patient experience with care scores mortality in each racial/ethnic group. RESULTS: Within our cohort of 2603 lung cancer patients, Hispanic patients reported lower adjusted mean score with their ability to get needed care compared to white patients (B: - 5.21, 95% CI: - 9.03, - 1.39). Asian patients reported lower adjusted mean scores with their ability to get care quickly (- 4.25 (- 8.19, - 0.31)), get needed care (- 7.06 (- 10.51, - 3.61)), get needed drugs (- 9.06 (- 13.04, - 5.08)). For Hispanic patients, a 1-unit score increase in their ability to get all needed care (HR: 1.02, 1.00-1.03) care coordination (1.06, 1.02-1.09) was associated with higher risk of mortality. Among black patients, a 1-unit score increase in their ability to get needed care (HR: 0.99, 95% CI 0.98-0.99) care coordination (0.97, 0.94-0.99) was associated with lower risk mortality. CONCLUSIONS: There are racial/ethnic disparities in lung cancer patient experiences with care that may impact mortality. Patient experiences with care are important risk factors of mortality for certain racial/ethnic groups.

Forjaz, G., et al. (2020). "Regional differences in tobacco smoking and lung cancer in Portugal in 2018: a population-based analysis using nationwide incidence and mortality data." BMJ Open **10**(10): e038937.

OBJECTIVES: This study aims to estimate the proportion of lung cancer cases and deaths attributable to tobacco smoking in Portugal in 2018, complemented by trends in incidence and mortality, by sex and region. DESIGN: Cancer cases for 1998-2011 and cancer deaths for 1991-2018 were obtained from population-based registries and Statistics Portugal, respectively. We projected cases for 2018 and used reported deaths for the same year to estimate, using Peto's method, the number and proportion of lung cancer cases and deaths caused by tobacco smoking in 2018. We calculated the age-adjusted incidence and mortality rates in each year of diagnosis and death. We fitted a joinpoint regression to the observed data to estimate the annual percentage change (APC) in the rates. SETTING: Portugal. RESULTS: In 2018, an estimated 3859 cases and 3192 deaths from lung cancer were attributable to tobacco smoking in Portugal, with men presenting a population attributable fraction (PAF) of 82.6% (n=3064) for incidence and 84.1% (n=2749) for mortality, while in women those values were 51.0% (n=795) and 42.7% (n=443), respectively. In both sexes and metrics, the Azores were the region with the highest PAF and the Centre with the lowest. During 1998-2011, the APC for incidence ranged from 0.6% to 3.0% in men and 3.6% to 7.9% in women, depending on region, with mortality presenting a similar pattern between sexes. CONCLUSION: Exposure to tobacco smoking has accounted for most of the lung cancer cases and deaths estimated in Portugal in 2018.

Differential patterns of tobacco consumption across the country, varying implementation of primary prevention programmes and differences in personal cancer awareness may have contributed to the disparities observed. Primary prevention of lung cancer remains a public health priority, particularly among women.

Forjaz, G., et al. (2020). "Measuring progress against cancer in the Azores, Portugal: Incidence, survival, and mortality trends and projections to 2025." Cancer Epidemiol **69**: 101810.

BACKGROUND: Measuring progress against cancer is more accurate when trends in incidence, survival, and mortality are interpreted simultaneously. Our study aims to analyze how these key metrics have evolved over time in the Azores, Portugal. METHODS: Data for incident cases diagnosed in 1997-2016 and followed up through December 31, 2017 were obtained from the Azores Cancer Registry. Data for cancer deaths that occurred in 1991-2016 were obtained from Statistics Portugal. To estimate temporal trends, we applied a joinpoint model to age-adjusted rates. We estimated five-year net survival within the framework of relative survival using the Pohar-Perme estimator and predicted the number of cases and deaths in 2025. RESULTS: In men, incidence and mortality decreased for stomach, larynx, and prostate cancer. In women, mortality decreased for breast and cervical cancer. Five-year relative survival improved for several cancers, with the most pronounced improvements for prostate cancer in men and colorectal cancer in women (24.1 and 27.9 percentage point absolute increase, respectively). Conversely, incidence and mortality increased for colorectal cancer in men and lung cancer in women. The incidence and mortality burdens are both expected to increase in 2025. CONCLUSION: Overall, progress against cancer in the Azores has been mixed, and much of the progress has been driven by advances in treatment. Statistics for lung cancer in women and colorectal cancer in men are a call to action for policymakers. Reducing tobacco use and tackling the obesity epidemic are the two public health priorities for cancer control within the region.

Formigosa, L. A. C., et al. (2022). "Impact of screening on cervical cancer incidence and mortality in a Northern Brazilian city." Ecancermedicalscience **16**: 1418.

OBJECTIVE: To analyse the impact of screening actions on the incidence and mortality rates of cervical cancer (CC) in the city of Belem, Brazil. METHODS: Based on the cancer registry data from 1998 to 2017, collected from the Belem Population-Based Cancer Registry, combined with local population data for the interval 1998-2017, CC incidence and mortality were calculated. The Segi world population 1960 was used for age-standardised incidence/mortality rates. RESULTS: In the period analysed, there were 4,469 new cases and 1,660 deaths from CC. The median age at diagnosis of invasive cases was 51 years. The age-adjusted incidence rate decreased from 18.65/100,000 in 1998 to 11.79/100,000 in 2017, despite the increase observed in the first 5 years of the historical series, while there was stability in mortality rates in the same time lapse. CONCLUSION: CC is still one of the most common malignant tumours that threaten public health in northern Brazil. The trend of the disease depends on comprehensive prevention and control strategies regarding the local situation and age groups, with emphasis on the organisation of the screening programme and vaccination against human papillomavirus.

Forster, R. B., et al. (2022). "Association between medical androgen deprivation therapy and long-term cardiovascular disease and all-cause mortality in nonmetastatic prostate cancer." Int J Cancer **151**(7): 1109-1119.

Studies have suggested that prostate cancer (PCa) patients receiving androgen deprivation therapy (ADT) are at increased risk of developing or exacerbating cardiovascular disease (CVD). We aimed to explore the association between ADT for PCa and subsequent CVD and all-cause mortality in this nationwide, longitudinal study. We also evaluated the role of cardiovascular risk and ADT duration to determine effect modification. Norwegian registry data were used to identify patients with PCa from 2008-18 and who received primary ADT in the first year after diagnosis. The associations between ADT and composite cardiovascular events, and the individual components of myocardial infarction, stroke and heart failure, in addition to atrial fibrillation and all-cause mortality, were explored using time-varying Cox regression models. We included 30 923 PCa patients, of whom 8449 (27%) received primary ADT. Mean follow-up was 2.9 and 3.8 years for CVD events and mortality, respectively. We found an association between ADT and composite CVD (adjusted HR 1.13: 95% CI 1.05-1.21), myocardial infarction (1.18: 1.05-1.32), stroke (1.21: 1.06-1.38), heart failure (1.23: 1.13-1.35) and all-cause mortality (1.49: 1.39-1.61). These associations persisted in those with low and moderate CVD risk and ADT longer than 7 months. A relationship between ADT and composite CVD and all-cause mortality was observed, especially in those with moderate CVD risk and longer treatment duration. Future studies with more detailed cancer data are needed to verify the clinical relevance of these results, especially when considering all-cause mortality within

the context of treatment guidelines and benefits of ADT.

Forster, R. B., et al. (2022). "Treatment and 30-day mortality after myocardial infarction in prostate cancer patients: A population-based study from Norway." Cardiology.

INTRODUCTION: There is limited knowledge about the use of invasive treatment and mortality after acute myocardial infarction (AMI) in prostate cancer patients. We therefore wanted to compare rates of invasive treatment and 30-day mortality between AMIs in patients with prostate cancer (PCa) and AMIs in the general Norwegian male population. METHODS: Norwegian population-based registry data from 2013-2019 were used in this cohort study to identify AMIs in patients with a preceding PCa diagnosis. We compared invasive treatment rates and 30-day mortality in AMI patients with PCa to the same outcomes in all male AMI patients in Norway. Invasive treatment was defined as performed angiography with or without percutaneous coronary intervention or coronary artery bypass graft surgery. Standardized mortality (SMR) and incidence ratios (SIR), and logistic regression were used to evaluate the association between PCa risk groups and invasive treatment. RESULTS: In 1018 patients with PCa of all risk groups, the total rates of invasive treatment for AMIs were similar to the rates in the general AMI population. In patients with ST-segment elevation AMIs, rates were lower in metastatic PCa compared to localized PCa (OR 0.15, 95% CI 0.04-0.49). For non-ST-segment elevation AMIs there were no differences between PCa risk groups. The 30-day mortality after AMI was lower in PCa patients than in the total population of similarly aged AMI patients (SMR 0.77, 95% CI 0.61-0.97). CONCLUSION: Except for patients with metastatic PCa experiencing an ST-segment elevation AMI, PCa patients were treated as frequent with invasive treatment for their AMI as the general AMI population. 30-day all-cause mortality was lower after AMI in PCa patients compared to the general AMI population.

Fossa, S. D., et al. (2022). "Mortality and Second Cancer Incidence After Treatment for Testicular Cancer: Psychosocial Health and Lifestyle Are Modifiable Prognostic Factors." J Clin Oncol **40**(23): 2588-2599.

PURPOSE: To evaluate whether selected modifiable patient-reported adverse health outcomes (AHOs) in testicular cancer survivors (TCSs) represent prognostic factors of overall mortality, cancer mortality, and first-time non-germ cell second cancer (SecCa) incidence. PATIENTS AND METHODS: In 775 long-term TCSs (diagnosis: 1980-1994) who previously participated in a quality-of-life survey, 20-year mortality and SecCa incidence were compared between the surgery group (n = 272) and TCSs after platinum-based chemotherapy (PBCT; n = 503). A PBCT standard group (total cisplatin: </= 630 mg: n = 124) was separated from a PBCT high subgroup (total cisplatin: > 630 mg; n = 379). Univariate and multivariate analyses (Kaplan-Meier; Cox proportional hazard analyses) included age, treatment, and prior major physical comorbidity as nonmodifiable factors, whereas low socioeconomic status, unhealthy lifestyle, probable depression disorder, and neurotoxicity were modifiable AHOs. RESULTS: For all TCSs, the cumulative overall 20-year mortality was 14% (95% CI, 11.8 to 16.8). Rising age, PBCT high, and comorbidity significantly increased the risk of overall mortality rate. Compared with a low-risk group (no AHO; n = 446) and with exception of neurotoxicity, this risk was further significantly enhanced by 80% in TCSs of a medium-risk group (one or two AHOs; n = 278). In men of a high-risk group (three AHOs; n = 47), the probability of overall mortality and of cancer mortality was eight-fold and five-fold increased, respectively. Risk grouping did not influence on SecCa incidence. CONCLUSION: Self-reported unfavorable modifiable AHO concerning lifestyle and psychosocial health are in TCSs independently and significantly associated with increased overall mortality and cancer mortality. Health professionals and the TCSs themselves, particularly those after PBCT high, should continuously be aware of these risk factors attempting maximal reduction of these AHOs and thereby supporting long-term survival.

Foster, S., et al. (2021). "Damaged Masculinity: How Honor Endorsement Can Influence Prostate Cancer Screening Decision-Making and Prostate Cancer Mortality Rates." Pers Soc Psychol Bull: 1461672211065293.

Prior research has established factors that contribute to the likelihood that men seek out prostate cancer screenings. The current study addresses how endorsing the ideology found in cultures of honor may serve as a barrier to prostate cancer screenings. Two studies were conducted which analyzed the impact of stigma on men's decisions to seek out prostate cancer screenings (Study 1) as well as how prostate cancer deaths may be higher in the culture of honor regions due to men's reticence to seek out screenings (Study 2). Results suggest that older, honor-endorsing men are less likely to have ever sought out a prostate cancer screening due to screening stigma and that an honor-oriented region (southern and western United States) displays higher rates of prostate cancer death than a non-honor-oriented region (northern United States). These findings suggest that honor may be a cultural

framework to consider when practitioners address patients' screening-related concerns.

Frater, J. L. (2022). "Re: Hazem Orabi, Lauren Howard, Christopher L. Amling, et al. Red Blood Cell Distribution Width Is Associated with All-cause Mortality but Not Adverse Cancer-specific Outcomes in Men with Clinically Localized Prostate Cancer Treated with Radical Prostatectomy: Findings Based on a Multicenter Shared Equal Access Regional Cancer Hospital Registry. Eur Urol Open Sci 2022;37:106-12." Eur Urol Open Sci **42**: 9.

Freire, A. R., et al. (2021). "Socioeconomic indicators and economic investments influence oral cancer mortality in Latin America." BMC Public Health **21**(1): 377.

BACKGROUND: It is necessary to recognize the influence of socioeconomic factors on oral cancer indicators in Latin American countries. This study aimed to analyze the influence of socioeconomic indicators and economical investments on oral cancer mortality rates in Latin American countries. METHODS: This cross-sectional study considered the age-standardized mortality rate (ASR) of oral cancer within the period 2000-2015. The oral cancer mortality rate (for both sexes and age groups 40-59 and 60 years old or more), socioeconomic aspects (Gini Inequality Index, unemployment rate and Gross Domestic Product (GDP) per capita) and investments in different sectors (%GDP invested in health per capita and by the government, %GDP invested in education by the government and %GDP invested in research and development) were considered. Tweedie multivariate regression was used to estimate the effect of independent variables on the mortality rate of oral cancer, considering $p < 0.05$. RESULTS: This study showed that being male and aged 60 or over (PR = 14.7) was associated with higher mortality rate for oral cancer. In addition, greater inequality (PR = 1.05), higher health expenditure per capita (PR =1.09) and greater investment in research and development (PR = 1.81) were associated with a higher mortality rate from oral cancer. CONCLUSION: Socioeconomic factors and economical investments influence the mortality rate of oral cancer in Latin American countries. This emphasizes oral cancer is a socioeconomic-mediated disease.

Freudenburg, E., et al. (2022). "Geographic distribution of racial differences in mortality in muscle-invasive bladder cancer patients: an opportunity for improvement." Cancer Causes Control **33**(4): 613-622.

OBJECTIVES: To determine the geographic distribution of muscle-invasive bladder cancer mortality according to race in the United States (US). African Americans (AAs) have up to two times the risk of bladder cancer mortality compared to Caucasians. Bladder cancer mortality increases exponentially once it invades the muscle. Geographic heterogeneity in bladder cancer mortality according to race remains to be determined. DESIGN: Analysis of Surveillance, Epidemiology, and End Results (SEER)-Medicare data for 6,044 patients aged 66-85 diagnosed with clinical stage T2-T4 N0M0 bladder cancer from 1 January 2002 to 31 December 2011. Fine and Gray-competing risks regression models were used to assess the association of race with bladder cancer-specific mortality (BCSM) according to tumor registry. RESULTS: Out of 6,044 patients, 5,408 (89.5%) were Caucasian, 352 (5.82%) were non-Hispanic AA, 85 (1.4%) were Hispanic, and 199 (3.29%) were other. Of the 18 registries, AAs with bladder cancer were largely concentrated in Louisiana (19%), New Jersey (17.9%), and Georgia (17.6%). New Jersey was the only registry where AAs had increased risk of BCSM than Caucasians and only for stage T2 disease: (AHR, 1.74; 95% CI 1.22-2.47, $p = 0.002$). According to treatment, AAs in New Jersey had worse BCSM than Caucasians when they underwent radical cystectomy (AHR, 2.05; 95% CI 1.26-3.35, $p = 0.0039$) and radiotherapy or chemotherapy alone (AHR, 1.55; 95% CI 1.03-2.35, $p = 0.0367$). CONCLUSIONS: We observed geographic variation in bladder cancer mortality which impacted only one registry with one of the largest population of AAs. These findings support further investigation into the social determinants of race (i.e., socioeconomic status and distance to healthcare facility) and culturally centered healthcare decision making which may drive these results.

Friedman-Jimenez, G., et al. (2022). "Low-dose ionizing radiation and cancer mortality among enlisted men stationed on nuclear-powered submarines in the United States Navy." Int J Radiat Biol **98**(10): 1542-1550.

BACKGROUND: Men stationed on nuclear-powered submarines are occupationally exposed to external ionizing radiation at very low levels and radiation dose for each individual is closely monitored. Little is known about ionizing radiation (IR) risks of cancer mortality for populations with levels of cumulative ionizing radiation exposure this low. MATERIALS AND METHODS: This historical cohort study followed 85,033 enlisted men who had served on a nuclear-powered submarine in the U.S. Navy between 1969 and 1982 to determine patterns of cancer mortality. Occupational radiation doses were measured by badge dosimeters for each individual for all periods of Navy service potentially involving radiation exposure. Deaths were ascertained through 1995 by searches of multiple national mortality databases.

Within-cohort dose-response relationships for cancer mortality were estimated using linear Poisson regression models. Individual-level smoking status was not available so cancer risks were estimated separately for cancers with and without previously published evidence of consistently moderate or strong associations with smoking. RESULTS: A total of 584 cancer deaths occurred during a follow-up period of up to 27 years. The mean and median cumulative occupational radiation doses received while in the Navy were 5.7 and 1.1 milliSieverts (mSv), respectively, range 0-242 mSv. Mortality Excess Relative Risks (ERRs) per 10 mSv and 95% confidence intervals (CI) were 0.053 (CI -0.03, 0.17) for all cancers, 0.052 (CI -0.03, 0.18) for all solid cancers, and 0.003 (CI -0.29, 0.30) for leukemias excluding chronic lymphocytic leukemia. The ERRs per 10 mSv were 0.052 (CI -0.07, 0.17) for cancers previously associated with smoking and 0.012 (CI -0.10, 0.12) for cancers that were not. CONCLUSIONS: The ERR point estimates for solid cancers and leukemia were statistically compatible with those reported in previously published studies of other ionizing radiation-exposed and monitored cohorts, albeit with wide confidence intervals. This study, with high-quality measurements of in-Navy occupational external IR doses, high follow-up proportion, and detailed IR dose-response analyses, is consistent with the premise of small excess cancer risks from low-dose IR.

Ganatra, S., et al. (2022). "Impact of Social Vulnerability on Comorbid Cancer and Cardiovascular Disease Mortality in the United States." JACC CardioOncol **4**(3): 326-337.

BACKGROUND: Racial and social disparities exist in outcomes related to cancer and cardiovascular disease (CVD). OBJECTIVES: The aim of this cross-sectional study was to study the impact of social vulnerability on mortality attributed to comorbid cancer and CVD. METHODS: The Centers for Disease Control and Prevention Wide-Ranging Online Data for Epidemiologic Research database (2015-2019) was used to obtain county-level mortality data attributed to cancer, CVD, and comorbid cancer and CVD. County-level social vulnerability index (SVI) data (2014-2018) were obtained from the CDC's Agency for Toxic Substances and Disease Registry. SVI percentiles were generated for each county and aggregated to form SVI quartiles. Age-adjusted mortality rates (AAMRs) were estimated and compared across SVI quartiles to assess the impact of social vulnerability on mortality related to cancer, CVD, and comorbid cancer and CVD. RESULTS: The AAMR for comorbid cancer and CVD was 47.75 (95% CI: 47.66-47.85) per 100,000 person-years, with higher mortality in counties with greater social vulnerability. AAMRs for cancer and CVD were also significantly greater in counties with the highest SVIs. However, the proportional increase in mortality between the highest and lowest SVI counties was greater for comorbid cancer and CVD than for either cancer or CVD alone. Adults <45 years of age, women, Asian and Pacific Islanders, and Hispanics had the highest relative increase in comorbid cancer and CVD mortality between the fourth and first SVI quartiles, without significant urban-rural differences. CONCLUSIONS: Comorbid cancer and CVD mortality increased in counties with higher social vulnerability. Improved education, resource allocation, and targeted public health interventions are needed to address inequities in cardio-oncology.

Ganguli, R., et al. (2022). "Machine learning models to prognose 30-Day Mortality in Postoperative Disseminated Cancer Patients." Surg Oncol **44**: 101810.

Patients with disseminated cancer at higher risk for postoperative mortality see improved outcomes with altered clinical management. Being able to risk stratify patients immediately after their index surgery to flag high risk patients for healthcare providers is vital. The combination of physician uncertainty and a demonstrated optimism bias often lead to an overestimation of patient life expectancy which can precent proper end of life counseling and lead to inadequate postoperative follow up. In this cohort study of 167,474 postoperative patients with multiple types of disseminated cancer, patients at high risk of 30-day postoperative mortality were accurately identified using our machine learning models based solely on clinical features and preoperative lab values. Extreme Gradient Boosting, Random Forest, and Logistic Regression machine learning models were developed on the cohort. Among 167,474 disseminated cancer patients, 50,669 (30.3%) died within 30 days of their index surgery; After preprocessing, 28 features were included in the model development. The cohort was randomly divided into 133,979 patients (80%) for training the models and 33,495 patients (20%) for testing. The extreme gradient boosting model had an AUC of 0.93 (95% CI: 0.926-0.931), the random forest model had an AUC of 0.93 (95% CI: 0.930-0.934), and the logistic regression model had an AUC of 0.90 (95% CI: 0.900-0.906 the index operation. Ultimately, Machine learning models were able to accurately predict short-term postoperative mortality among a heterogenous population of disseminated cancer patients using commonly accessible medical features. These models can be included in electronic health systems to guide clinical judgements that affect direct patient care, particularly in low-resource settings.

Gao, J., et al. (2021). "Exploratory analysis on the association of mental health disorders with in-hospital postoperative complications and mortality in head and neck cancer surgery." Head Neck **43**(10): 3022-3031.

BACKGROUND: The objective was to assess the association of mental health disorders with in-hospital complication and mortality rates in patients undergoing head and neck cancer surgery. METHODS: In this exploratory retrospective study, the Nationwide Inpatient Sample was queried from 2003 to 2014 for all patients with a diagnosis of head and neck cancer who underwent surgery. Univariate cross-tabulation, logistic regression, and propensity score matching (PSM) were used to compare demographics, procedure-related variables, and in-hospital postoperative complications and mortality between patients with and without selected comorbid mental health disorders. RESULTS: Of 39 600 included patients, 3390 (8.6%) had a selected comorbid mental health disorder diagnosis. After PSM, patients with selected mental health disorders had increased risk of overall medical complications on multivariable analysis (OR 1.28 [CI 1.12-1.46], P < 0.001) but not overall surgical complications or mortality. CONCLUSIONS: Patients with a mental health disorder diagnosis have increased risk of in-hospital medical, certain surgical, and total complications.

Gao, Y., et al. (2020). "Assessing the Relationship Between Leukocyte Telomere Length and Cancer Risk/Mortality in UK Biobank and TCGA Datasets With the Genetic Risk Score and Mendelian Randomization Approaches." Front Genet **11**: 583106.

BACKGROUND: Telomere length is an important indicator of tumor progression and survival for cancer patients. Previous work investigated the associations between genetically predicted telomere length and cancers; however, the types of cancers investigated in those studies were relatively limited or the telomere length-associated genetic variants employed often came from genome-wide association studies (GWASs) with small sample sizes. METHODS: We constructed the genetic risk score (GRS) for leukocyte telomere length based on 17 associated genetic variants available from the largest telomere length GWAS up to 78,592 individuals. Then, a comprehensive analysis was undertaken to evaluate the association between the constructed GRS and the risk or mortality of a wide range of cancers [i.e., 37 cancers in the UK Biobank and 33 cancers in The Cancer Genome Atlas (TCGA)]. We further applied the two-sample Mendelian randomization (MR) to estimate the causal effect of leukocyte telomere length on UK Biobank cancers via summary statistics. RESULTS: In the UK Biobank dataset, we found that the GRS of leukocyte telomere length was associated with a decreased risk of nine types of cancer (i.e., significant association with multiple myeloma, chronic lymphocytic leukemia, kidney/renal cell cancer, bladder cancer, malignant melanoma, basal cell carcinoma, and prostate cancer and suggestive association with sarcoma/fibrosarcoma and Hodgkin's lymphoma/Hodgkin's disease). In addition, we found that the GRS was suggestively associated with an increased risk of leukemia. In the TCGA dataset, we observed suggestive evidence that the GRS was associated with a high death hazard of rectum adenocarcinoma (READ), sarcoma (SARC), and skin cutaneous melanoma (SKCM), while the GRS was associated with a low death hazard of kidney renal papillary cell carcinoma (KIRP). The results of MR further supported the association for leukocyte telomere length on the risk of malignant melanoma, Hodgkin's lymphoma/Hodgkin's disease, chronic lymphocytic leukemia and multiple myeloma. CONCLUSION: Our study reveals that telomere played diverse roles in different types of cancers. However, further validations in large-scale prospective studies and deeper investigations of the biologic mechanisms are warranted.

Gapare, C. R., et al. (2022). "Ecologic Analysis of Correlates of Cervical Cancer Morbidity and Mortality in Sub-Saharan Africa." Cancer Epidemiol Biomarkers Prev **31**(9): 1804-1811.

BACKGROUND: Cervical cancer is the fourth leading cause of death among women worldwide, with 85% of the burden falling on low- to middle- income countries. We studied the correlates of cervical cancer incidence and mortality, and case-fatality in Sub-Saharan Africa. METHODS: Country-level data on 16 putative cervical cancer correlates for 37 Sub-Saharan African countries were collected from publicly available data sources. We performed univariate and multiple (stepwise) linear regression analyses to identify correlates of cervical cancer incidence and mortality, and case-fatality. RESULTS: In univariate analyses, incidence and mortality rates were significantly correlated with contraceptive use, penile cancer incidence, and human immunodeficiency virus prevalence. Incidence rates were also correlated with literacy rates, whereas mortality rates were correlated with the proportion of rural population and screening coverage. Multiple regression analyses showed contraceptive use (P = 0.009) and penile cancer incidence (P = 0.004) as associated with cervical cancer incidence. Penile cancer incidence (P = 9.77 x 10-5) and number of medical doctors (P = 0.0433) were associated with mortality. The goodness of fit of the incidence and mortality models was moderate at best, explaining 49% and 37% of variability in the data, respectively. However, the case-fatality model had the

best fit explaining most of the variation (adjusted R2 = 0.948; P = 6.822 x 10-16). CONCLUSIONS: To reduce the burden of cervical cancer in Sub-Saharan Africa, it would be important to design multimodal interventions that not only target screening and HPV vaccination, but also focus on cervical cancer correlates. IMPACT: Identifying contextual factors associated with cervical cancer in this region could inform targeted interventions.

Garau, M., et al. (2022). "Cancer incidence and mortality in Uruguay: 2013-2017." Colomb Med (Cali) **53**(1): e2014966.

BACKGROUND: Uruguay has the highest cancer incidence and mortality rates in Latin America. The National Cancer Registry of Uruguay, which has been in operation since 1992, provides epidemiological information on incidence and mortality at the country level. OBJECTIVE: The objective of this article is to update the incidence and mortality figures by reporting the information for the period 2013-2017. METHODS: All incident cases of invasive neoplasias except non melanoma of the skin and all cancer deaths occurred in from 2013 to 2017 were analyzed. Age standardized rates were calculated by the direct method, using the world standard population. Complementary, incidence (2002-2017) and mortality (1990-2017) trends were studied for the leading sites. RESULTS: Among females, the most common cancers are breast, colon and rectum, lung, cervix and thyroid. The most frequent cancers in males are prostate, lung, colon and rectum, bladder and kidney. Lung, prostate and colorectal cancer are the leading causes of cancer death in males while breast cancer is the first cause of cancer death among females. CONCLUSIONS: Although cancer mortality has declined monotonously since 1990, cancer control is a challenge for Uruguay, wherein breast, lung and prostate cancer have very high incidence while the country must still make an effort to reduce other cancers that are very common in economically less favored countries.

Garcia-Suarez, J., et al. (2020). "Impact of hematologic malignancy and type of cancer therapy on COVID-19 severity and mortality: lessons from a large population-based registry study." J Hematol Oncol **13**(1): 133.

BACKGROUND: Patients with cancer have been shown to have a higher risk of clinical severity and mortality compared to non-cancer patients with COVID-19. Patients with hematologic malignancies typically are known to have higher levels of immunosuppression and may develop more severe respiratory viral infections than patients with solid tumors. Data on COVID-19 in patients with hematologic malignancies are limited. Here we characterize disease severity and mortality and evaluate potential prognostic factors for mortality. METHODS: In this population-based registry study, we collected de-identified data on clinical characteristics, treatment and outcomes in adult patients with hematologic malignancies and confirmed severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infection within the Madrid region of Spain. Our case series included all patients admitted to 22 regional health service hospitals and 5 private healthcare centers between February 28 and May 25, 2020. The primary study outcome was all-cause mortality. We assessed the association between mortality and potential prognostic factors using Cox regression analyses adjusted for age, sex, comorbidities, hematologic malignancy and recent active cancer therapy. RESULTS: Of 833 patients reported, 697 were included in the analyses. Median age was 72 years (IQR 60-79), 413 (60%) patients were male and 479 (69%) and 218 (31%) had lymphoid and myeloid malignancies, respectively. Clinical severity of COVID-19 was severe/critical in 429 (62%) patients. At data cutoff, 230 (33%) patients had died. Age >/= 60 years (hazard ratios 3.17-10.1 vs < 50 years), > 2 comorbidities (1.41 vs </= 2), acute myeloid leukemia (2.22 vs non-Hodgkin lymphoma) and active antineoplastic treatment with monoclonal antibodies (2.02) were associated with increased mortality; conventional chemotherapy showed borderline significance (1.50 vs no active therapy). Conversely, Ph-negative myeloproliferative neoplasms (0.33) and active treatment with hypomethylating agents (0.47) were associated with lower mortality. Overall, 574 (82%) patients received antiviral therapy. Mortality with severe/critical COVID-19 was higher with no therapy vs any antiviral combination therapy (2.20). CONCLUSIONS: In this series of patients with hematologic malignancies and COVID-19, mortality was associated with higher age, more comorbidities, type of hematological malignancy and type of antineoplastic therapy. Further studies and long-term follow-up are required to validate these criteria for risk stratification.

Gariazzo, C., et al. (2021). "Predictors of Lung Cancer Risk: An Ecological Study Using Mortality and Environmental Data by Municipalities in Italy." Int J Environ Res Public Health **18**(4).

Lung cancer (LC) mortality remains a consistent part of the total deaths occurring worldwide. Its etiology is complex as it involves multifactorial components. This work aims in providing an epidemiological assessment on occupational and environmental factors associated to LC risk by means of an ecological study involving the 8092 Italian municipalities for the period 2006-2015. We consider mortality data from mesothelioma as proxy of asbestos

exposure, as well as PM(2.5) and radon levels as a proxy of environmental origin. The compensated cases for occupational respiratory diseases, urbanization and deprivation were included as predictors. We used a negative binomial distribution for the response, with analysis stratified by gender. We estimated that asbestos is responsible for about 1.1% (95% CI: 0.8, 1.4) and 0.5% (95% CI: 0.2, 0.8) of LC mortality in males and females, respectively. The corresponding figures are 14.0% (95% CI: 12.5, 15.7) and 16.3% (95% CI: 16.2, 16.3) for PM(2.5) exposure, and 3.9% (95% CI: 3.5, 4.2) and 1.6% (95% CI: 1.4, 1.7) for radon exposure. The assessment of determinants contribution to observed LC deaths is crucial for improving awareness of its origin, leading to increase the equity of the welfare system.

Gedeborg, R., et al. (2022). "Androgen deprivation therapy, comorbidity, cancer stage and mortality from COVID-19 in men with prostate cancer." Scand J Urol **56**(2): 104-111.

BACKGROUND: Androgens facilitate entrance of the severe acute respiratory syndrome coronavirus 2 into respiratory epithelial cells, and male sex is associated with a higher risk of death from corona virus disease (COVID-19). Androgen deprivation therapy (ADT) could possibly improve COVID-19 outcomes. METHODS: In a case-control study nested in the Prostate Cancer data Base Sweden (PCBaSe) RAPID 2019, we evaluated the association between ADT and COVID-19 as registered cause of death in men with prostate cancer. Each case was matched to 50 controls by region. We used conditional logistic regression to adjust for confounders and also evaluated potential impact of residual confounding. RESULTS: We identified 474 men who died from COVID-19 in March-December 2020. In crude analyses, ADT exposure was associated with an increased risk of COVID-19 death (odds ratio [OR] 5.05, 95% CI: 4.18-6.10); however, the OR was substantially attenuated after adjustment for age, comorbidity, prostate cancer characteristics at diagnosis, recent healthcare use, and indicators of advanced cancer (adjusted OR 1.25, 95% CI: 0.95-1.65). If adjustment has accounted for at least 85% of confounding, then the true effect could be no more than a 5% reduction of the odds for COVID-19 death. CONCLUSIONS: The increased mortality from COVID-19 in men with prostate cancer treated with ADT was mainly related to high age, comorbidity, and more advanced prostate cancer. There was no evidence to support the hypothesis that ADT is associated with improved COVID-19 outcomes.

Gedeborg, R., et al. (2021). "Androgen deprivation therapy and excess mortality in men with prostate cancer during the initial phase of the COVID-19 pandemic." PLoS One **16**(10): e0255966.

BACKGROUND: Men have a higher risk of death from COVID-19 than women and androgens facilitate entrance of the SARS-CoV-2 virus into respiratory epithelial cells. Thus, androgen deprivation therapy may reduce infection rates and improve outcomes for COVID-19. In the spring of 2020, Sweden was highly affected by COVID-19. The aim was to estimate the impact of androgen deprivation therapy on mortality from COVID-19 in men with prevalent prostate cancer by comparing all-cause mortality in the spring of 2020 to that in previous years. PATIENTS AND METHODS: Using the Prostate Cancer data Base Sweden all men with prostate cancer on March 1 each year in 2015-2020 were followed until June 30 the same year. Exposure to androgen deprivation therapy was ascertained from filled prescriptions for bicalutamide monotherapy, gonadotropin-releasing hormone agonists (GnRH), or bilateral orchidectomy. RESULTS: A total of 9,822 men died in March-June in the years 2015-2020, of whom 5,034 men were on androgen deprivation therapy. There was an excess mortality in 2020 vs previous years in all men. The crude relative mortality rate ratio for 2020 vs 2015-2019 was 0.93 (95% confidence interval (CI) 0.83 to 1.04) in men on GnRH, and 0.90 (95% CI 0.78 to 1.05) in men on bicalutamide monotherapy. After multivariable adjustment these ratios were attenuated to 1.00 (95% CI 0.89 to 1.12) and 0.97 (95% CI 0.84 to 1.12), respectively. When restricting the analysis to the regions with the highest incidence of COVID-19 or to the time period between 2 April to 10 June when mortality in 2020 was increased >30% compared to previous years, the results were similar to the main analysis. CONCLUSIONS: In this large national population-based cohort of men with prevalent prostate cancer, there was no clear evidence in support for an effect of androgen deprivation therapy on COVID-19 mortality.

Gendarme, S., et al. (2021). "Impact on All-Cause and Cardiovascular Mortality Rates of Coronary Artery Calcifications Detected during Organized, Low-Dose, Computed-Tomography Screening for Lung Cancer: Systematic Literature Review and Meta-Analysis." Cancers (Basel) **13**(7).

Although organized, low-dose, computed-tomography (CT) scan lung-cancer screening has been shown to lower all-cause and lung-cancer-specific mortality, the primary cause of death for subjects eligible for such screening remains cardiovascular (CV) mortality. This meta-analysis study was undertaken to evaluate the impact of screening-scan-detected coronary artery calcifications (CACs) on CV and all-cause mortality. We conducted a systematic

review and meta-analysis of studies reporting CV mortality according to the Agatson CAC score for participants in a lung-cancer screening program of randomized clinical or cohort studies. PubMed, Embase, and Cochrane databases were screened in June 2020. Two authors independently selected articles and extracted data. Six studies, including 20,175 subjects, were retained. CV and all-cause mortality rates were higher for subjects with CAC scores >0, with respective relative risks of 2.02 [95% CI 1.23-3.32] and 2.29 [95% CI 1.00-5.21]. Both mortality rates were even higher for those with high CAC scores (>400 or >1000). CACs are more common in men than in women, with an odds ratio of 1.49 [95% CI 1.40-1.59]. The presence of CAC is associated with CV mortality with an RR of 2.05 [95% CI 1.20-3.57] in men and 2.37 [CI 95% 1.29-5.09] in women, respectively. Analysis of lung-cancer-screening scans for CACs is a tool able to predict CV mortality. Prospective studies within those programs are needed to assess the benefit of primary CV prevention based on CAC detection.

Gillezeau, C., et al. (2022). "Interferon gamma expression and mortality in unselected cohorts of urothelial bladder cancer patients." PLoS One **17**(8): e0271339.

BACKGROUND: The role of interferon gamma (IFN-gamma) expression in long-term survival has not been studied in patients with urinary bladder cancer (UBC). IFN-gamma expression was characterized among various UBC patient cohorts to assess if IFN-gamma status is associated with overall survival (OS). METHODS: A tumor-based IFN-gamma gene signature was evaluated among adult UBC patients newly diagnosed between 2004 and 2017 from two hospital systems in New York. Patient cohorts included metastatic (stage IV or progressing to stage IV [MBC]), muscle-invasive (stages T2a to T4a [MIBC]), and non-muscle-invasive (carcinoma in situ or stages 0a, 0is, and I [NMIBC]) disease. Descriptive analyses were conducted comparing IFN-gamma signature in the highest tertile to those in the lowest two tertiles. RESULTS: 234 patients with bladder cancer were evaluated (56 MBC, 38 MIBC, and 140 NMIBC). Median OS was only reached in the MIBC cohort for those with an IFN-gamma signature in the lowest two tertiles (15.03 months [95% CI, 8.50-50.60]). Those with an IFN-gamma signature in the highest tertile had a decreased risk of mortality in all cohorts indicating better survival, but this was statistically significant in only the MIBC cohort (adjusted HR = 0.09 [95% CI, 0.01-0.73]). CONCLUSION: IFN-gamma signature status was associated with a decreased mortality risk in all cohorts, particularly MIBC, indicating that it may be a prognostic marker of survival in patients with UBC.

Gillies, M. and R. G. E. Haylock (2022). "Mortality and cancer incidence 1952-2017 in United Kingdom participants in the United Kingdom's atmospheric nuclear weapon tests and experimental programmes." J Radiol Prot **42**(2).

This study examines the mortality and cancer incidence experience among men who took part in the United Kingdom's atmospheric nuclear weapon tests between 1952-67. A cohort of 21 357 servicemen and male civilians from the UK who participated in the tests and a group of 22 312 controls were followed between 1952 and 2017. Analyses of mortality and cancer incidence were conducted. The overall mortality rate in the test participants was slightly higher relative risk (RR = 1.02, 90% CI 1.00-1.05,p= 0.04) than that in the control group. This difference was driven by similar increased risks for both all cancers combined (RR 1.03, 90% CI 1.00-1.07) and all non-cancer diseases (RR = 1.02, 90% CI 1.00-1.05). Leukaemia excluding chronic lymphatic incidence showed evidence of being raised relative to controls (RR = 1.38, 90% CI 1.10-1.75,p= 0.01). Leukaemia risks were driven by increased risks for chronic myeloid leukaemia (CML) (RR = 2.43, 90% CI 1.43-4.13,p= 0.003). Among non-cancer outcomes only cerebrovascular diseases showed increases in participants relative to controls. UK nuclear weapon tests participants have lower mortality rates compared to the national population although rates are slightly (2%) higher than in the study control group. Variation in background characteristics, that could not be accounted for in the analysis (e.g. smoking habits, diet), are a possible explanation for this difference. For leukaemia evidence of increased risk in the early years after the test has generally continued to diminish with time although for CML risks have persisted. There was some evidence that participants had higher mortality rates from cerebrovascular diseases than those in the control group. Assuming recorded radiation exposures (generally very low) are a true reflection of actual exposures then it is unlikely that any observed health effect will have been caused by radiation exposure.

Gillis, R. D., et al. (2021). "Carvedilol blocks neural regulation of breast cancer progression in vivo and is associated with reduced breast cancer mortality in patients." Eur J Cancer **147**: 106-116.

PURPOSE: The sympathetic nervous system drives breast cancer progression through beta-adrenergic receptor signalling. This discovery has led to the consideration of cardiac beta-blocker drugs as novel strategies for anticancer therapies. Carvedilol is a beta-blocker used in the management of cardiovascular disorders, anxiety, migraine and chemotherapy-induced cardiotoxicity. However, little is known about how

carvedilol affects cancer-related outcomes. METHODS: To address this, we investigated the effects of carvedilol on breast cancer cell lines, in mouse models of breast cancer and in a large cohort of patients with breast cancer (n = 4014). RESULTS: Treatment with carvedilol blocked the effects of sympathetic nervous system activation, reducing primary tumour growth and metastasis in a mouse model of breast cancer and preventing invasion by breast cancer cell lines. A retrospective analysis found that women using carvedilol at breast cancer diagnosis (n = 136) had reduced breast cancer-specific mortality compared with women who did not (n = 3878) (5-year cumulative incidence of breast cancer deaths: 3.1% versus 5.7%; p = 0.024 and 0.076 from univariate and multivariable analyses, respectively) after a median follow-up of 5.5 years. CONCLUSIONS: These findings provide a rationale to further explore the use of the beta-blocker carvedilol as a novel strategy to slow cancer progression.

Giovannucci, E. L., et al. (2021). "Muscle-strengthening activities and risk of cardiovascular disease, type 2 diabetes, cancer and mortality: A review of prospective cohort studies." J Intern Med **290**(4): 789-805.

The benefits of aerobic moderate-to-vigorous physical activity (MVPA) on major non-communicable diseases (NCDs) are well established. However, much less is known whether muscle-strengthening activities (i.e., resistance/weight/strength training) confer similar benefits. Herein, we conducted a narrative literature review and summarized the existing evidence from large prospective cohort studies on muscle strengthening activities and risk of major chronic diseases and mortality in adults generally free of major NCDs at baseline. Current epidemiologic evidence suggests that engagement in muscle-strengthening activities over 1-2 sessions (or approximately 60-150 min) per week was associated with reduced risk of cardiovascular disease (seven studies; approximately 20%-25% reduction), type 2 diabetes (four studies; approximately 30% reduction), cancer mortality (four studies; approximately 15%-20% reduction) as well as all-cause mortality (six studies; approximately 20%-25% reduction). For diabetes, the risk appears to lower further with even higher levels of muscle-strengthening activities, but some studies for cardiovascular and all-cause mortality suggest a reversal whereby higher levels (>/=2.5 h/week) have less benefit, or are even harmful, relative to lower levels of activity. The likely mechanisms contributing to a benefit include improvement in body composition, lipid profile, insulin resistance and inflammation. The evidence supports engaging in 1-2 sessions (up to 2.5 h) per week, preferably performed complementary to the recommended levels of aerobic MVPA. Although data are limited, caution is suggested for training exceeding 2.5 h per week. Further studies are required to better understand the influence of frequency, duration and intensity of muscle-strengthening activities on major NCDs and mortality in diverse populations.

Giraldo-Osorio, A., et al. (2022). "[Lung cancer mortality trends in Colombia, 1985-2018Tendencias na mortalidade por cancer de pulmao na Colombia de 1985 a 2018]." Rev Panam Salud Publica **46**: e127.

OBJECTIVE: To determine lung cancer mortality trends in Colombia during the period 1985-2018 in the population aged 35 years and over and identify changes in the trend. METHODS: Analysis of mortality time series. The specific standardized rates by sex and age group were calculated. Using joinpoint regression, the annual percentage change in the rates was estimated and points of change were identified. RESULTS: During the period 1985-2018, 105 553 deaths from lung cancer were reported in the population aged 35 and over. The standardized rates exhibit a downward trend during the period 1985-2005, except in people over the age of 64. CONCLUSIONS: Lung cancer death rates in Colombia are trending downward. Primary and secondary prevention measures with respect to tobacco use need to be enhanced and other risk factors, such as residential radon or occupation, monitored.

Girardi, P., et al. (2022). "Mortality for Lung Cancer among PVC Baggers Employed in the Vinyl Chloride Industry." Int J Environ Res Public Health **19**(10).

Vinyl-chloride monomer (VCM) is classified as a known carcinogen of the liver; for lung cancer, some results suggest a potential association with polyvinyl chloride (PVC) dust. We evaluated the relationship between lung cancer mortality and exposure as PVC baggers in a cohort of workers involved in VCM production and polymerization in Porto Marghera (Venice, Italy) considering both employment status and smoking habits. The workers were studied between 1973 and 2017. A subset of them (848 over 1658) was interviewed in the 2000s to collect information about smoking habits and alcohol consumption. Missing values were imputed by the Multivariate Imputation by Chained Equations (MICE) algorithm. We calculated standardized mortality ratios (SMR) and 95% confidence intervals (95% CIs) using regional reference rates by task (never, ever, and exclusively baggers) and by smoking habits. Mortality rate ratios (MRR), adjusted for age, calendar time, time since first exposure, and smoking habits, were obtained via Poisson regression using Rubin's rule to combine results from imputed datasets calculating the fraction of information due to non-response. Lung cancer

mortality was lower than the regional reference in the whole cohort (lung cancer SMR = 0.92; 95% CI 0.75-1.11). PVC baggers showed a 50% increase in lung cancer mortality compared to regional rates (SMR = 1.48; 95% CI 0.82-2.68). In the cohort analyses, a doubled risk of lung cancer mortality among PVC baggers was confirmed after adjustment for smoking and time-dependent covariates (MRR = 1.99, 95% CI 1.04-3.81). Exposure to PVC dust resulting from activity as bagger in a polymerization PVC plant was associated with an increase in lung cancer mortality risk after adjustment for smoking habits.

Global Burden of Disease Cancer, C., et al. (2022). "Cancer Incidence, Mortality, Years of Life Lost, Years Lived With Disability, and Disability-Adjusted Life Years for 29 Cancer Groups From 2010 to 2019: A Systematic Analysis for the Global Burden of Disease Study 2019." JAMA Oncol **8**(3): 420-444.

IMPORTANCE: The Global Burden of Diseases, Injuries, and Risk Factors Study 2019 (GBD 2019) provided systematic estimates of incidence, morbidity, and mortality to inform local and international efforts toward reducing cancer burden. OBJECTIVE: To estimate cancer burden and trends globally for 204 countries and territories and by Sociodemographic Index (SDI) quintiles from 2010 to 2019. EVIDENCE REVIEW: The GBD 2019 estimation methods were used to describe cancer incidence, mortality, years lived with disability, years of life lost, and disability-adjusted life years (DALYs) in 2019 and over the past decade. Estimates are also provided by quintiles of the SDI, a composite measure of educational attainment, income per capita, and total fertility rate for those younger than 25 years. Estimates include 95% uncertainty intervals (UIs). FINDINGS: In 2019, there were an estimated 23.6 million (95% UI, 22.2-24.9 million) new cancer cases (17.2 million when excluding nonmelanoma skin cancer) and 10.0 million (95% UI, 9.36-10.6 million) cancer deaths globally, with an estimated 250 million (235-264 million) DALYs due to cancer. Since 2010, these represented a 26.3% (95% UI, 20.3%-32.3%) increase in new cases, a 20.9% (95% UI, 14.2%-27.6%) increase in deaths, and a 16.0% (95% UI, 9.3%-22.8%) increase in DALYs. Among 22 groups of diseases and injuries in the GBD 2019 study, cancer was second only to cardiovascular diseases for the number of deaths, years of life lost, and DALYs globally in 2019. Cancer burden differed across SDI quintiles. The proportion of years lived with disability that contributed to DALYs increased with SDI, ranging from 1.4% (1.1%-1.8%) in the low SDI quintile to 5.7% (4.2%-7.1%) in the high SDI quintile. While the high SDI quintile had the highest number of new cases in 2019, the middle SDI quintile had the highest number of cancer deaths and DALYs. From 2010 to 2019, the largest percentage increase in the numbers of cases and deaths occurred in the low and low-middle SDI quintiles. CONCLUSIONS AND RELEVANCE: The results of this systematic analysis suggest that the global burden of cancer is substantial and growing, with burden differing by SDI. These results provide comprehensive and comparable estimates that can potentially inform efforts toward equitable cancer control around the world.

GlobalSurg, C. and S. National Institute for Health Research Global Health Research Unit on Global (2021). "Global variation in postoperative mortality and complications after cancer surgery: a multicentre, prospective cohort study in 82 countries." Lancet **397**(10272): 387-397.

BACKGROUND: 80% of individuals with cancer will require a surgical procedure, yet little comparative data exist on early outcomes in low-income and middle-income countries (LMICs). We compared postoperative outcomes in breast, colorectal, and gastric cancer surgery in hospitals worldwide, focusing on the effect of disease stage and complications on postoperative mortality. METHODS: This was a multicentre, international prospective cohort study of consecutive adult patients undergoing surgery for primary breast, colorectal, or gastric cancer requiring a skin incision done under general or neuraxial anaesthesia. The primary outcome was death or major complication within 30 days of surgery. Multilevel logistic regression determined relationships within three-level nested models of patients within hospitals and countries. Hospital-level infrastructure effects were explored with three-way mediation analyses. This study was registered with ClinicalTrials.gov, NCT03471494. FINDINGS: Between April 1, 2018, and Jan 31, 2019, we enrolled 15 958 patients from 428 hospitals in 82 countries (high income 9106 patients, 31 countries; upper-middle income 2721 patients, 23 countries; or lower-middle income 4131 patients, 28 countries). Patients in LMICs presented with more advanced disease compared with patients in high-income countries. 30-day mortality was higher for gastric cancer in low-income or lower-middle-income countries (adjusted odds ratio 3.72, 95% CI 1.70-8.16) and for colorectal cancer in low-income or lower-middle-income countries (4.59, 2.39-8.80) and upper-middle-income countries (2.06, 1.11-3.83). No difference in 30-day mortality was seen in breast cancer. The proportion of patients who died after a major complication was greatest in low-income or lower-middle-income countries (6.15, 3.26-11.59) and upper-middle-income countries (3.89, 2.08-7.29). Postoperative death after complications was partly explained by patient factors (60%) and partly by

hospital or country (40%). The absence of consistently available postoperative care facilities was associated with seven to 10 more deaths per 100 major complications in LMICs. Cancer stage alone explained little of the early variation in mortality or postoperative complications. INTERPRETATION: Higher levels of mortality after cancer surgery in LMICs was not fully explained by later presentation of disease. The capacity to rescue patients from surgical complications is a tangible opportunity for meaningful intervention. Early death after cancer surgery might be reduced by policies focusing on strengthening perioperative care systems to detect and intervene in common complications. FUNDING: National Institute for Health Research Global Health Research Unit.

Gnagnarella, P., et al. (2021). "Vitamin D Supplementation and Cancer Mortality: Narrative Review of Observational Studies and Clinical Trials." Nutrients **13**(9).

Several studies have investigated the beneficial effects of vitamin D on survival of cancer patients. Overall evidence has been accumulating with contrasting results. This paper aims at narratively reviewing the existing articles examining the link between vitamin D supplementation and cancer mortality. We performed two distinct searches to identify observational (ObS) studies and randomized clinical trials (RCTs) of vitamin D supplementation (VDS) in cancer patients and cohorts of general population, which included cancer mortality as an outcome. Published reports were gathered until March 2021. We identified 25 papers published between 2003 and 2020, including n. 8 RCTs on cancer patients, n. 8 population RCTs and n. 9 ObS studies. There was some evidence that the use of VDS in cancer patients could improve cancer survival, but no significant effect was found in population RCTs. Some ObS studies reported evidence that VDS was associated with a longer survival among cancer patients, and only one study found an opposite effect. The findings do not allow conclusive answers. VDS may have the potential as treatment to improve survival in cancer patients, but further investigations are warranted. We strongly support investment in well-designed and sufficiently powered RCTs to fully evaluate this association.

Godono, A., et al. (2022). "The association between occupational asbestos exposure with the risk of incidence and mortality from prostate cancer: a systematic review and meta-analysis." Prostate Cancer Prostatic Dis **25**(4): 604-614.

BACKGROUND: There is conflicting evidence on the association between asbestos exposure and prostate cancer (PCa). Two recent meta-analyses have claimed that exposure is associated with increased PCa incidence and mortality, but they suffer from some methodological flaws. Given the potential importance of this research question, we aimed to perform a methodologically sound systematic review and meta-analysis to investigate the association between occupational asbestos exposure and the incidence of and mortality from PCa. METHODS: We followed PRISMA guidelines to systematically search for pertinent articles in three relevant electronic databases: Pubmed, Scopus, and Embase, from their inception to July 2020. The methodological quality of included articles was evaluated using the US National Institutes of Health tool. Standardized incidence ratios (SIRs) and standardized mortality ratios (SMRs) for PCa, as well as respective 95% confidence intervals (CIs), were extracted or calculated for each included cohort. Main and subgroup meta-analyses according to first year of employment, industry, asbestos type, and geographic region were performed. RESULTS: Sixty-five articles comprising 68 cohorts were included. PCa incidence and mortality were not significantly associated with occupational asbestos exposure (pooled SIR: 1.06, 95% CI: 1.00-1.13, P = 0.062; pooled SMR: 1.03, 95% CI: 0.99-1.06, P = 0.115). PCa incidence was higher among workers employed after 1960 (SIR: 1.10, 95% CI: 1.01-1.20). Pooled SIR was elevated in European (SIR: 1.09, 95% CI: 1.01-1.18) and UK cohorts (SIR: 1.05, 95% CI: 1.02-1.09). Mortality was elevated in North American cohorts (SMR: 1.06, 95% CI: 1.02-1.10). Studies of lower methodological quality appeared to yield elevated SIRs or SMRs. CONCLUSIONS: This systematic review and meta-analysis provides evidence that men with occupational asbestos exposure have a PCa incidence and mortality similar to that of the general population. Temporal and geographical variables seem to be related to higher SMR or SIR.

Grieshober, L., et al. (2020). "AHRR methylation in heavy smokers: associations with smoking, lung cancer risk, and lung cancer mortality." BMC Cancer **20**(1): 905.

BACKGROUND: A low level of methylation at cg05575921 in the aryl-hydrocarbon receptor repressor (AHRR) gene is robustly associated with smoking, and some studies have observed associations between cg05575921 methylation and increased lung cancer risk and mortality. To prospectively examine whether decreased methylation at cg05575921 may identify high risk subpopulations for lung cancer screening among heavy smokers, and mortality in cases, we evaluated associations between cg05575921 methylation and lung cancer risk and mortality, by histotype, in heavy smokers. METHODS: The beta-Carotene and Retinol Efficacy Trial (CARET) included enrollees ages 45-69 with >/= 20 pack-year smoking

histories and/or occupational asbestos exposure. A subset of CARET participants had cg05575921 methylation available from HumanMethylationEPIC assays of blood collected on average 4.3 years prior to lung cancer diagnosis in cases. Cg05575921 methylation beta-values were treated continuously for a 10% methylation decrease and as quintiles, where quintile 1 (Q1, referent) represents high methylation and Q5, low methylation. We used conditional logistic regression models to examine lung cancer risk overall and by histotype in a nested case-control study including 316 lung cancer cases (diagnosed through 2005) and 316 lung cancer-free controls matched on age (+/-5 years), sex, race/ethnicity, enrollment year, current/former smoking, asbestos exposure, and follow-up time. Mortality analyses included 372 lung cancer cases diagnosed between 1985 and 2013 with available methylation data. We used Cox proportional hazards models to examine mortality overall and by histotype. RESULTS: Decreased cg05575921 methylation was strongly associated with smoking, even in our population of heavy smokers. We did not observe associations between decreased pre-diagnosis cg05575921 methylation and increased lung cancer risk, overall or by histotype. We observed linear increasing trends for lung cancer-specific mortality across decreasing cg05575921 methylation quintiles for adenocarcinoma and small cell carcinoma (P-trends = 0.01 and 0.04, respectively). CONCLUSIONS: In our study of heavy smokers, decreased cg05575921 methylation was strongly associated with smoking but not increased lung cancer risk. The observed association between cg05575921 methylation and increased mortality in adenocarcinoma and small cell histotypes requires further examination. Our results do not support using decreased cg05575921 methylation as a biomarker for lung cancer screening risk stratification.

Grilli, R., et al. (2021). "The effects of centralizing cancer surgery on postoperative mortality: A systematic review and meta-analysis." J Health Serv Res Policy **26**(4): 289-301.

OBJECTIVES: To review the evidence of the effects of centralization of cancer surgery on postoperative mortality. METHODS: We searched Medline, Embase, Cinahl, Cochrane and Scopus (up to November 2019) for studies that (i) assessed the effects of centralization of cancer surgery policies on in-hospital or 30-day mortality, or (ii) described changes in both postoperative mortality for a surgical intervention and degree of centralization using reduction in the number of hospitals or increases in the proportion of patients undergoing cancer surgery at high volume hospitals as proxy. PRISMA guidelines were followed. We estimated pooled odds ratios (OR) and conducted meta-regression to assess the relationship between degree of centralization and mortality. RESULTS: A total of 41 studies met our inclusion criteria of which 15 evaluated the effect of centralization policies on postoperative mortality after cancer surgery and 26 described concurrent changes in the degree of centralization and postoperative mortality. Policy evaluation studies mainly used before-after designs (n = 13) or interrupted time series analysis (n = 2), mainly focusing on pancreatic, oesophageal and gastric cancer. All but one showed some degree of reduction in postoperative mortality, with statistically significant effects demonstrated by six studies. The pooled odds ratio for centralization policy effect was 0.68 (95% Confidence interval: 0.54-0.85; I(2) = 80%). Meta-regression analysis of the 26 descriptive studies found that an increase of the proportion of patients treated at high volume hospitals was associated with greater reduction in postoperative mortality. CONCLUSIONS: Centralization of cancer surgery is associated with reduced postoperative mortality. However, existing evidence tends to be of low quality and estimates of the effect size are likely inflated. There is a need for prospective studies using more robust approaches, and for centralization efforts to be accompanied by well-designed evaluations of their effectiveness.

Grytten, N., et al. (2022). "Cancer related mortality in multiple sclerosis. A population based cohort study." Mult Scler Relat Disord **69**: 104417.

BACKGROUND: Cancer is a major cause of death, but how cancer influences mortality risk in Multiple Sclerosis (MS) is unclear. OBJECTIVES: Determine all-cause mortality and mortality following a cancer diagnosis among MS patients compared with matched population controls. METHODS: Norwegian MS patients born 1930 - 1979 (n= 6950) followed-up 1953 - 2016, were matched with 37 922 controls. We compared incident cancer diagnosis from the Cancer Registry of Norway, date of death from the Cause of Death Registry, education from the National Education Database, by multivariate Cox proportional hazard regression. RESULTS: Hazard ratio (HR) and 95% confidence interval (CI) for all-cause mortality among MS patients was 4.97 (4.64 - 5.33), and 2.61 (2.29 - 2.98) for mortality following a cancer diagnosis. Mortality in MS was highest following urinary- (2.53: 1.55 - 4.14), colorectal- (2.14: 1.47 - 3.11), hematological- (1.76: 1.08 - 2.88), ovarian - 2.30 (1.73-3.06) and breast cancer diagnosis (2.61: 1.85 - 3.68), compared to controls. High education was inversely associated with mortality among MS patients. CONCLUSIONS: All-cause mortality was five- fold and mortality following a cancer diagnosis was two-fold increased among MS patients. Mortality following

specific cancers raises the possibility of diagnostic neglect.

Gu, B., et al. (2021). "Variations in incidence and mortality rates of endometrial cancer at the global, regional, and national levels, 1990-2019." Gynecol Oncol **161**(2): 573-580.

BACKGROUND: Endometrial cancer (EC) is a commonly diagnosed cancer in women. A comprehensive knowledge of its epidemiological features is essential for understanding the disease burden and guiding prevention strategies. METHODS: We retrieved the incidence and mortality data of EC from the Global Burden of Disease database. Estimated average percentage change (EAPC) was used to quantify the trends of the age-standardized incidence and mortality rates (ASIR and ASMR, respectively) of EC from 1990 to 2019. RESULTS: Globally, the ASIR of EC significantly increased by 0.69% (95% confidence interval [CI] 0.57-0.81%) per year between 1990 and 2019. This increasing trend was also observed in 160 countries or territories, regardless of the sociodemographic status. The most pronounced increase was found in Italy (EAPC = 4.81, 95% CI, 4.10-5.53), followed by Saudi Arabia and Singapore. Between 1990 and 2019, the ASMR of EC decreased significantly worldwide (EAPC = -0.85, 95% CI, -0.93 to -0.76) but increased significantly in 91 countries or territories, with the highest increase in Lesotho (EAPC = 3.27, 95% CI, 2.81-3.74). The ASMR-ASIR ratio of EC was higher in developing countries than in developed countries. This ratio showed a decreasing trend at the national level over the past three decades. CONCLUSIONS: EC incidence has ubiquitously increased worldwide. EC mortality has decreased at the global level but increased in many countries. More efforts are required to alleviate the disease burden of EC.

Gu, W., et al. (2022). "The association between biomarkers of acrylamide and cancer mortality in U.S. adult population: Evidence from NHANES 2003-2014." Front Oncol **12**: 970021.

The association between acrylamide (AA) and the development of cancer has been extensively discussed but the results remained controversial, especially in population studies. Large prospective epidemiological studies on the relationship of AA exposure with cancer mortality were still lacking. Therefore, we aimed to assess the association between AA biomarkers and cancer mortality in adult population from National Health and Nutrition Examination Survey (NHANES) 2003-2014. We followed 3717 participants for an average of 10.3 years. Cox regression models with multivariable adjustments were performed to determine the relationship of acrylamide hemoglobin adduct (HbAA) and glycidamide hemoglobin adduct (HbGA) with cancer mortality. Mediation analysis was conducted to demonstrate the mediated role of low-grade inflammation score (INFLA-score) in this correlation. Compared with the lowest quintile, participants with the highest quintile of HbAA, HbGA and HbAA+HbGA had increased cancer mortality risk, and the hazard ratios(HRs) were 2.07 (95%CI:1.04-4.14) for HbAA, 2.39 (95%CI:1.29-4.43) for HbGA and 2.48 (95%CI:1.28-4.80) for HbAA+HbGA, respectively. And there was a considerable non-linearity association between HbAA and cancer mortality (p (for non-linearity) = 0.0139). We further found that increased INFLA-score significantly mediated 71.67% in the effect of HbGA exposure on increased cancer mortality risk. This study demonstrates that hemoglobin biomarkers of AA are positively associated with cancer mortality in adult American population and INFLA-score plays a mediated role in this process. Our findings can raise public awareness of environmental and dietary exposure to acrylamide and remind people to refrain from smoking or having acrylamide-rich foods.

Guan, T., et al. (2022). "Long-Term Cardiovascular Mortality among 80,042 Older Patients with Bladder Cancer." Cancers (Basel) **14**(19).

BACKGROUND: To identify the risk of death from cardiovascular disease (CVD) in older patients with bladder cancer (BC). METHODS: This population-based study included 80,042 older BC patients (>/=65 years) diagnosed between 1975 and 2018, with a mean follow-up of 17.2 years. The proportion of deaths, competing risk models, standardized mortality ratio (SMR), and absolute excess risk (AER) per 10,000 person-years were applied to identify the risk of CVD-related deaths among older BC patients. RESULTS: For older patients with BC, CVD-related death was the chief cause of death, and cumulative CVD-related mortality also exceeded primary BC as the leading cause of death mostly 5-10 years after BC diagnosis, especially in localized-stage and low-grade subgroups. The risk of short- and long-term CVD-related death in older BC patients was higher than in the general older adult population (SMR = 1.30, 95% CI 1.28-1.32; AER = 105.68). The risk of sex-specific CVD-related deaths also increased compared to the general population of older adults, including heart disease, cerebrovascular diseases, hypertension without heart disease, atherosclerosis, aortic aneurysm and dissection, and other diseases of the arteries, arterioles, and capillaries. CONCLUSIONS: CVD-related death is an important competing risk among older BC patients and has surpassed primary BC as the chief cause of death,

mainly 5-10 years after BC diagnosis. The risk of CVD-related death in older patients with BC was greater than in the general population. The management of older patients with BC should focus not only on the primary cancer but also on CVD-related death.

Guerville, F., et al. (2022). "Does Inflammation Contribute to Cancer Incidence and Mortality during Aging? A Conceptual Review." Cancers (Basel) **14**(7).

Aging is associated with chronic low-grade inflammation, cancer incidence and mortality. As inflammation contributes to cancer initiation and progression, one could hypothesize that age-associated chronic low-grade inflammation contributes to the increase in cancer incidence and/or mortality observed during aging. Here, we review the evidence supporting this hypothesis: (1) epidemiological associations between biomarkers of systemic inflammation and cancer incidence and mortality in older people, (2) therapeutic clues suggesting that targeting inflammation could reduce cancer incidence and mortality and (3) experimental evidence from animal models highlighting inflammation as a link between various mechanisms of aging and cancer initiation and progression. Despite a large body of literature linking aging, inflammation and cancer, convincing evidence for the clear implication of specific inflammatory pathways explaining cancer incidence or mortality during aging is still lacking. Further dedicated research is needed to fill these gaps in evidence and pave the way for the development of applications in clinical care.

Guo, K., et al. (2022). "Association between chronic kidney disease and cancer including the mortality of cancer patients: national health and nutrition examination survey 1999-2014." Am J Transl Res **14**(4): 2356-2366.

PURPOSE: This study aimed to investigate the association between chronic kidney disease (CKD) and different types of cancer and the effect of CKD on mortality among types of cancer. METHODS: 30559 participants from NHANES 1999-2014 were included in our analysis, which had 2824 participants with cancer. Subgroups were grouped by cancer location. The association of different types of cancer with CKD was assessed using logistic regression models. Kaplan-Meier estimates and Cox proportional hazards models were used to evaluate the correlation between CKD and all-cause mortality in different cancer groups. RESULTS: Age, gender, race, education level, income level, hypertension, diabetes, smoking status, alcohol consumption, TG, HDL-C, UA and eGFR were significantly different between the cancer and non-cancer group. The three cancers with highest prevalence of CKD were kidney cancer (72.3%), bladder cancer (54.7%), and colon cancer (43.0%) in this study. The prevalence of CKD was higher in cancer patients compared to non-cancer ones. Only genitourinary cancer showed a positive association with CKD (OR=1.23, 95% CI: 1.05-1.44) after adjusting for confounding factors. However, CKD was an independent risk factor for mortality from cancer regardless of the type of cancer. CONCLUSION: CKD is significantly associated only with genitourinary cancer among different types of cancer. CKD is an independent risk factor for survival in cancer patients, regardless of the type of cancer. Monitoring and maintaining the renal function of cancer patients is essential for prolonging their life.

Guo, M., et al. (2022). "Metformin Use and Mortality in Women with Ovarian Cancer: An Updated Meta-Analysis." Int J Clin Pract **2022**: 9592969.

BACKGROUND: Previous observational studies and meta-analysis suggested a possible association between metformin use and reduced mortality in women with ovarian cancer (OC). However, clinical factors that may influence the relationship remain poorly evaluated. We performed an updated meta-analysis to systematically evaluate the above association and to observe the potential influences of study characteristics on the association. METHODS: Relevant studies reporting the association between metformin use and mortality in women with OC in the multivariate adjusted model were identified by search of electronic databases that included PubMed, Embase, and Web of Science. The random-effects model was adopted to combine the results. RESULTS: Nine studies including 10030 women with OC were included. Overall, metformin use was independently associated with reduced overall mortality (hazard ratio (HR): 0.72, 95% confidence interval (CI): 0.55-0.93, P=0.01; I (2) = 62%). Consistent results were observed for studies comparing metformin users with nondiabetic women and studies comparing metformin users with diabetic women who did not use metformin (P for subgroup analysis = 0.70). Further subgroup analyses showed consistent results in studies with metformin use before or after the diagnosis of OC, with or without adjustment of body mass index (BMI) and with or without adjustment of concurrent medications (P for subgroup analyses all >0.10). CONCLUSION: Metformin use is associated with reduced mortality in women with OC, which may be independent of the diabetic status of the controls, timing of metformin use, or adjustment of BMI and concurrent medications. Clinical trials are needed to validate the potential benefits of metformin on survival of OC.

Guo, M., et al. (2021). "Trends in cervical cancer mortality in China from 1989 to 2018: an age-period-cohort study and Joinpoint analysis." BMC Public Health **21**(1): 1329.

BACKGROUND: Worldwide, cervical cancer is the second-most-common malignancy of the female reproductive system. Due to its large population, China accounted for 11.9% of cervical cancer deaths, and 12.3% of global cervical cancer DALYs in 2017. In 2009, China launched a nationwide screening program, yet mortality from cervical cancer has shown an upward trend in recent years. The aim of this study was to explore factors affecting cervical cancer mortality rates in China, and contribute to their future reduction. METHODS: In this descriptive study, a Joinpoint regression analysis and age-period-cohort (APC) model based on the intrinsic estimator (IE) algorithm were utilized. Data from the period 1989-2018 were extracted from the International Agency for Research on Cancer (IARC) Database of WHO (1989-2000) and China Health Statistical Yearbook database (2002-2018). RESULTS: Our study found mortality from cervical cancer to have initially declined, but increase thereafter over the entire observation period in both rural and urban China. The influence of age, period and cohort effect on the mortality rate had statistical significance. The effect of age increased with years, becoming a contributing factor in women aged over 45 years countrywide. Conversely, the cohort effect became a protective factor for women born after 1938 in urban areas, and for women born after 1958 in rural areas. The period effect was relatively less impactful. CONCLUSIONS: The study indicates that organized cervical screening projects facilitated the identification of potential patients, or patients with comorbidities. Correspondingly, mortality was found to increase with incidence, particularly among elderly women, indicating that newly diagnosed patients were at an advanced stage of cervical cancer, or were not receiving appropriate treatment. Therefore, the coverage of cervical cancer screening should be improved, and women's health awareness promoted. Early diagnosis and treatment is critical to reduce the disease burden and improve outcomes.

Guo, Q., et al. (2021). "Relationship between particulate matter exposure and female breast cancer incidence and mortality: a systematic review and meta-analysis." Int Arch Occup Environ Health **94**(2): 191-201.

OBJECTIVES: The associations of PM with the risk and prognosis of breast cancer have not been determined. This systematic review aimed to provide an updated understanding of the relationship between PM exposure level and breast cancer incidence and mortality. METHODS: Articles from Web of Science and PubMed databases were methodically inspected until March 8, 2020. In final, 15 studies were kept for analysis, which provided necessary information to estimate the impact of PM on breast cancer risk and prognosis. These studies were combined for quantitative analyses to evaluate the effect of per 10 mug /m(3) increment exposure of PM(2.5) (< 2.5 mum in aerodynamic diameter) and PM(10) (< 10 mum in aerodynamic diameter) using random-effects model. RESULTS: PM(2.5) exposure was associated with increased breast cancer mortality (relative risk [RR] = 1.09; 95% confidence interval [CI]: 1.02, 1.16; P(Q-test) = 0.158). No association of PM(2.5) (1.02; 0.97, 1.18; 0.308) and PM(10) (1.03; 0.98, 1.09; 0.009) with the increase incidence of breast cancer was observed. Stratified analysis suggested that PM(2.5) was associated with the increase mortality of breast cancer (1.10; 1.03, 1.17; 0.529) in subgroup of developed country. PM(10) was associated with breast cancer incidence based on studies published after 2017 (1.08; 1.00, 1.15; 0.157) and European studies (1.15; 1.06, 1.25; 0.502). CONCLUSIONS: Our study indicated that PM(2.5) exposure was related to breast cancer mortality. Further researches in this field are needed to validate the conclusion.

Guo, X., et al. (2022). "Association of urinary or blood heavy metals and mortality from all causes, cardiovascular disease, and cancer in the general population: a systematic review and meta-analysis of cohort studies." Environ Sci Pollut Res Int **29**(45): 67483-67503.

Amounting epidemiological evidence has shown detrimental effects of heavy metals on a wide range of diseases. However, the effect of heavy metal exposure on mortality in the general population remains unclear. The primary objective of this study was to clarify the associations between heavy metals and mortality from all causes, cardiovascular disease (CVD), and cancer based on prospective studies. We comprehensively searched Pubmed, Embase, and Web of Science electronic databases to identify studies published from their inception until 1 March 2022. Investigators identified inclusion criteria, extracted study characteristics, and assessed the methodological quality of included studies according to standardized guidelines. Meta-analysis was conducted if the effect estimates of the same outcome were reported in at least three studies. Finally, 42 original studies were identified. The results of meta-analysis showed that cadmium and lead exposure was significantly associated with mortality from all causes, CVD, and cancer in the general population. Moderate evidence suggested there was a link between arsenic exposure and mortality. The adverse effects of mercury and other heavy metals on mortality were inconclusive.

Epidemiological evidence for the joint effect of heavy metal exposure on mortality was still indeterminate. In summary, our study provided compelling evidence that exposure to cadmium, lead, and arsenic were associated with mortality from all causes, CVD, and cancer, while the evidence on other heavy metals, for example mercury, was insignificant or indeterminate. Nevertheless, further prospective studies are warranted to explore the joint effects of multiple metal exposure on mortality.

Guo, Z., et al. (2022). "Association between vitamin D supplementation and cancer incidence and mortality: A trial sequential meta-analysis of randomized controlled trials." Crit Rev Food Sci Nutr: 1-15.

Observational studies and clinical trials have evaluated the associations between vitamin D supplementation and cancer incidence/mortality and obtained mixed results. Previous meta-analyses have also yielded inconsistent conclusions. In this paper, we conduct an updated meta-analysis by including current randomized clinical trials (RCTs) to assess the association between vitamin D supplementation and cancer incidence and mortality. The PubMed, Scopus and Embase databases were systematically searched from their inception to 6 February 2022. Fixed-effects meta-analyses were conducted. Trial sequential analyses were performed using a risk ratio reduction threshold of 10% for cancer incidence and mortality. Twenty-six RCTs were eligible, and pooled results indicated that vitamin D supplementation, compared to placebo with/without calcium, was not associated with a reduction in total cancer incidence (risk ratio: 0.98, 95% CI: 0.94, 1.02; I(2) = 0%). In contrast, vitamin D supplementation significantly reduced total cancer mortality (risk ratio: 0.88, 95% CI: 0.8, 0.96; I(2) = 0%). Moreover, trial sequential analysis provided reliable evidence that supplementation with vitamin D lowered the relative risk of total cancer mortality by 10%. Our updated meta-analysis suggested that vitamin D supplementation did not reduce total cancer incidence but significantly lowered total cancer mortality.

Guven, D. C., et al. (2021). "Newly diagnosed cancer and the COVID-19 pandemic: tumour stage migration and higher early mortality." BMJ Support Palliat Care.

BACKGROUND: We compared the new outpatient clinic referrals during the first 10 months of the COVID-19 pandemic with the year before. METHODS: We compared baseline characteristics of the 2208 new referrals in 2020 (n=922) and 2019 (n=1286) with Chi(2) and Mann-Whitney U tests and calculated ORs with binary logistic regression. To evaluate the expected changes in the cancer survival secondary to stage migration, we used the 5-year survival data of Survival, Epidemiology and End Results (SEER) Program 2010-2016. RESULTS: The percentage of patients with inoperable or metastatic disease was significantly increased during the pandemic (49.8% vs 39%, OR: 1.553, 95% CI: 1.309 to 1.843, p<0.001). We observed a significant decrease in the percentage of patients diagnosed via the screening methods (18.8% vs 28.7%, OR: 1.698, 95% CI: 1.240 to 2.325, p=0.001). The 90-day mortality after the cancer diagnosis was significantly higher during the pandemic (10.5% vs 6.6%, OR: 1.661, 95% CI: 1.225 to 2.252, p=0.001). Due to the increased advanced-stage disease rate at first referral, significant decreases in 5-year survival rates were expected for breast cancer (-8.9%), colorectal cancer (-11.1%), cervix cancer (-10.3%) and melanoma (-7%). CONCLUSION: We think that collaborative efforts are paramount to prevent the pandemic of late cancer diagnoses and ensure patient safety during the pandemic.

Hamers, P. A. H., et al. (2022). "External Validation of the Colon Life Nomogram for Predicting 12-Week Mortality in Dutch Metastatic Colorectal Cancer Patients Treated with Trifluridine/Tipiracil in Daily Practice." Cancers (Basel) **14**(20).

BACKGROUND: Predicting prognosis in refractory metastatic colorectal cancer (mCRC) patients is needed to guide decision making. The Colon Life nomogram was developed to predict 12-week mortality in refractory mCRC patients. The aim of this study is to validate the Colon Life nomogram in last line/refractory patients receiving trifluridine/tipiracil (FTD/TPI) in daily practice. METHODS: The validation cohort consists of 150 QUALITAS study patients, an observational substudy of the Prospective Dutch CRC cohort, who were treated with FTD/TPI between 2016 and 2019. Model performance was assessed on discrimination, calibration, and clinical usefulness. The additional prognostic value of baseline quality of life (QoL) and thymidine kinase (TK1) expression in tissue was explored. RESULTS: Of the 150 patients, 25 (16.7%) died within 12 weeks of starting FTD/TPI treatment. The C-statistic was 0.63 (95% C.I. 0.56-0.70). The observed/expected ratio was 0.52 (0.37-0.73). The calibration intercept and slope were -1.06 (-1.53 to -0.58) and 0.41 (0.01-0.81), respectively, which indicated overestimation of 12-week mortality by the nomogram. Decision curve analysis showed the nomogram did not yield a positive net benefit at clinically meaningful thresholds for predicted 12-week mortality. Addition of QoL to the nomogram improved the C-statistic to 0.85 (0.81-0.89). TK1 expression was associated with progression-free survival but not with overall survival. CONCLUSION: We demonstrated evident miscalibration of the Colon Life nomogram upon external validation, which

hampers its use in clinical practice. We recommend conducting a study with a sufficiently large sample size to update the Colon Life nomogram or to develop a new model including QoL.

Han, D., et al. (2022). "Association of Dietary Total Antioxidant Capacity with Cancer Recurrence and Mortality among Breast Cancer Survivors: A Prospective Cohort Study." Nutr Cancer **74**(9): 3253-3262.

Antioxidants decrease the risk of breast cancer by reducing oxidative stress, but the association between dietary total antioxidant capacity (DTAC) and cancer recurrence has not yet been investigated. The present study aimed to test the hypothesis that DTAC is inversely associated with cancer recurrence and mortality in breast cancer patients. Breast cancer patients (n = 603) who underwent breast cancer surgery and a dietary survey within 5 years after surgery were recruited. This study observed disease-free survival (DFS) and mortality in breast cancer patients according to DTAC calculated based on 24-hr dietary recall. Total DTAC was significantly lower in patients with cancer recurrence than in those without. DFS was positively associated with the total DTAC (p = 0.005) and DTAC of vegetables and legumes (p = 0.001 and p = 0.010), respectively. However, total DTAC was not associated with mortality. Cox proportional hazards regression analysis showed that total DTAC (HR: 0.44, 95% CI 0.26-0.94) and DTAC of vegetables (HR: 0.30, 95% CI 0.14-0.65) and legumes (HR: 0.38, 95% CI 0.18-0.73) were inversely associated with cancer recurrence after adjusting for confounding factors. This study was the first to indicate that total DTAC and DTAC of vegetables and legumes could be beneficial in decreasing breast cancer recurrence.

Han, K. T., et al. (2022). "Association of institutional transition of cancer care with mortality in elderly patients with lung cancer: a retrospective cohort study using national claim data." BMC Cancer **22**(1): 452.

BACKGROUND: Although survival based outcomes of lung cancer patients have been well developed, institutional transition of cancer care, that is, when patients transfer from primary visiting hospitals to other hospitals, and mortality have not yet been explored using a large-scale representative population-based sample. METHODS: Data from the Korean National Elderly Sampled Cohort survey were used to identify patients with lung cancer who were diagnosed during 2005-2013 and followed up with for at least 1 year after diagnosis (3738 patients with lung cancer aged over 60 years). First, the authors examined the distribution of the study population by mortality, and Kaplan-Meier survival curves/log-rank test were used to compare mortality based on institutional transition of cancer care. Survival analysis using the Cox proportional hazard model was conducted after controlling for all other variables. RESULTS: Results showed that 1-year mortality was higher in patients who underwent institutional transition of cancer care during 30 days after diagnosis (44.2% vs. 39.7%, p = .027); however, this was not associated with 5-year mortality. The Cox proportional hazard model showed that patients who underwent institutional transition of cancer care during 30 days after diagnosis exhibited statistically significant associations with high mortality for 1 year and 5 years (1-year mortality, Hazard ratio [HR]: 1.279, p = .001; 5-year mortality, HR: 1.158, p = .002). CONCLUSION: This study found that institutional transition of cancer care was associated with higher mortality among elderly patients with lung cancer. Future consideration should also be given to the limitation of patients' choice when opting for institutional transition of care since there are currently no control mechanisms in this regard. Results of this study merit health policymakers' attention.

Han, K. T., et al. (2022). "Impact of Cardiovascular Diseases on Mortality in Gastric Cancer Patients with Preexisting Chronic Disease." Yonsei Med J **63**(11): 1043-1049.

PURPOSE: Chronic diseases and cardiovascular diseases (CVD) have been independently linked to poorer cancer outcomes. This study investigated whether gastric cancer patients with hypertension, diabetes, or dyslipidemia have higher mortality if diagnosed with CVD in the past year before cancer diagnosis. MATERIALS AND METHODS: Data were obtained from the National Health Insurance database for 2002 to 2019. The study population consisted of gastric cancer patients with hypertension, diabetes, or dyslipidemia. The outcome measure was 5-year mortality in relation to incident status of CVD within 1 year before cancer diagnosis. A survival analysis was conducted using the Cox proportional hazards model. Subgroup analysis was conducted according to age, economic status, and type of hospital first visited for cancer treatment. RESULTS: Of a total of 6458 individuals, 2123 (32.7%) were diagnosed with CVDs in the past year before cancer diagnosis. Compared to participants without a history of CVD, those who were diagnosed with CVD showed a higher risk of 5-year mortality (hazard ratio 1.259, 95% confidence interval 1.138-1.394). The extent to which the mortality risk differed between those with and without CVD was greater for individuals of low economic status and in those receiving their initial cancer treatment in a general hospital. CONCLUSION: Patients with gastric cancer and hypertension, diabetes, or dyslipidemia diagnosed with CVD within 1 year before their cancer diagnosis

had a higher mortality risk, emphasizing the importance of managing cancer patients with chronic disease and subsequent incidence of CVDs.

Han, K. T. and S. Kim (2021). "Post-Diagnostic Statin Use Reduces Mortality in South Korean Patients with Dyslipidemia and Gastrointestinal Cancer." J Clin Med **10**(11).

BACKGROUND: Statins play a role in lowering serum cholesterol and are known to have pleiotropic effects in a variety of diseases, including cancer. Despite the beneficial effects of statins in dyslipidemia patients, the treatment rate for dyslipidemia in Korea remains low, and evidence supporting the continued use of statins is lacking. The purpose of this study was to evaluate the effect of continued statin use and dosage on patient mortality after diagnosis of dyslipidemia and gastrointestinal (GI) cancer. METHODS: We used data from the National Health Insurance Sampling (NHIS) cohort to evaluate patients diagnosed with dyslipidemia from 2002 to 2015. A total of 901 GI cancer patients with dyslipidemia and 62,727 non-cancer dyslipidemia patients were included in the study. During the study period, each patient's medication possession ratio (MPR) after diagnosis was evaluated as a measure of continued statin use. Statin dosage was measured based on a defined daily dose (DDD). Finally, we used Cox-proportional hazard ratios to identify associations between the continual use of statins and mortality in patients with dyslipidemia and GI cancer. RESULTS: In our study, mortality decreased with increasing MPR and reached significance in MPRs exceeding 50% for GI cancer patients and 75% for dyslipidemia patients compared to patients that did not use statins. Moreover, patients with high MPRs had significantly reduced 5-year mortality compared to non-users, and cause-specific mortality analyses revealed that high MPR was associated with decreased colorectal cancer death. We did not find a significant dose-response relationship between statins and mortality. CONCLUSION: Our findings suggest that continued statin use after diagnosis is associated with reduced patient mortality. Altogether, these results support the continued use of statins in dyslipidemia patients with and without GI cancer and highlight the importance of patient education by healthcare providers.

Han, K. T., et al. (2021). "Does Delaying Time in Cancer Treatment Affect Mortality? A Retrospective Cohort Study of Korean Lung and Gastric Cancer Patients." Int J Environ Res Public Health **18**(7).

The aim of this study is to investigate the association between delays in surgical treatment and five- and one- year mortality in patients with lung or gastric cancer. The National Health Insurance claims data from 2006 to 2015 were used. The association between time to surgical treatment, in which the cut-off value was set at average time (30 or 50 days), and five year mortality was analyzed using the Cox proportional hazard model. Subgroup analysis was performed based on treatment type and location of medical institution. A total of 810 lung and 2659 gastric cancer patients were included, in which 74.8% of lung and 71.2% of gastric cancer patients received surgery within average. Compared to lung cancer patients who received treatment within 50 days, the five-year (HR 1.826, 95% CI 1.437-2.321) mortality of those who received treatment afterwards was higher. The findings were not significant for gastric cancer based on the after 30 days standard (HR: 1.003, 95% CI: 0.822-1.225). In lung cancer patients, time-to-treatment and mortality risk were significantly different depending on region. Delays in surgical treatment were associated with mortality in lung cancer patients. The findings imply the importance of monitoring and assuring timely treatment in lung cancer patients.

Han, K. T., et al. (2021). "Is time-to-treatment associated with higher mortality in Korean elderly lung cancer patients?" Health Policy **125**(8): 1047-1053.

Lung cancer is a leading cause of cancer-related deaths in many countries, including South Korea. As treatment delays after diagnosis may correlate with survival, this study aimed to investigate the association between time-to-treatment and one-and five-year overall mortality in patients aged 60 years or above. Survival analysis using the Cox proportional hazard model were conducted after controlling for all independent variables. Of a total of 1,535 individuals who received surgical treatment due to lung cancer, 837 patients received treatment within 30 days and 698 after 30 days of initial diagnosis. Individuals who received surgical treatment after 30 days of diagnosis were more likely to die within 1-year (Hazard Ratio, HR: 1.15, 95% Confidence Interval, CI: 1.01-1.32) and 5-year (HR: 1.16, 95% CI: 1.02-1.33) compared to those who received treatment within 30 days. The increase in mortality risk with time delay persisted when applying other cut-off times, including standards at 2, 3, and 6 months. We also found that the mortality rate of lung cancer patients differs depending on age (74 years or younger), household income (<80 percentile), patient severity, and the residing region. Our findings show that time delay is an important factor that can influence the outcome of lung cancer patients, highlighting the importance of monitoring and providing appropriate and timely treatment.

Han, M., et al. (2022). "Cardiorespiratory fitness and mortality from all causes, cardiovascular disease and

cancer: dose-response meta-analysis of cohort studies." Br J Sports Med **56**(13): 733-739.

OBJECTIVE: Current evidence of the associations between cardiorespiratory fitness (CRF) and mortality is limited. We performed a meta-analysis to assess the dose-response association of CRF with mortality from all causes, cardiovascular disease (CVD) and cancer in healthy population. METHODS: PubMed, EMBASE and Web of Science were searched up to 26 December 2019 for reports of cohort studies giving risk estimates for all-cause, CVD and cancer mortality by level of CRF. Cohort studies were included if CRF was assessed by an exercise stress test and reported as at least three levels or per incremental increase, and the association of CRF with all-cause, CVD and cancer mortality was evaluated. Generalised least-squares regression models were used to assess the quantitative relation of CRF with all-cause, CVD and cancer mortality. RESULTS: 34 cohort studies were eligible for the meta-analysis. The pooled relative risks (RRs) for all-cause, CVD and cancer mortality per one-metabolic equivalent increase in CRF were 0.88 (95% CI 0.83 to 0.93), 0.87 (95% CI0.83 to 0.91) and 0.93 (95% CI 0.91 to 0.96), respectively. As compared with lowest CRF, with intermediate CRF, the summary RRs for all-cause, CVD and cancer mortality were 0.67 (95% CI 0.61 to 0.74), 0.60 (95% CI 0.51 to 0.69) and 0.76 (95% CI 0.69 to 0.84), respectively, and with highest CRF were 0.47 (95% CI 0.39 to 0.56), 0.49 (95% CI 0.42 to 0.56) and 0.57 (95% CI 0.46 to 0.70), respectively. CONCLUSION: Our analysis showed inverse dose-response associations of CRF with all-cause, CVD and cancer mortality, which provides evidence for public health recommendations for preventing all-cause, CVD and cancer mortality. PROSPERO REGISTRATION NUMBER: CRD42020208883.

Han, Y., et al. (2021). "Breast Cancer Mortality Hot Spots Among Black Women With de Novo Metastatic Breast Cancer." JNCI Cancer Spectr **5**(1).

BACKGROUND: Black women living in southern states have the highest breast cancer mortality rate in the United States. The prognosis of de novo metastatic breast cancer is poor. Given these mortality rates, we are the first to link nationally representative data on breast cancer mortality hot spots (counties with high breast cancer mortality rates) with cancer mortality data in the United States and investigate the association of geographic breast cancer mortality hot spots with de novo metastatic breast cancer mortality among Black women. METHODS: We identified 7292 Black women diagnosed with de novo metastatic breast cancer in Surveillance, Epidemiology, and End Results (SEER). The county-level characteristics were obtained from 2014 County Health Rankings and linked to SEER. We used Cox proportional hazards models to calculate adjusted hazard ratios (aHRs) and 95% confidence intervals (CIs) for mortality between hot spot and non-hot spot counties. RESULTS: Among 7292 patients, 393 (5.4%) resided in breast cancer mortality hot spots. Women residing in hot spots had similar risks of breast cancer-specific mortality (aHR = 0.99, 95% CI = 0.85 to 1.15) and all-cause mortality (aHR = 0.97, 95% CI = 0.84 to 1.11) as women in non-hot spots after adjusting for individual and tumor-level factors and treatments. Additional adjustment for county-level characteristics did not impact mortality. CONCLUSION: Living in a breast cancer mortality hot spot was not associated with de novo metastatic breast cancer mortality among Black women. Future research should begin to examine variation in both individual and population-level determinants, as well as in molecular and genetic determinants that underlie the aggressive nature of de novo metastatic breast cancer.

Heath, A. K., et al. (2021). "Soft Drink and Juice Consumption and Renal Cell Carcinoma Incidence and Mortality in the European Prospective Investigation into Cancer and Nutrition." Cancer Epidemiol Biomarkers Prev **30**(6): 1270-1274.

BACKGROUND: Renal cell carcinoma (RCC) accounts for more than 80% of kidney cancers in adults, and obesity is a known risk factor. Regular consumption of sweetened beverages has been linked to obesity and several chronic diseases, including some types of cancer. It is uncertain whether soft drink and juice consumption is associated with risk of RCC. We investigated the associations of soft drink and juice consumption with RCC incidence and mortality in the European Prospective Investigation into Cancer and Nutrition (EPIC). METHODS: A total of 389,220 EPIC participants with median age of 52 years at recruitment (1991-2000) were included. Cox regression yielded adjusted HRs and 95% confidence intervals (CI) for RCC incidence and mortality in relation to intakes of juices and total, sugar-sweetened, and artificially sweetened soft drinks. RESULTS: A total of 888 incident RCCs and 356 RCC deaths were identified. In models including adjustment for body mass index and energy intake, there was no higher risk of incident RCC associated with consumption of juices (HR per 100 g/day increment = 1.03; 95% CI, 0.97-1.09), total soft drinks (HR = 1.01; 95% CI, 0.98-1.05), sugar-sweetened soft drinks (HR = 0.99; 95% CI, 0.94-1.05), or artificially sweetened soft drinks (HR = 1.02; 95% CI, 0.96-1.08). In these fully adjusted models, none of the beverages was associated with RCC mortality (HR, 95% CI per 100 g/day increment 1.06, 0.97-1.16; 1.03, 0.98-1.09; 0.97, 0.89-1.07; and 1.06, 0.99-1.14, respectively). CONCLUSIONS: Consumption of juices or soft drinks was not associated

with RCC incidence or mortality after adjusting for obesity. IMPACT: Soft drink and juice intakes are unlikely to play an independent role in RCC development or mortality.

Hejazi, E., et al. (2021). "Dietary acid load and mortality from all causes, CVD and cancer: results from the Golestan Cohort Study." Br J Nutr: 1-7.

Given the limited studies and controversial results on association between dietary acid load and mortality from CVD and cancers, we aimed to investigate this association in a large population cohort study in Middle East, with a wide range of dietary acid load. The study was conducted on the platform of the Golestan Cohort Study (GCS), which enrolled 50 045 participants in 2004-2008. Dietary intake was assessed using a validated FFQ. Dietary potential renal acid load (PRAL) score was calculated from nutrient intake. Death and its causes were identified and confirmed by two or three physicians. Cox proportional hazards regression was used to estimate hazard ratio (HR) and 95 % CI for total and cause-specific mortalities. Then, the associations were modelled using restricted cubic splines. PRAL range was -57.36 to +53.81 mEq/d for men and -76.70 to +49.08 for women. During 555 142 person-years of follow-up, we documented 6830 deaths, including 3070 cardiovascular deaths, 1502 cancer deaths and 2258 deaths from other causes. For overall deaths, in final model after adjustment for confounders, participants in the first and fifth quintiles of PRAL had a higher risk of mortality compared with the second quintile of PRAL (HR: 1.08; 95 % CI1.01, 1.16 and HR: 1.07; 95 % CI 1.01, 1.15, respectively); Pfor trend < 0.05). Participants in the first and fifth quintiles of PRAL had a 12 % higher risk of CVD mortality compared with the Q2 of PRAL (HR: 1.12; 95 % CI 1.01-1.25 and HR: 1.12; 95 % CI 1.01, 1.26, respectively; Pfor trend < 0.05). We found that all-cause and CVD mortality rates were higher in the lowest and highest PRAL values, in an approximately U-shaped relation (P-values for the overall association and the non-linear association of energy-adjusted PRAL with total mortality were < 0.001 and < 0.001, and with CVD mortality were 0.008 and 0.003, respectively). Our results highlight unfavourable associations of high acidity and alkalinity of diet with the increased total and CVD mortality risk. It may be important to consider a balanced acid-base diet as a protective strategy to prevent pre-mature death, especially from CVD.

Hektoen, H. H., et al. (2021). "Prediagnostic Serum 25-Hydroxyvitamin D and Mortality Among Bladder Cancer Patients in the Janus Serum Bank Cohort." Clin Epidemiol **13**: 801-811.

PURPOSE: Circulating 25-hydroxyvitamin D (25(OH)D) is inversely associated with overall cancer mortality and selected cancers, while for urothelial bladder cancer (BC) this relationship is unclear. We aimed to examine the association between 25(OH)D and BC mortality. MATERIALS AND METHODS: We used prediagnostic serum from 378 BC cases within the population-based Janus Cohort. Cox regression models estimated hazard ratios (HRs), with 95% confidence intervals (CIs), for the association between 25(OH)D and BC-specific and all-cause mortality. Restricted cubic splines were assessed to examine non-linear risk associations. Analyses were stratified by tumor invasiveness (non-muscle invasive BC (NMIBC) and muscle invasive BC (MIBC)). Additionally, the association between 25(OH)D and all-cause mortality was assessed for 378 cancer-free matched controls. RESULTS: 25(OH)D deficiency (<50 nmol/L) was associated with higher BC-specific mortality (HR 1.87, 95% CI 1.10-3.20), when compared with insufficient levels (50-74 nmol/L). Stratification by tumor invasiveness revealed that this result was evident for NMIBC only, both with respect to BC-specific mortality (HR 2.84, 95% CI 1.14-7.12) and all-cause mortality (HR 1.97, 95% CI 1.06-3.65). No association between 25(OH)D levels and all-cause mortality was found in cancer-free controls. CONCLUSION: 25(OH)D deficiency (<50 nmol/L) prior to a BC diagnosis was associated with increased risk of BC-specific mortality, when compared to insufficient levels (50-74 nmol/L). The results were evident among NMIBC patients only, suggesting a more critical role of vitamin D deficiency in an early stage of the disease.

Hellesnes, R., et al. (2021). "Testicular Cancer in the Cisplatin Era: Causes of Death and Mortality Rates in a Population-Based Cohort." J Clin Oncol **39**(32): 3561-3573.

PURPOSE: Using complete information regarding testicular cancer (TC) treatment burden, this study aimed to investigate cause-specific non-TC mortality with impact on previous treatment with platinum-based chemotherapy (PBCT) or radiotherapy (RT). METHODS: Overall, 5,707 men identified by the Cancer Registry of Norway diagnosed with TC from 1980 to 2009 were included in this population-based cohort study. By linking data with the Norwegian Cause of Death Registry, standardized mortality ratios (SMRs), absolute excess risks (AERs; [(observed number of deaths - expected number of deaths)/person-years of observation] x10,000), and adjusted hazard ratios (HRs) were calculated. RESULTS: Median follow-up was 18.7 years, during which non-TC death was registered for 665 (12%) men. Overall excess non-TC mortality was 23% (SMR, 1.23; 95% CI, 1.14 to

1.33; AER, 11.14) compared with the general population, with increased risks after PBCT (SMR, 1.23; 95% CI, 1.07 to 1.43; AER, 7.68) and RT (SMR, 1.28; 95% CI, 1.15 to 1.43; AER, 19.55). The highest non-TC mortality was observed in those < 20 years at TC diagnosis (SMR, 2.27; 95% CI, 1.32 to 3.90; AER, 14.42). The most important cause of death was non-TC second cancer with an overall SMR of 1.53 (95% CI, 1.35 to 1.73; AER, 7.94), with increased risks after PBCT and RT. Overall noncancer mortality was increased by 15% (SMR, 1.15; 95% CI, 1.04 to 1.27; AER, 4.71). Excess suicides appeared after PBCT (SMR, 1.65; 95% CI, 1.01 to 2.69; AER, 1.39). Compared with surgery, increased non-TC mortality appeared after 3 (HR, 1.47; 95% CI, 0.91 to 2.39), 4 (HR, 1.41; 95% CI, 1.01 to 1.99), and more than four (HR, 2.04; 95% CI, 1.25 to 3.35) cisplatin-based chemotherapy cycles after > 10 years of follow-up. CONCLUSION: TC treatment with PBCT or RT is associated with a significant excess risk of non-TC mortality, and increased risks emerged after more than two cisplatin-based chemotherapy cycles after > 10 years of follow-up.

Helo, D., et al. (2021). "The association of skipping breakfast with cancer-related and all-cause mortality in a national cohort of United States adults." Cancer Causes Control **32**(5): 505-513.

PURPOSE: Many lifestyle and dietary factors have been recognized as risk factors for cancer morbidity and mortality. However, investigations of the association of the frequency of breakfast consumption and cancer are limited. This study aimed to examine the association of skipping breakfast with all-cause and cancer-related mortality in a national cohort of United States men and women. METHODS: Data were from 7,007 adults aged >/= 40 years who participated in the third National Health and Nutrition Examination Survey (1988-1994) and had follow-up information on mortality up until 31 December 2015. Cox proportional hazards regression models were used to calculate hazard ratios (HR) and 95% confidence intervals (CI). RESULTS: The mean age of participants was 55.4 years, with 54.4% and 79% being women and non-Hispanic whites, respectively. Approximately, 16% of participants rarely consumed breakfast, 23.0% consumed breakfast some days, and 61% consumed breakfast every day. During a median follow-up of 22.2 years, 3,573 deaths occurred with 795 being related to cancer. In models adjusting for sociodemographic factors, smoking, physical activity, body mass index, hypertension, diabetes, cholesterol levels, total energy intake and diet quality, persons who rarely consumed breakfast had a higher risk of cancer-related mortality (HR = 1.52; CI:1.06-2.18) and all-cause (HR = 1.69; CI: 1.42-2.02) compared to those who took breakfast every day. CONCLUSION: In this nationally representative sample, skipping breakfast was associated with elevated risks for all-cause and cancer-related mortality. This study provides evidence for the benefits of regular breakfast consumption in reducing the risk of all-cause and cancer mortality.

Hemu, M., et al. (2021). "Associations between sinus tachycardia and adverse cardiovascular outcomes and mortality in cancer patients." J Thorac Dis **13**(8): 4845-4852.

BACKGROUND: Sinus tachycardia in cancer reflects a significant multi-system organ stressor and disease, with sparse literature describing its clinical significance. We assessed cardiovascular (CV) and mortality prognostic implications of sinus tachycardia in cancer patients. METHODS: We conducted a case-control study of 622 cancer patients at a U.S. urban medical center from 2008 to 2016. Cases had ECG-confirmed sinus tachycardia [heart rate (HR) >/=100 bpm] in >/=3 different clinic visits within 1 year of cancer diagnosis excluding a history of pulmonary embolism, thyroid dysfunction, left ventricular ejection fraction <50%, atrial fibrillation/flutter, HR >180 bpm. Adverse CV outcomes (ACVO) were heart failure with preserved ejection fraction (HFpEF), HF with reduced EF (HFrEF), hospital admissions for HF exacerbation (AHFE), acute coronary syndrome (ACS). Regression analyses were conducted to examine the effect of sinus tachycardia on overall ACVO and survival. RESULTS: There were 51 cases, age and sex-matched with 571 controls (mean age 70+/-10, 60.5% women, 76.4% Caucasian). In multivariate analysis over a 10-year follow-up period, sinus tachycardia (HR >/=100 vs. <100 bpm) was an independent predictor of overall ACVO (OR 2.8, 95% CI: 1.4-5.5; P=0.006). There was increased incidence of HFrEF (OR 3.3, 95% CI: 1.6-6.5; P=0.004) and AHFE (OR 6.3, 95% CI: 1.6-28; P=0.023), but not HFpEF or ACS (P>0.05) compared with controls. Sinus tachycardia was a significant predictor of overall mortality after adjusting for significant covariates (HR 2.9, 95% CI 1.8-5; P<0.001). CONCLUSIONS: Independent of typical factors that affect cardiovascular disease, sinus tachycardia around the time of cancer treatment is associated with increased ACVO and mortality in cancer patients at 10 years of follow-up.

Hendrick, R. E., et al. (2021). "Breast Cancer Mortality Rates Have Stopped Declining in U.S. Women Younger than 40 Years." Radiology **299**(1): 143-149.

Background National Center for Health Statistics (NCHS) data for U.S. women have shown a steady decline in breast cancer mortality rates since 1989. Purpose To analyze U.S. breast cancer mortality rates by age decade in women aged 20-79 years and in

women aged 20-39 years and women aged 40-69 years. Materials and Methods The authors conducted a retrospective analysis of (a) female breast cancer mortality rates from NCHS data for 1969-2017 for all races and by race and (b) age- and delay-adjusted invasive breast cancer incidence rates from the Surveillance, Epidemiology, and End Results program. Joinpoint analysis was used to determine trends in breast cancer mortality, invasive breast cancer incidence, and distant-stage (metastatic) breast cancer incidence rates. Results Between 1989 and 2010, breast cancer mortality rates decreased by 1.5%-3.4% per year for each age decade from 20 to 79 years ($P < .001$ for each). After 2010, breast cancer mortality rates continued to decline by 1.2%-2.2% per year in women in each age decade from 40 to 79 years ($P < .001$ for each) but stopped declining in women younger than 40 years. After 2010, breast cancer mortality rates demonstrated nonsignificant increases of 2.8% per year in women aged 20-29 years ($P = .11$) and 0.3% per year in women aged 30-39 years ($P = .70$), results attributable primarily to changes in mortality rates in White women. A contributing factor is that distant-stage breast cancer incidence rates increased by more than 4% per year after the year 2000 in women aged 20-39 years. Conclusion Female breast cancer mortality rates have stopped declining in women younger than 40 years, ending a trend that existed from 1987 to 2010. Conversely, mortality rates have continued to decline in women aged 40-79 years. Rapidly rising distant-stage breast cancer rates have likely contributed to ending the decline in mortality rates in women younger than 40 years. (c) RSNA, 2021 Online supplemental material is available for this article.

Hendrick, R. E., et al. (2021). "Age distributions of breast cancer diagnosis and mortality by race and ethnicity in US women." Cancer **127**(23): 4384-4392.

BACKGROUND: Surveillance, Epidemiology, and End Results (SEER) data from 1973-2010 have been used to show that minority women have disproportionately higher percentages of breast cancers diagnosed at younger ages in comparison with White women. METHODS: The authors analyzed SEER 21 invasive breast cancer incidence data for 2014-2017 and National Center for Health Statistics mortality data for 2014-2018 and compared invasive incidence and mortality by age in non-Hispanic Black (NH-Black), Asian American/Pacific Islander (AAPI), Native American, and Hispanic women with those in non-Hispanic White (NH-White) women. They evaluated incidence rates and percentages of invasive breast cancer cases and breast cancer deaths occurring before the age of 50 years along with advanced-stage incidence rates and percentages in minority women versus NH-White women. RESULTS: Recent SEER data showed that invasive breast cancers were diagnosed at significantly younger ages in minority women versus NH-White women. Among women diagnosed with invasive breast cancer, compared with NH-White women, minority women were 72% more likely to be diagnosed under the age of 50 years (relative risk [RR], 1.72; 95% confidence interval [CI], 1.70-1.75), 58% more likely to be diagnosed with advanced-stage breast cancer under the age of 50 years (RR, 1.58; 95% CI, 1.55-1.61), and 24% more likely to be diagnosed with advanced-stage (regional or distant) breast cancer at all ages (RR, 1.24; 95% CI, 1.23-1.25). Among women dying of breast cancer, minority women were 127% more likely to die under the age of 50 years than NH-White women. CONCLUSIONS: NH-Black, AAPI, Native American, and Hispanic women have higher proportions of invasive breast cancers at younger ages and at advanced stages and breast cancer deaths at younger ages than NH-White women. LAY SUMMARY: This study analyzes the most recently available data on invasive breast cancers and breast cancer deaths in US women by age and race/ethnicity. Its findings show that non-Hispanic Black, Asian American/Pacific Islander, Native American, and Hispanic women have a higher percentage of invasive breast cancers at younger ages and at more advanced stages and a higher percentage of breast cancer deaths at younger ages than non-Hispanic White women.

Herbert, C., et al. (2022). "Association of Community Economic Distress and Breast and Colorectal Cancer Screening, Incidence, and Mortality Rates Among US Counties." Ann Surg Oncol **29**(2): 837-848.

INTRODUCTION: Not all Americans may benefit equally from current improvements in breast and colorectal cancer screening and mortality rates. METHODS: We performed a cross-sectional retrospective review of county-level screening, incidence, and mortality rates for breast and colon cancer utilizing three publicly available data sources from the Centers for Disease Control and Prevention (CDC), and their association with the Distressed Communities Index (DCI), a measure of local economic prosperity across communities. RESULTS: After controlling for other factors, DCI was associated with county-level screening, incidence, and death rates per 100,000 for breast and colorectal cancer. There was an absolute increase of 0.77 (95% confidence interval [CI] 0.67-0.85, $p < 0.001$) in the proportion of women aged 40 years or older who had a screening mammogram for every 10-point decrease in DCI, which in turn correlated with an increase in the age-adjusted incidence by 1.68 per 100,000 (95% CI 1.37-2.00, $p < 0.001$). While the age-adjusted death rate for

breast cancer was highest in the most distressed communities, the overall incidence of age-adjusted death decreased by 0.28 per 100,000 (95% CI -0.37 to -0.19, p < 0.001) with every 10-point decrease in DCI. For colorectal cancer, every 10-point decrease in DCI was similarly associated with an absolute 0.60 (95% CI 0.52-0.69, p < 0.001) increase in the proportion of individuals who had screening endoscopy. Increased colorectal screening in low-DCI counties was associated with a lower age-adjusted incidence rate (-0.80 per 100,000; 95% CI -0.94 to -0.65) and age-adjusted death rate (-0.55 per 100,000; 95% CI -0.62 to -0.49) of colorectal cancer per every 10-point decrease in DCI (p < 0.001). CONCLUSION: The association of county-level socioeconomic and healthcare factors with breast and colorectal cancer outcomes was notable, with level of community distress impacting cancer screening, incidence, and mortality rates.

Hermanns, I., et al. (2022). "Mortality during In-Hospital Treatment for Head and Neck Cancer in Germany: A Diagnosis-Related Group-Based Nationwide Analysis, 2005-2018." J Oncol **2022**: 1387860.

BACKGROUND: Data on in-hospital MR (IHMR) of head and neck cancer (HNC) are sparse. METHODS: IHMR was determined in Germany between 2005 and 2018 using nationwide population-based diagnosis-related group (DRG) data of 1,090,596 HNC. RESULTS: The overall average IHMR was 0.04 +/- 0.02. IHMR increased with older age to 0.04 +/- 0.01 for patients of 65-79 years of age (relative risk [RR] in relation to patients of 35-49 years of age = 1.767; 95%confidence interval [CI] = 1.040 to3.001) to a maximum of 0.07 +/- 0.01 for patients of 80 years and older (RR = 2.826; CI = 1.663 to 4.803). IHMR was the highest when no HNC-specific treatment, i.e., best supportive and palliative care, was applied (0.11 +/- 0.01; RR in relation to tumor biopsy surgery = 7.241; CI = 3.447 to 5.211). IHMR was not different between surgery, radiotherapy, or chemotherapy/biologicals. CONCLUSIONS: IHMR did not change over time. Efforts are needed to decrease the IHMR for HNC.

Hernandez Vargas, J. A., et al. (2020). "Patterns of breast, prostate and cervical cancer incidence and mortality in Colombia: an administrative registry data analysis." BMC Cancer **20**(1): 1097.

BACKGROUND: Cancer is widely recognized as a global public health problem. Breast, prostate, and cervical cancer are among the most frequent types in developing countries. Assessing their incidence and mortality by regions and municipalities is important to guide evidence-based health policy. Our aim was to describe the incidence and mortality trends for breast, cervical, and prostate cancer across regions and municipalities in Colombia during 2018. METHODS: We performed a cross-sectional analysis with data from people with breast, prostate, or cervical cancer, reported to the National Administrative Cancer Registry during 2018. A descriptive analysis was performed. Age-standardized incidence and mortality rates were estimated at national, regional, and municipal levels. Finally, we identify the regions and municipalities with significantly higher or lower incidence and mortality rates compared to national estimations. RESULTS: Breast cancer was the most frequent type among all new cases and deaths in Colombia. Breast, prostate and cervical cancer incidence and mortality rates per 100,000 were: 18.69 (CI 95%: 18.15-19.25) and 10.48 (CI 95%: 10.07-10.91); 11.34 (CI 95%: 10.90-11.78) and 7.58 (CI 95%: 7.22-7.96); 5.93 (CI 95%: 5.62-6.25) and 4.31 (CI 95%: 4.05-4.58), respectively. Eastern region had both, incidence and mortality rates, significantly lower than national for all types of cancer. By municipalities, there was a heterogeneous pattern. Nonetheless, Agua de Dios (Cundinamarca), had one of the highest incidence rates for all types. CONCLUSIONS: We observed clear differences in cancer incidence and mortality across regions and municipalities, depending on each type of cancer. Our findings are important to improve screening coverage, early detection, and treatment in the country.

Hernandez-Regino, L. M., et al. (2022). "Clinical characteristics and mortality predictors of patients with cancer hospitalized by COVID-19 in a pediatric third-level referral center." Front Pediatr **10**: 960334.

BACKGROUND: More than 135 million COVID-19 cases (coronavirus disease 2019) have been reported worldwide until today, with over 2.9 million deaths. Several studies have demonstrated that disease severity is lower in the pediatric population than in adults; however, differences are described in patients with chronic diseases, including oncological patients. Current world literature suggests patients with comorbidities, including cancer, have an increased risk of unfortunate outcomes. Therefore, our objective was to describe the clinical characteristics and epidemiological factors associated with mortality in a cohort of pediatric cancer patients hospitalized for COVID-19. METHODS: This is a retrospective, descriptive study of the cases of patients with cancer hospitalized for COVID-19. A total of 40 pediatrics were included in the analysis. Data from pediatric patients with COVID-19 included clinical and epidemiological records, laboratory, imaging studies, COVID-19 diagnostic methods, and medical treatment. RESULTS: Of the 40 pediatric patients admitted with cancer with a confirmed diagnosis of COVID-19,

42.5% were solid tumors, 40% leukemias, and 17.5% lymphomas. The clinical parameters associated with mortality were stage IV tumor ($p = 0.029$) and intubation ($p < 0.001$). The biochemical factors associated with lower survival were thrombocytopenia under 25,000 cells/mm(3) ($p < 0.001$), D-dimer over 1 mug/ml ($p = 0.003$), clinical malnutrition ($p = 0.023$), and disseminated intravascular coagulation ($p = 0.03$). CONCLUSION: Our findings showed that the fever was the most frequent symptom, and the clinical parameters associated with mortality were stage IV tumor, intubation, saturation percentage, RDW, platelets, creatinine, ALT, D-dimer, ferritin, and FiO2 percentage. The thrombocytopenia, D-dimer, nutritional status, and disseminated intravascular coagulation were significantly associated with lower survival.

Hirano, Y., et al. (2021). "Impact of Body Mass Index on Major Complications, Multiple Complications, In-hospital Mortality, and Failure to Rescue Following Esophagectomy for Esophageal Cancer: A Nationwide Inpatient Database Study in Japan." Ann Surg.

OBJECTIVE: To examine the association of BMI with mortality and related outcomes after oncologic esophagectomy. SUMMARY BACKGROUND DATA: Previous studies showed that high BMI was a risk factor for anastomotic leakage and low BMI was a risk factor for respiratory complications after esophagectomy. However, the association between BMI and in-hospital mortality after oncologic esophagectomy remains unclear. METHODS: Data for patients who underwent esophagectomy for esophageal cancer between July 2010 and March 2019 were extracted from a Japanese nationwide inpatient database. Multivariate regression analyses and restricted cubic spline analyses were used to investigate the associations between BMI and short-term outcomes, adjusting for potential confounders. RESULTS: Among 39,406 eligible patients, in-hospital mortality, major complications, and multiple complications (>/=2 major complications) occurred in 1069 (2.7%), 14,824 (37.6%), and 3621 (9.2%), respectively. Compared with normal weight (18.5-22.9 kg/m2), severe underweight (<16.0 kg/m2), mild/moderate underweight (16.0-18.4 kg/m2), and obese (>/=27.5 kg/m2) were significantly associated with higher in-hospital mortality [odds ratio 2.20 (95% confidence interval 1.65-2.94), 1.25 (1.01-1.49), and 1.48 (1.05-2.09), respectively]. BMI showed U-shaped dose-response associations with mortality, major complications, and multiple complications. BMI also showed a reverse J-shaped association with failure to rescue (death after major complications). CONCLUSIONS: Both high BMI and low BMI were associated with mortality, major complications, and multiple complications after esophagectomy for esophageal cancer. Patients with low BMI were more likely to die once a major complication occurred. The present results can assist with risk stratification in patients undergoing oncologic esophagectomy.

Hirano, Y., et al. (2022). "Impact of Prophylactic Corticosteroid Use on In-hospital Mortality and Respiratory Failure after Esophagectomy for Esophageal Cancer: Nationwide Inpatient Data Study in Japan." Ann Surg.

OBJECTIVE: To assess the effect of preoperative prophylactic corticosteroid use on short-term outcomes after oncologic esophagectomy. SUMMARY BACKGROUND DATA: Previous studies have shown that prophylactic corticosteroid use may decrease the risk of respiratory failure following esophagectomy by attenuating the perioperative systemic inflammation response. However, its effectiveness has been controversial, and its impact on mortality remains unknown. METHODS: Data of patients who underwent oncologic esophagectomy between July 2010 and March 2019 were extracted from a Japanese nationwide inpatient database. Stabilized inverse probability of treatment weighting (IPTW), propensity score matching, and instrumental variable analyses were performed to investigate the associations between prophylactic corticosteroid use and short-term outcomes, such as in-hospital mortality and respiratory failure, adjusting for potential confounders. RESULTS: Among 35,501 eligible patients, prophylactic corticosteroids were used in 22,620 (63.7%) patients. In-hospital mortality, respiratory failure, and severe respiratory failure occurred in 924 (2.6%), 5440 (15.3%), and 2861 (8.1%) patients, respectively. In stabilized IPTW analyses, corticosteroids were significantly associated with decreased in-hospital mortality (odds ratio 0.80 [95% confidence interval 0.69-0.93]), respiratory failure (0.84 [0.79-0.90]), and severe respiratory failure (0.87 [0.80-0.95]). Corticosteroids were also associated with decreased postoperative length of stay and total hospitalization costs. The proportion of anastomotic leakage did not differ with the use of methylprednisolone. Propensity score matching and instrumental variable analysis demonstrated similar results. CONCLUSIONS: Prophylactic corticosteroid use in oncologic esophagectomy was associated with lower in-hospital mortality as well as decreased respiratory failure and severe respiratory failure, suggesting a potential benefit for preoperative corticosteroid use in esophagectomy.

Hird, A. E., et al. (2021). "Association between chronic bladder catheterisation and bladder cancer incidence

and mortality: a population-based retrospective cohort study in Ontario, Canada." BMJ Open **11**(9): e050728.

OBJECTIVES: To compare the risk of bladder cancer and bladder cancer mortality among patients with chronic bladder catheterisation (indwelling or intermittent) to patients from the general population. DESIGN: Retrospective cohort study. SETTING: Population-based study in Ontario, Canada between 2003 and 2018. PARTICIPANTS: Adult patients 18-90 years of age with chronic bladder catheterisation were hard matched to patients from the general population without a history of bladder catheterisation. INTERVENTIONS: The presence of a chronic catheter was defined as a minimum of two physician encounters for bladder catheterisation, suprapubic tube insertion or home care for catheter care separated by at least 28 days. Urinary tract infection (UTI) rates were collected. MAIN OUTCOME MEASURES: Bladder cancer and bladder cancer-specific mortality after a 1-year lag period were compared between groups. RESULTS: We identified 36 903 patients with chronic catheterisation matched to 110 709 patients without a history of catheterisation. Patients were followed for a median of 8.8 years (IQR: 5.2-11.9 years). The median age was 62 years (IQR: 50-71) and 52% were female. More patients in the catheter group developed bladder cancer (393 (1.1%) vs 304 (0.3%),p<0.001). There were 106 (0.3%) bladder cancer deaths in the catheter group and 59 (0.1%) in the comparison group (p<0.001). Chronic catheterisation (adjusted subdistribution HR (sdHR)=4.80, 95% CI: 4.26 to 5.42,p<0.001) and the number of UTIs (adjusted sdHR=1.04 per UTI, 95% CI: 1.04 to 1.05,p<0.001) were independent predictors of bladder cancer. The relative rate of bladder cancer-specific death was more than eightfold higher among patients with chronic catheterisation (adjusted sdHR=8.68, 95% CI: 6.97 to 10.81,p<0.001). Subgroup analysis among patients with neurogenic bladder and bladder calculi similarly revealed an increased risk of bladder cancer diagnosis and mortality. Bladder cancer risk was highest among patients in the two longest catheter duration quintiles (2.9-5.9 and 5.9-15.5 years). CONCLUSIONS: This is the first study to quantify the increase in bladder cancer incidence and mortality in a large, diverse cohort of patients with chronic indwelling or intermittent bladder catheterisation. The risk was highest among patients with a chronic catheter beyond 2.9 years.

Hirose, N., et al. (2022). "Association between nurse aide staffing and patient mortality after major cancer surgeries in acute care settings: A retrospective cohort study." Nurs Health Sci **24**(1): 283-292.

This study examined the association between adding nurse aides and patient mortality in acute care settings. We conducted a retrospective cohort study using a national healthcare administrative claims database. We identified patients who underwent planned surgery for six types of cancer from 2010 to 2017. Multivariable logistic analyses were used to examine the association between the nurse aide staffing level and patient outcomes. The primary outcomes were failure to rescue and 30-day hospital mortality. We examined 330 666 in-hospital patients. The median number of nurse aides per 100 occupied beds was 6.60 (interquartile range, 4.61-8.43). In the multivariable analysis, nurse aide staffing level was not significantly associated with failure to rescue or 30-day hospital mortality. The Japanese government provides economic incentives to hospitals that hire more nurse aides, expecting that a higher nurse aide staffing level will help licensed nurses concentrate on the tasks that need their specialties. However, our findings suggest that adding nurse aides may not be associated with lower rates of failure to rescue or 30-day hospital mortality in acute care settings.

Hjelholt, T. J., et al. (2021). "Risk of infections and mortality in Danish patients with cancer diagnosed with bone metastases: a population-based cohort study." BMJ Open **11**(12): e049831.

OBJECTIVES: Risk of infections in patients with solid cancers and bone metastases (BM) and the subsequent impact on prognosis is unclear. We examined the risk of infections among patients with cancer diagnosed with BM and the subsequent impact of infections on mortality. DESIGN: Population-based cohort study. SETTING: Danish medical databases holding information on all hospital contacts in Denmark. PARTICIPANTS: Adult patients with solid cancers and BM between 1 January 1994 and 30 November 2013. OUTCOME MEASURES: In the risk analyses, the outcome was time to hospitalisation for common severe infections, pneumonia, sepsis and urinary tract infections. In the mortality analysis, we used Cox regression to compute HRs of death, modelling infection as time-varying exposure, stratifying for primary cancer type and adjusting for age, sex and comorbidities. RESULTS: Among 23 336 patients with cancer and BM, cumulative incidences of common severe infections were 4.6%, 14.0% and 20.0% during 1 month, 1 year and 10 years follow-up. The highest incidence was observed for pneumonia, followed by urinary tract infections and sepsis. Infection was a strong predictor of 1 month mortality (adjusted HR: 2.1 (95% CI 1.8 to 2.3)) and HRs increased after 1 and 10 years: 2.4 (95% CI 2.3 to 2.6) and 2.4 (95% CI 2.4 to 2.6). Sepsis and pneumonia were the strongest predictors of death. Results were consistent across cancer types. CONCLUSION: Patients with cancer and BM were at high risk of

infections, which was associated with a more than twofold increased risk of death for up to 10 years of follow-up. The findings underscore the importance of preventing infections in patients with cancer and BM.

Hjortebjerg, R., et al. (2020). "Pregnancy-Associated Plasma Protein-A2 Is Associated With Mortality in Patients With Lung Cancer." Front Endocrinol (Lausanne) **11**: 614.

Pregnancy-associated plasma protein-A (PAPP-A) and its homolog PAPP-A2 are enzymes that modulate the availability and mitogenic activity of insulin-like growth factor-I (IGF-I). PAPP-A has been implicated in numerous cancers but reports on PAPP-A2 in malignancy are non-existent. In a prospective observational study of 689 patients under suspicion of lung cancer, we examined levels of PAPP-A and PAPP-A2 and their relationship with mortality. Serum PAPP-A and PAPP-A2 concentrations were determined in pre-diagnostic blood samples using ELISA, and immunohistochemical staining of PAPP-A and PAPP-A2 was performed in malignant tissue from five operable patients. A total of 144 patients were diagnosed with lung cancer, whereas the diagnosis was rejected in 545 subjects, who served as a control group. PAPP-A2 concentrations were higher in patients with lung cancer [median (IQR): 0.33 (0.21-0.56) ng/mL] than in controls [0.27 (0.17-0.39) ng/mL], $p < 0.001$, whereas PAPP-A levels did not differ. Presence of PAPP-A and PAPP-A2 were confirmed in tumor specimens, and staining occurred in a heterogeneous pattern. Patients were observed for a median (range) of 7 (6; 8) years, during which 114 patients (79.2%) died. Patient mortality differed according to PAPP-A2 tertile ($p < 0.001$). PAPP-A2 was associated with mortality with an unadjusted hazard ratio (95% CI) per doubling in protein concentration of 1.30 (1.12; 1.53), $p = 0.001$. In a multivariable model adjusted for age, sex, and BMI, PAPP-A2 remained predictive of the endpoint with a hazard ratio per doubling in protein concentration of 1.25 (1.05; 1.48), $p = 0.013$. Collectively, PAPP-A2, but not PAPP-A, is elevated in patients with lung cancer and associated with mortality. This novel role of PAPP-A2 in cancer warrants further functional studies as well as validation in external cohorts.

Ho, K. L., et al. (2022). "County-level geographic disparities in cardiovascular disease mortality among U.S. breast cancer survivors, 2000-2018." JNCI Cancer Spectr.

BACKGROUND: Disparities in cardiovascular disease mortality among breast cancer survivors are documented, but geographic factors by county-level socioeconomic status (SES) and rurality are not well described. METHODS: We analyzed 724,518 women diagnosed with localized or regional stage breast cancer between 2000-2017 within SEER-18 with follow-up until 2018. We calculated relative risks (RR) of cardiovascular disease mortality using Poisson regression, accounting for age- and race-specific rates in the general population, according to county-level quintiles of SES (measured by Yost index), median income, and rurality at breast cancer diagnosis. We also calculated ten-year cumulative mortality risk of cardiovascular disease accounting for competing risks. RESULTS: Cardiovascular disease mortality was 41% higher among breast cancer survivors living in the lowest SES (RR = 1.41, 95%CI=1.36-1.46, p-trend<0.001) and poorest (RR = 1.41, 95%CI=1.36-1.47, p-trend<0.001) counties compared to the highest SES and wealthiest counties, and 24% higher for most rural relative to most urban counties (RR = 1.24, 95%CI=1.17-1.30; p-trend<0.001). Disparities for lowest SES relative to highest SES counties were greatest among younger women: age 18-49 (RR = 2.32, 95%CI=1.90-2.83) and age 50-59 (RR = 2.01, 95% CI = 1.77-2.28), and within the first 5 years of breast cancer diagnosis (RR = 1.53, 95%CI=1.44-1.64). In absolute terms, however, disparities were widest for women aged 60+ with approximately 2% higher ten-year cumulative cardiovascular disease mortality risk in the poorest compared to wealthiest counties. CONCLUSION: Geographic factors at breast cancer diagnosis were associated with increased cardiovascular disease mortality risk. Studies with individual and county-level information are needed to inform public health interventions and reduce disparities among breast cancer survivors.

Hoang, T., et al. (2020). "Dietary Intake in Association with All-Cause Mortality and Colorectal Cancer Mortality among Colorectal Cancer Survivors: A Systematic Review and Meta-Analysis of Prospective Studies." Cancers (Basel) **12**(11).

We carried out a systematic review and meta-analysis to determine the effects of both prediagnostic and postdiagnostic dietary intake on all-cause mortality and CRC-specific mortality among CRC survivors. An extensive search of PubMed and Embase was conducted to identify eligible studies. We applied a random-effects model to estimate the pooled relative risks (RRs)/hazard ratios (HRs) and their 95% confidence intervals (CIs). As a result, a total of 45 studies were included in the final analysis. Pooled effect sizes from at least three study populations showed that whole grains and calcium were inversely associated with all-cause mortality, with RRs/HRs (95% CIs) of 0.83 (0.69-0.99) and 0.84 (0.73-0.97), respectively. In contrast, a positive association between an unhealthy dietary pattern and both all-cause

mortality (RR/HR = 1.47, 95% CI = 1.05-2.05) and CRC-specific mortality (RR/HR = 1.52, 95% CI = 1.13-2.06) was observed among CRC survivors. In the subgroup analysis by CRC diagnosis, prediagnostic and postdiagnostic dietary intake such as carbohydrates, proteins, lipids, and fiber were observed to have different effects on all-cause mortality. Overall, an unhealthy dietary pattern increased the risks of both all-cause mortality and CRC-specific mortality. The role of prediagnostic and postdiagnostic intake of dietary elements such as macronutrients and fatty acids could be different in the risk of all-cause mortality.

Hoang, T., et al. (2022). "Descriptive Analysis of Gastric Cancer Mortality in Korea, 2000-2020." Cancer Res Treat.

PURPOSE: This study aimed to examine secular trends, age-period-cohort effects, and geographical differences in gastric cancer (GC) mortality in Korea. MATERIALS AND METHODS: Using cause of death data from the Korean Statistical Information Service for GC from 2000 to 2020, we calculated average annual percentage changes (AAPCs) in the age-standardized mortality of GC in 17 cities and provinces through joinpoint regression. Decomposition of age, period, and cohort effects on GC mortality were elucidated by applying a log-linear model and an intrinsic estimate method. Spatial patterns and the degree of spatial clustering in 250 administrative regions were explored via Moran's I statistics. Stratification by sex was performed for all analyses. RESULTS: The age-standardized mortality of GC per 100,000 persons declined from 29.0 in 2000 to 7.9 in 2020 (AAPC, -6.28%). Age-period-cohort analyses of GC mortality showed a downward trend among five-year age groups from age 20-89 years across five-year periods from 2005-2020 and five-year birth cohorts from 1920-2000. Overall, the younger birth cohort showed lower mortality rates than the older cohort within the same period. In 2020, clusters of high GC mortality were observed in the central area for men (Chungcheongbuk, Jeollabuk, Gyeongsangbuk, and Gyeongsangnam) and in the eastern area for women (Gyeongsangbuk). CONCLUSION: This study identified a downward trend in GC mortality among men and women from 2000 to 2020 in Korea. This trend was mainly attributed to birth cohort rather than period effects. Spatial analysis showed high GC mortality in the Chungcheong and Gyeongsangbuk areas.

Hoeh, B., et al. (2022). "Effect of Neoadjuvant Chemotherapy on Complications, in-Hospital Mortality, Length of Stay and Total Hospital Costs in Bladder Cancer Patients Undergoing Radical Cystectomy." Cancers (Basel) **14**(5).

BACKGROUND: To test for differences in complication rates, in-hospital mortality, length of stay (LOS) and total hospital costs (THCs) in patients treated with neoadjuvant chemotherapy (NAC) prior to radical cystectomy (RC). METHODS: Within the National (Nationwide) Inpatient Sample (NIS) database (2016-2019), we identified RC-treated, non-metastatic, lymph-node negative bladder cancer patients, stratified by NAC status. Trend analyses, multivariable logistic, multivariable Poisson and multivariable linear regression models were used. RESULTS: We identified 4347 RC-treated bladder cancer patients. Of those, 805 (19%) received NAC prior to RC. Overall, complications rates did not differ (65 vs. 66%; p = 0.7). However, NAC patients harbored lower rates of surgical site (6 vs. 9%), cardiac (13 vs. 19%) and genitourinary (5.5 vs. 9.7%) complications. In-hospital mortality (<1.7 vs. 1.8%) and LOS (6 vs. 7 days) was lower in NAC patients (all p < 0.05). Moreover, NAC was an independent predictor of shorter LOS in multivariable Poisson regression models (Risk ratio: 0.86; p < 0.001) and an independent predictor for higher THCs in multivariable linear regression models (Odds ratio: 1474$; p = 0.02). CONCLUSION: NAC was not associated with higher complication rates and in-hospital mortality. Contrary, NAC was associated with shorter LOS, yet moderately higher THCs. The current analysis suggests no detriment from NAC in the context of RC.

Hoeh, B., et al. (2022). "Cancer-specific mortality after radical prostatectomy vs external beam radiotherapy in high-risk Hispanic/Latino prostate cancer patients." Int Urol Nephrol **54**(1): 81-87.

PURPOSE: To test for differences in cancer-specific mortality (CSM) rates in Hispanic/Latino prostate cancer patients according to treatment type, radical prostatectomy (RP) vs external beam radiotherapy (EBRT). METHODS: Within the Surveillance, Epidemiology, and End Results database (2010-2016), we identified 2290 NCCN (National Comprehensive Cancer Network) high-risk (HR) Hispanic/Latino prostate cancer patients. Of those, 893 (39.0%) were treated with RP vs 1397 (61.0%) with EBRT. First, cumulative incidence plots and competing risks regression models tested for CSM differences after adjustment for other cause mortality (OCM). Second, cumulative incidence plots and competing risks regression models were refitted after 1:1 propensity score matching (according to age, PSA, biopsy Gleason score, cT-stage, cN-stage). RESULTS: In NCCN HR patients, 5-year CSM rates for RP vs EBRT were 2.4 vs 4.7%, yielding a multivariable hazard ratio of 0.37 (95% CI 0.19-0.73, p = 0.004) favoring RP. However, after propensity score matching, the hazard ratio of 0.54 was no longer

statistically significant (95% CI 0.21-1.39, p = 0.2). CONCLUSION: Without the use of strictest adjustment for population differences, NCCN high-risk Hispanic/Latino prostate cancer patients appear to benefit more of RP than EBRT. However, after strictest adjustment for baseline patient and tumor characteristics between RP and EBRT cohorts, the apparent CSM benefit of RP is no longer statistically significant. In consequence, in Hispanic/Latino NCCN high-risk patients, either treatment modality results in similar CSM outcome.

Holland, L. R., et al. (2021). "Cancer Incidence, Mortality, and Survival for Children, Adolescents, and Young Adults in Queensland Between 1987 and 2016." J Adolesc Young Adult Oncol **10**(6): 629-644.

Purpose: Cancer remains the most common cause of disease-related death among young people and carries a significant burden. In the absence of prior state-based Australian epidemiological studies, this retrospective cohort study reviewed all cases of invasive cancer diagnosed in Queensland children, adolescents, and young adults (AYAs) (0-39 years) from 1987 to 2016 using the Queensland Oncology Repository (QOR). Methods: Cancers were classified according to Surveillance, Epidemiology and End Results (SEER) AYA site recode. Age-standardized rates (ASRs) were calculated. JoinPoint regression examined trends in ASRs across three age cohorts, for three decades (1987-1996, 1997-2006, and 2007-2016). Results: In total, 3,576 children aged 0-14 years (ASR = 15.2/100,000), 6,441 aged 15-24 years (ASR = 39.3/100,000), and 29,923 (ASR = 122.6/100,000) aged 25-39 years were diagnosed. Incidence increased for female children, and leukemia was the most common diagnosis. For those 15-24 years, incidence increased initially before decreasing and was higher than other nationally reported rates. For those 25-39 years, incidence increased. For the older cohorts, the most common diagnosis was melanoma. All cohorts demonstrated a decline in mortality and improvement in 5-year relative survival, with those 0-14 years demonstrating the greatest gains. The lowest survival for all cohorts was associated with central nervous system tumors. Conclusion: These results highlight areas in need of further investigation to improve survival, reduce the burden of cancer for young people, and aid service delivery. Future studies should focus on cancer biology, early detection, barriers in access to clinical trials, innovative models of care, improved data collection, and patient-reported outcomes.

Holmberg, D., et al. (2022). "Incidence and Mortality in Upper Gastrointestinal Cancer After Negative Endoscopy for Gastroesophageal Reflux Disease." Gastroenterology **162**(2): 431-438 e434.

BACKGROUND AND AIMS: Gastroesophageal reflux disease (GERD) is associated with an increased risk of cancer of the upper gastrointestinal tract. This study aimed to assess whether and to what extent a negative upper endoscopy in patients with GERD is associated with decreased incidence and mortality in upper gastrointestinal cancer (ie, esophageal, gastric, or duodenal cancer). METHODS: We conducted a population-based cohort study of all patients with newly diagnosed GERD between July 1, 1979 and December 31, 2018 in Denmark, Finland, Norway, and Sweden. The exposure, negative upper endoscopy, was examined as a time-varying exposure, where participants contributed unexposed person-time from GERD diagnosis until screened and exposed person-time from the negative upper endoscopy. The incidence and mortality in upper gastrointestinal cancer were assessed using parametric flexible models, providing adjusted hazard ratios (HRs) with 95% confidence intervals (CIs). RESULTS: Among 1,062,740 patients with GERD (median age 58 years; 52% were women) followed for a mean of 7.0 person-years, 5324 (0.5%) developed upper gastrointestinal cancer and 4465 (0.4%) died from such cancer. Patients who had a negative upper endoscopy had a 55% decreased risk of upper gastrointestinal cancer compared with those who did not undergo endoscopy (HR, 0.45; 95% CI, 0.43-0.48), a decrease that was more pronounced during more recent years (HR, 0.34; 95% CI, 0.30-0.38 from 2008 onward), and was otherwise stable across sex and age groups. The corresponding reduction in upper gastrointestinal mortality among patients with upper endoscopy was 61% (adjusted HR, 0.39; 95% CI, 0.37-0.42). The risk reduction after a negative upper endoscopy in incidence and mortality lasted for 5 and at least 10 years, respectively. CONCLUSIONS: Negative upper endoscopy is associated with strong and long-lasting decreases in incidence and mortality in upper gastrointestinal cancer in patients with GERD.

Hong, S., et al. (2021). "Cancer Statistics in Korea: Incidence, Mortality, Survival, and Prevalence in 2018." Cancer Res Treat **53**(2): 301-315.

PURPOSE: The current study provides national cancer statistics and their secular trends in Korea, including incidence, mortality, survival, and prevalence in 2018. MATERIALS AND METHODS: Incidence, survival, and prevalence rates of cancer were calculated using the Korea National Cancer Incidence Database, from 1999 to 2018, with survival follow-up until December 31, 2019. Deaths from cancer were assessed using causes-of-death data obtained from Statistics Korea. Crude and age-standardized rates (ASRs) for incidence, mortality, prevalence, and 5-year relative survival rates were

calculated, and temporal trends for incidence and mortality rates were evaluated, with annual percentage changes. RESULTS: In 2018, newly diagnosed cancer cases and deaths from cancer were reported as 243,837 (ASR, 270.4 per 100,000) and 79,153 (ASR, 73.3 per 100,000), respectively. The overall cancer incidence rates increased by 3.3% annually from 1999 to 2012, and decreased by 5.4% annually from 2012 to 2015, thereafter, followed by nonsignificant changes. Cancer mortality rates have been decreasing since 2002, with more rapid decline in recent years (annual decrease of 2.7% from 2007 to 2014; 3.7% from 2014 to 2018). The 5-year relative survival between 2014 and 2018 was 70.3%, which contributed to prevalent cases reaching over 2 million by the end of 2018. CONCLUSION: Cancer statistics have improved significantly during the past two decades. However, there remain important challenges to be solved, such as controlling cancers with low survival rates. Cancer statistics can be used to discover blind spots in cancer control, and as evidence for developing and implementing future cancer control strategies.

Hong, S. Y., et al. (2022). "Incidence, mortality, and survival of liver cancer using Korea central cancer registry database: 1999-2019." Ann Hepatobiliary Pancreat Surg **26**(3): 211-219.

BACKGROUNDS/AIMS: Historically, incidence and survival analysis and annual traits for primary liver cancer (LC) has not been investigated in a population-based study in Korea. The purpose of the current study is to determine incidence, survival rate of patients with primary LC in Korea. METHODS: We conducted a retrospective cohort study using Korea Central Cancer Registry based on the Korea National Cancer Incidence Database. Statistical analysis including crude rate and age-standadized rate (ASR) of incidence and mortality was performed for LC patients registered with C22 code in International Classification of Diseases, tenth revision from 1999 to 2019. Subgroup analysis was performed for hepatocellular carcinoma (HCC, C22.0) and intrahepatic cholangiocarcinoma (IHCC, C22.1). RESULTS: The crude incidence rate of HCC (21.0 to 22.8 per 100,000) and IHCC (2.3 to 5.6 per 100,000) increased in the observed period from 1999 to 2019. The ASR decreased in HCC (20.7 to 11.9 per 100,000) but remained unchanged in IHCC (2.4 to 2.7 per 100,000). The proportion of HCC patients diagnosed in early stages (localized or regional Surveillance, Epidemiology, and End Results or SEER stage) increased significantly over time. As expected, 5-yeat survival rate of HCC was greatly improved, reaching 42.4% in the period between 2013 and 2019. This trait was more prominent in localized SEER stage. On the other hand, the proportion of IHCC patients diagnosed in localized stage remained unchanged (22.9% between 2013 and 2019), although ASR and 5-year survival rate showed minor improvements. CONCLUSIONS: A great improvement in survival rate was observed in patients with newly diagnosed HCCs. It was estimated to be due to an increase in early detection rate. On the contrary, detection rate of an early IHCC was stagnant with a minor improvement in prognosis.

Hong, Y., et al. (2022). "Projection of Cancer Incidence and Mortality From 2020 to 2035 in the Korean Population Aged 20 Years and Older." J Prev Med Public Health **55**(6): 529-538.

OBJECTIVES: This study aimed to identify the current patterns of cancer incidence and estimate the projected cancer incidence and mortality between 2020 and 2035 in Korea. METHODS: Data on cancer incidence cases were extracted from the Korean Statistical Information Service from 2000 to 2017, and data on cancer-related deaths were extracted from the National Cancer Center from 2000 to 2018. Cancer cases and deaths were classified according to the International Classification of Diseases, 10th edition. For the current patterns of cancer incidence, age-standardized incidence rates (ASIRs) and age-standardized mortality rates were investigated using the 2000 mid-year estimated population aged over 20 years and older. A joinpoint regression model was used to determine the 2020 to 2035 trends in cancer. RESULTS: Overall, cancer cases were predicted to increase from 265 299 in 2020 to 474 085 in 2035 (growth rate: 1.8%). The greatest increase in the ASIR was projected for prostate cancer among male (7.84 vs. 189.53 per 100 000 people) and breast cancer among female (34.17 vs. 238.45 per 100 000 people) from 2000 to 2035. Overall cancer deaths were projected to increase from 81 717 in 2020 to 95 845 in 2035 (average annual growth rate: 1.2%). Although most cancer mortality rates were projected to decrease, those of breast, pancreatic, and ovarian cancer among female were projected to increase until 2035. CONCLUSIONS: These up-to-date projections of cancer incidence and mortality in the Korean population may be a significant resource for implementing cancer-related regulations or developing cancer treatments.

Hoppmann, A. L., et al. (2022). "Persistent Child Poverty and Mortality in a Cohort of Children with Cancer in Alabama." Cancer Epidemiol Biomarkers Prev.

BACKGROUND: One fifth of US counties are designated persistent child poverty counties (>/=20% of children in poverty since 1980). The association between a persistent child poverty environment and mortality in children with cancer is

unknown. METHODS: Our cohort includes 2,089 children with cancer (2000-2016) in Alabama. We used multivariable cox proportional hazards modeling (adjusted for sociodemographics/clinical characteristics) to assess mortality by persistent child poverty designation at 1, 5 and 10 years from diagnosis. Distance to treatment was subsequently explored. RESULTS: Forty-two percent of the cohort lived in a persistent child poverty county; they were more likely to be African American (P<0.0001), have public/no insurance (P=0.0009), and live >100 miles to treatment (P<0.0001). Children in persistent child poverty counties were 30% more likely to die by 5 years (95%CI=1.06-1.59, P=0.012). Distance (per 20-mile increase) to treatment was associated with a 9% increased mortality risk (P<0.0001). Children with both exposures (distance >100 miles and persistent child poverty) faced the highest mortality risk at 5 years (HR=1.80, 95%CI=1.39-2.33, P<0.0001). In sub-analysis, children exposed to persistent child poverty were at higher risk for cancer-related mortality. However, the risk of health-related mortality did not differ. CONCLUSION: Among children with cancer from the Deep South, persistent child poverty was a prevalent exposure associated with inferior overall survival. Distance to treatment was independently associated with inferior survival. Children with both exposures had the highest risk of mortality. IMPACT: Persistent child poverty is associated with inferior survival among children with cancer; mechanisms underlying this disparity warrant investigation.

Hoskins, K. F., et al. (2021). "Association of Race/Ethnicity and the 21-Gene Recurrence Score With Breast Cancer-Specific Mortality Among US Women." JAMA Oncol **7**(3): 370-378.

IMPORTANCE: Given the widespread use of the 21-gene recurrence score for identifying candidates for adjuvant chemotherapy, it is important to examine the performance of the Oncotype DX Breast Recurrence Score test in diverse patient populations to validate this approach for tailoring treatment in women in racial/ethnic minority groups. OBJECTIVE: To examine whether breast cancer-specific mortality for women with hormone-dependent breast cancer differs by race/ethnicity across risk categories defined by the Oncotype DX Breast Recurrence Score test and whether the prognostic accuracy of the 21-gene recurrence score differs by race/ethnicity. DESIGN, SETTING, AND PARTICIPANTS: This retrospective, population-based cohort study used the Surveillance, Epidemiology, and End Results Oncotype DX 2004-2015 database to obtain breast cancer-specific survival data on US women 18 years and older who were diagnosed with first primary stage I to III, estrogen receptor-positive breast cancer between January 1, 2004, and December 31, 2015, and had tumor testing through the Genomic Health Clinical Laboratory. Data were analyzed from April 20 to September 27, 2020. MAIN OUTCOMES AND MEASURES: The primary outcome was breast cancer-specific mortality among women from different racial/ethnic groups stratified by the 21-gene recurrence score risk categories. Secondary analyses compared the prognostic accuracy of the recurrence score among the different racial/ethnic groups. RESULTS: A total of 86 033 patients with breast cancer (mean [SD] age, 57.6 [10.6] years) with Oncotype DX Breast Recurrence Score test information were available for the analysis, including 64 069 non-Hispanic White women (74.4%), 6719 non-Hispanic Black women (7.8%), 7944 Hispanic women (9.2%), 6950 Asian/Pacific Islander women (8.0%), and 351 American Indian/Alaska Native women (0.4%). Black women were significantly more likely than non-Hispanic White women to have a recurrence score greater than 25 (17.7% vs 13.7%; P < .001). Among women with axillary node-negative tumors, competing risk models adjusted for age, tumor characteristics, and treatment found higher breast cancer-specific mortality for Black compared with non-Hispanic White women within each recurrence score risk stratum, with subdistribution hazard ratios of 2.54 (95% CI, 1.44-4.50) for Black women with recurrence scores of 0 to 10, 1.64 (95% CI, 1.23-2.18) for Black women with recurrence scores of 11 to 25, and 1.48 (95% CI, 1.10-1.98) for Black women with scores greater than 25. The prognostic accuracy of the recurrence score was significantly lower for Black women, with a C index of 0.656 (95% CI, 0.592-0.720) compared with 0.700 (95% CI, 0.677-0.722) (P = .002) for non-Hispanic Whites. CONCLUSIONS AND RELEVANCE: In this cohort study, Black women in the US were more likely to have a high-risk recurrence score and to die of axillary node-negative breast cancer compared with non-Hispanic White women with comparable recurrence scores. The Oncotype DX Breast Recurrence Score test has lower prognostic accuracy in Black women, suggesting that genomic assays used to identify candidates for adjuvant chemotherapy may require model calibration in populations with greater racial/ethnic diversity.

Hoydahl, O., et al. (2022). "Octogenarian patients with colon cancer - postoperative morbidity and mortality are the major challenges." BMC Cancer **22**(1): 302.

BACKGROUND: Few studies have addressed colon cancer surgery outcomes in an unselected cohort of octogenarian patients. The present study aimed to evaluate the relative survival of octogenarian patients after a major resection of colon cancer with a curative intent. METHODS: All patients diagnosed with colon cancer at Levanger Hospital between 1980 and 2016

were included. We performed logistic regression to test for associations between 90-day mortality and explanatory variables. We performed a relative survival analysis to identify factors associated with short- and long-term survival. RESULTS: Among 237 octogenarian patients treated with major resections with curative intent, the 90-day mortality was 9.3%. Among 215 patients that survived the first 90 days, the 5 year relative survival rate was 98.7%. The 90-day mortality of octogenarian patients was significantly higher than that of younger patients, but the long-term survival converged with that of younger patients. Among octogenarian patients, the incidence of colon cancer more than doubled during our 37-year observation period. The relative increase in patients undergoing surgery exceeded the increase in incidence; hence, more patients were selected for surgery over time. A high 90-day mortality was associated with older age, a high American Society of Anaesthesiologists (ASA) score, and emergency surgery. Moreover, worse long-term survival was associated with a high Charlson Comorbidity Index, a high ASA score, a worse TNM stage, emergency surgery and residual tumours. Both the 90-day and long-term survival rates improved over time. CONCLUSION: Among octogenarian patients with colon cancer that underwent major resections with curative intent, the 90-day mortality was high, but after surviving 90 days, the relative long-term survival rate was comparable to that of younger patients. Further improvements in survival will primarily require measures to reduce the 90-day mortality risk.

Hsu, T. H., et al. (2021). "Artificial intelligence to assess body composition on routine abdominal CT scans and predict mortality in pancreatic cancer- A recipe for your local application." Eur J Radiol **142**: 109834.

BACKGROUND: Body composition is associated with mortality; however its routine assessment is too time-consuming. PURPOSE: To demonstrate the value of artificial intelligence (AI) to extract body composition measures from routine studies, we aimed to develop a fully automated AI approach to measure fat and muscles masses, to validate its clinical discriminatory value, and to provide the code, training data and workflow solutions to facilitate its integration into local practice. METHODS: We developed a neural network that quantified the tissue components at the L3 vertebral body level using data from the Liver Tumor Challenge (LiTS) and a pancreatic cancer cohort. We classified sarcopenia using accepted skeletal muscle index cut-offs and visceral fat based its median value. We used Kaplan Meier curves and Cox regression analysis to assess the association between these measures and mortality. RESULTS: Applying the algorithm trained on LiTS data to the local cohort yielded good agreement [>0.8 intraclass correlation (ICC)]; when trained on both datasets, it had excellent agreement (>0.9 ICC). The pancreatic cancer cohort had 136 patients (mean age: 67 +/- 11 years; 54% women); 15% had sarcopenia; mean visceral fat was 142 cm(2). Concurrent with prior research, we found a significant association between sarcopenia and mortality [mean survival of 15 +/- 12 vs. 22 +/- 12 ($p < 0.05$), adjusted HR of 1.58 (95% CI: 1.03-3.33)] but no association between visceral fat and mortality. The detector analysis took 1 +/- 0.5 s. CONCLUSIONS: AI body composition analysis can provide meaningful imaging biomarkers from routine exams demonstrating AI's ability to further enhance the clinical value of radiology reports.

Hu, D., et al. (2020). "Synergistic effect of clinicopathological factors on mortality risk in patients with differentiated thyroid cancer: An analysis using the SEER database." Surg Oncol **34**: 96-102.

OBJECTIVES: In this study, we analyzed the effects of histology subtypes, lymph node N-stages, and the presence of extrathyroidal extensions on cancer-specific survival (CSS) and overall survival (OS) in patients with differentiated thyroid cancer. MATERIALS AND METHODS: Cox proportional hazards regression analyses were carried out to evaluate the correlations between clinicopathological factors and CSS/OS. The combined effects of these factors on CSS and OS were then analyzed to determine the relative excess risk, attributable proportion, and synergy index. Kaplan-Meier curves were used to evaluate the mortality rate. RESULTS: A total of 86033 cases were included in the analysis. Histology subtype, N-stage, and extrathyroidal extension were all found to be risk factors for CSS (hazard ratio [HR] = 1.8, 95% confidence intervals [CI]: 1.4-2.3, $p < 0.001$; HR = 1.9, 95% CI: 1.6-2.3, $p < 0.001$; HR = 1.4, 95% CI: 1.0-1.9, $p = 0.035$, respectively). The risk factors for OS were histology subtype and N-stage (HR = 1.3, 95% CI; 1.2-1.5, $p < 0.001$; HR = 1. 4, 95% CI: 1.3-1.5, $p < 0.001$, respectively) but not extrathyroidal extension (HR = 1.1, 95% CI: 0.9-1.3, $p = 0.228$). Furthermore, histology subtype and N-stage, histology subtype and extrathyroidal extension, and N stage and extrathyroidal extension (relative excess risk, attributable proportion, and synergy index: 48.8, 0.9, 7.6; 50.2, 0.7, 3.9; 7.0, 0.3, 1.6; respectively) were found to have significant synergistic effects. CONCLUSION: Patients with follicular thyroid carcinoma (FTC) and extrathyroidal extension or lymph node metastasis are at a higher risk of mortality. Histology subtype, N-stage, and extrathyroidal extension appear to have synergistic effects on the

increased risk of poor CSS in patients. This result can in the further development of treatment guidelines to improve the outcome of FTC patients.

Hu, X., et al. (2020). "Association of 5-alpha-reductase inhibitor and prostate cancer incidence and mortality: a meta-analysis." Transl Androl Urol **9**(6): 2519-2532.

BACKGROUND: 5-Alpha-reductase inhibitors (5-ARIs) have been suggested as potential chemopreventive agents for prostate cancer (PCa). This study was conducted to evaluate the effect of 5-ARIs on the incidence and mortality of PCa. METHODS: The PubMed, Embase and Cochrane Library databases were searched comprehensively from database inception to October 2019. The clinical outcomes included the incidence of overall PCa, high-grade (Gleason8-10) PCa, metastatic PCa, overall survival (OS), and cancer-specific survival (CSS). RESULTS: Overall, 23 studies were included in the present study, representing 11 cohort studies, 5 case-control studies, and 8 randomized controlled trials. The use of 5-ARIs was associated with a decreased risk of overall PCa [relative risk (RR) =0.77; 95% CI: 0.67-0.88; P<0.001] and increased risk of Gleason 8-10 PCa (RR=1.19; 95% CI: 1.01-1.40; P=0.036). In terms of metastatic PCa, there were no significant between-group differences (RR=1.23; 95% CI: 0.69-2.18; P=0.487). Furthermore, we found that prediagnostic 5-ARI usage was not associated with an increased risk of overall or prostate cancer mortality, with HRs of 1.00 (95% CI: 0.92-1.08; P=0.938) and 0.98 (95% CI: 0.80-1.21; P=0.881), respectively. CONCLUSIONS: In conclusion, while male 5-ARI users were associated with a decreased risk of overall prostate cancer and increased risk of high-grade prostate cancer (Gleason 8-10), they were not associated with an increased risk of overall or prostate cancer mortality. 5-ARIs should be recommended carefully for use as chemopreventive agents.

Huang, B. H., et al. (2022). "Sleep and physical activity in relation to all-cause, cardiovascular disease and cancer mortality risk." Br J Sports Med **56**(13): 718-724.

OBJECTIVES: Although both physical inactivity and poor sleep are deleteriously associated with mortality, the joint effects of these two behaviours remain unknown. This study aimed to investigate the joint association of physical activity (PA) and sleep with all-cause and cause-specific mortality risks. METHODS: 380 055 participants aged 55.9 (8.1) years (55% women) from the UK Biobank were included. Baseline PA levels were categorised as high, medium, low and no moderate-to-vigorous PA (MVPA) based on current public health guidelines. We categorised sleep into healthy, intermediate and poor with an established composited sleep score of chronotype, sleep duration, insomnia, snoring and daytime sleepiness. We derived 12 PA-sleep combinations, accordingly. Mortality risks were ascertained to May 2020 for all-cause, total cardiovascular disease (CVD), CVD subtypes (coronary heart disease, haemorrhagic stroke, ischaemic stroke), as well as total cancer and lung cancer. RESULTS: After an average follow-up of 11.1 years, sleep scores showed dose-response associations with all-cause, total CVD and ischaemic stroke mortality. Compared with high PA-healthy sleep group (reference), the no MVPA-poor sleep group had the highest mortality risks for all-cause (HR (95% CIs), (1.57 (1.35 to 1.82)), total CVD (1.67 (1.27 to 2.19)), total cancer (1.45 (1.18 to 1.77)) and lung cancer (1.91 (1.30 to 2.81))). The deleterious associations of poor sleep with all outcomes, except for stroke, was amplified with lower PA. CONCLUSION: The detrimental associations of poor sleep with all-cause and cause-specific mortality risks are exacerbated by low PA, suggesting likely synergistic effects. Our study supports the need to target both behaviours in research and clinical practice.

Huang, C. Y., et al. (2021). "Gender differences in trends of bladder cancer mortality-to-incidence ratios according to health expenditure in 55 countries." PLoS One **16**(2): e0244510.

The association between bladder cancer mortality-to-incidence ratios (MIRs) and healthcare disparities has gender differences. However, no evidence supports gender as an issue in the association between changes in the MIR and health expenditures on bladder cancer. Changes in the MIR were defined as the difference in data from the years 2012 and 2018, which was named deltaMIR. Current health expenditures (CHE) and the human development index (HDI) were obtained from the World Health Organization and the Human Development Report Office. The association between variables was analyzed by Spearman's rank correlation coefficient. In total, 55 countries were analyzed according to data quality and the exclusion of missing data. Globally, the MIR changed according to the HDI level in both genders. Among the 55 countries studied, a high HDI and CHE were significantly associated with a favorable age-standardized rate-based MIR (ASR-based MIR) in both genders and the subgroups according to gender (for both genders, MIR vs. HDI: rho = -0.720, p < 0.001; MIR vs. CHE per capita: rho = -0.760, p < 0.001; MIR vs. CHE as a percentage of gross domestic product (CHE/GDP): rho = -0.663, p < 0.001). Importantly, in females only, the CHE/GDP but neither the HDI score nor the CHE per capita was significantly associated with a favorable ASR-based deltaMIR (ASR-based deltaMIR vs. CHE/GDP: rho = 0.414, p =

0.002). In the gender subgroups, the association between the HDI and the CHE was statistically significant for females and less significant for males. In conclusion, favorable bladder ASR-based MIRs were associated with a high CHE; however, improvement of the ASR-based deltaMIR data was more correlated with the CHE in females. Further investigation of the gender differences via a cohort survey with detailed information of clinical-pathological characteristics, treatment strategies, and outcomes might clarify these issues and improve therapeutic and/or screening strategies for bladder cancer.

Huang, H. L., et al. (2021). "Ambient Cumulative PM2.5 Exposure and the Risk of Lung Cancer Incidence and Mortality: A Retrospective Cohort Study." Int J Environ Res Public Health **18**(23).

Smoking, sex, air pollution, lifestyle, and diet may act independently or in concert with each other to contribute to the different outcomes of lung cancer (LC). This study aims to explore their associations with the carcinogenesis of LC, which will be useful for formulating further preventive strategies. This retrospective, longitudinal follow-up cohort study was carried out by connecting to the MJ Health Database, Taiwan Cancer Registry database, and Taiwan cause of death database from 2000 to 2015. The studied subjects were persons attending the health check-ups, distributed throughout the main island of Taiwan. Cox proportional hazards regression models were used to investigate the risk factors associated with LC development and mortality after stratifying by smoking status, with a special emphasis on ambient two-year average PM(2.5) exposure, using a satellite-based spatiotemporal model at a resolution of 1 km(2), and on dietary habit including consumption of fruits and vegetables. After a median follow-up of 12.3 years, 736 people developed LC, and 401 people died of LC-related causes. For never smokers, the risk of developing LC (aHR: 1.32, 95%CI: 1.12-1.56) and dying from LC-related causes (aHR: 1.28, 95%CI: 1.01-1.63) rises significantly with every 10 mug/m(3) increment of PM(2.5) exposure, but not for ever smokers. Daily consumption of more than two servings of vegetables and fruits is associated with lowering LC risk in ever smokers (aHR: 0.68, 95%CI: 0.47-0.97), and preventing PM(2.5) exposure is associated with lowering LC risk for never smokers.

Huang, H. Y., et al. (2020). "Clinic image surveillance reduces mortality in patients with primary hepato-gastrointestinal cancer who develop second primary lung cancer: A STROBE-compliant retrospective study." Medicine (Baltimore) **99**(50): e23440.

Second primary cancer is prevalent in patients with gastrointestinal (GI) cancer, for which lung cancer is the most common and associated with high lethality. Image screening for lung cancer was proved to be effective in early diagnosis and lower mortality. However, trials of screen for lung cancer generally excluded patients with a previous diagnosis of malignancy. The study aimed to investigate the outcome of second primary lung cancer and the factor that improve survival in patients with hepato-GI cancer.A total of 276 patients with secondary lung cancer were found among 3723 newly-diagnosed lung cancer patients diagnosed in Chang Gung Memorial Hospital, between 2010 and 2014. Patients' clinical characteristics, stages and survival were recorded and analyzed. The patients were separated into 2 groups: Group I was defined as lung cancer detected in original primary cancer clinic and group II patients defined as lung cancer detected in other medical places.Sixty-nine cases with primary GI-hepatic and secondary lung cancer were diagnosed (42 (60.8%) in Group I and 27 (39.1%) in Group II). Although both groups had comparable primary cancer stages and treatment, more patients in Group I than Group II were diagnosed as early stage lung cancer (stage I-II: 40.5% vs 11.1%; P = .023). Group II had larger lung tumor sizes than Group I (4.7 vs 3.5 cm; P = .025). Group I showed better 5-year overall survival than Group II (P = .014, median survival: 27 vs 10 months). Among Group II, only 37% had received image follow up in clinic compared with 67% of Group I cases (P = .025). Patients with chest image follow up in clinics also had better 5-year overall survival (P = .043).GI-hepatic cancer was the most common primary malignancy in the lung cancer cohort. Patients had better survival outcome when secondary lung cancer was diagnosed in original primary cancer clinic. Chest image screening strategy may contribute better survival in secondary lung cancer due to detection at an earlier stage.

Huang, J., et al. (2021). "Global incidence and mortality of breast cancer: a trend analysis." Aging (Albany NY) **13**(4): 5748-5803.

This study aimed to evaluate the global incidence and mortality trends of breast cancer among females by region and age in the past decade. We retrieved country-specific incidence and mortality data from the Global Cancer Observatory up to 2018 and Cancer Incidence in Five Continents volumes I-XI, the Nordic Cancer Registries, the Surveillance, Epidemiology, and End Results, and WHO mortality database up to 2016. The temporal patterns were using Average Annual Percent Change (AAPC) with the 95% confidence interval (CI) by joinpoint regression analysis. Most countries showed an increasing trend in incidence. For the older population aged >/= 50 years, Japan (5.63, 4.90-6.36), Slovakia (3.63, 3.03-4.22), China (2.86, 2.00-3.72) reported the most prominent

increase. For young females (<50 years), Japan (AAPC=3.81, 95% CI=2.71-4.93), Germany (AAPC=2.60, 95% CI=1.41-3.81) and Slovakia (1.91, 1.13-2.69) reported the most drastic rise. Similarly, 12 countries showed an incidence increase among women aged <40 years. As for mortality, the Philippines (4.36, 3.65-5.07), Thailand (4.35, 3.12-5.59), Colombia (0.75, 0.08-1.42), and Brazil (0.44, 0.19-0.68) reported a significant increase. The disease burden of breast cancer showed an increasing trend in a large number of populations. More preventive efforts are recommended for these countries. Further research should explore the underlying reasons for these epidemiological trends.

Huang, J., et al. (2022). "Global incidence, mortality and temporal trends of cancer in children: A joinpoint regression analysis." Cancer Med.

BACKGROUND/METHODS: The Cancer Incidence in Five Continents Time Trends, Nordic Cancer Registries, Surveillance, Epidemiology and End Results, WHO Mortality databases were assessed to extract the Age-Standardised Rates (ASR) of cancer incidence and mortality among children aged 0-14 years old. By using the ASRs, the country-specific Average Annual Percentage Change (AAPC) and its corresponding 95% confidence interval (CI) were calculated to determine the epidemiological cancer trend. RESULTS: In 2020, the highest incidence of childhood cancer was found in countries with higher Human Development Index (HDI) (ASR = 15.7), yet the highest mortality was found in countries with lower HDIs (ASR = 4.8). As for incidence, seven countries had positive AAPC among boys; Slovakia (AAPC(2001-2010) = 4.98, 95% CI [1.66-8.40]), Ecuador (AAPC(2003-2012) = 4.07, 95% CI [0.67-7.59]) and Thailand (AAPC(2003-2012) = 3.69, 95% CI [0.37-7.11]) had the highest AAPC. Among girls, three countries had positive AAPC, which included Belarus (AAPC(2003-2012) = 3.18, 95% CI [1.11, 5.29]), Canada (AAPC(2003-2012) = 2.83, 95% CI [1.60, 4.07]) and Korea (AAPC(2003-2012) = 1.76, 95% CI [0.23-3.32]). There was an overall decreasing trend of mortality. However, increased mortality was observed in two countries: Ecuador for boys (AAPC(2007-2016) = 1.72, 95% CI [0.27-3.19]) and Austria for girls (AAPC(2008-2017) = 4.11, 95% CI [0.38-7.98]). CONCLUSIONS: The largest mortality and mortality to incidence ratio of childhood cancer were found in low-income countries. There was a substantial increasing trend of childhood cancer incidence, while overall its mortality has been decreasing over the past decade. More studies are needed to confirm the drivers behind these epidemiologic trends.

Huang, J., et al. (2022). "Worldwide Distribution, Risk Factors, and Temporal Trends of Testicular Cancer Incidence and Mortality: A Global Analysis." Eur Urol Oncol **5**(5): 566-576.

BACKGROUND: Testicular cancer is a common malignancy among young males in western countries. OBJECTIVE: To examine the global disease burden and trends of testicular cancer incidence and mortality by age and country, and their associations with human development index (HDI), gross domestic product (GDP), lifestyle habits, and metabolic risk factors. DESIGN, SETTING, AND PARTICIPANTS: We retrieved the Global Cancer Observatory database for the testicular cancer incidence and mortality in 2020; the World Bank for GDP per capita; the United Nations for HDI; the WHO Global Health Observatory for prevalence of smoking and alcohol drinking; and the Cancer Incidence in Five Continents, WHO mortality database, Surveillance, Epidemiology, and End Results programme and Nordic Cancer Registries (NORDCAN) for trend analysis. OUTCOME MEASUREMENTS AND STATISTICAL ANALYSIS: We presented the testicular cancer incidence and mortality using age-standardised rates. We examined their associations with HDI, GDP, smoking, alcohol drinking, physical inactivity, overweight, obesity, and medical conditions including diabetes, hypertension, and hypercholesterolaemia by linear regression. We estimated the 10-yr trend of incidence and mortality by joinpoint regression with average annual percentage change with 95% confidence intervals in different age groups. RESULTS AND LIMITATIONS: There was a wide variation in the testicular cancer burden with the highest mortality found in low-income countries, and the regions of Central America and South America, while the highest incidence was observed in high-income countries, especially in Western and Northern Europe. We found a positive association for HDI, GDP, alcohol drinking, inactivity, overweight, obesity, and hypercholesterolaemia with testicular cancer incidence, while a negative correlation was observed between GDP and mortality of testicular cancer. Globally, there was an overall increasing incidence trend of testicular cancer for the past decade, particularly in younger males; the mortality trends of testicular cancer were relatively stable. However, we did not analyse the trend of different stages and subtypes of testicular cancer due to data unavailability. CONCLUSIONS: There was a global variation in the testicular cancer burden associated with HDI, GDP, alcohol drinking, inactivity, overweight, obesity, and hypercholesterolaemia. Testicular cancer had an increasing incidence but decreasing mortality. The increasing testicular cancer incidence in the younger population is of concern and calls for early detection and preventive interventions.

PATIENT SUMMARY: Globally, testicular cancer incidence had been increasing particularly in the younger population, although its deaths rates had been decreasing. Socioeconomic indices, alcohol drinking, inactivity, overweight, obesity, and high plasma lipid levels are associated with testicular cancer incidence and mortality.

Huang, J., et al. (2022). "Distribution, Risk Factors, and Temporal Trends for Lung Cancer Incidence and Mortality: A Global Analysis." Chest **161**(4): 1101-1111.

BACKGROUND: Lung cancer ranks second for cancer incidence and first for cancer mortality. Investigation into its risk factors and epidemiologic trends could help describe geographical distribution and identify high-risk population groups. RESEARCH QUESTION: What is the global incidence, mortality, associated risk factors, and temporal trends of lung cancer by sex, age, and country? STUDY DESIGN AND METHODS: Data on incidence and mortality were retrieved from the Global Cancer Observatory (GLOBOCAN), Cancer Incidence in Five Continents series I-X, World Health Organization (WHO) mortality database, the Nordic Cancer Registries (NORDCAN), and the Surveillance, Epidemiology, and End Results Program (SEER). We searched the WHO Global Health Observatory data repository for age-adjusted prevalence of current smoking. The Average Annual Percentage Change (AAPC) of the trends were obtained by Joinpoint Regression. RESULTS: The age-standardized rate of incidence and mortality were 22.4 and 18.0 per 100,000 globally. The lung cancer incidence and mortality were associated with Human Development Index (HDI), Gross Domestic Products (GDP), and prevalence of smoking. For incidence, more countries had increasing trends in females but decreasing trends in males (AAPC, 1.06 to 6.43 for female; -3.53 to -0.64 for male). A similar pattern was found in those 50 years or older, whereas those aged younger than 50 years had declining incidence trends in both sexes in most countries. For mortality, similar to incidence, 17 of 48 countries showed decreasing trends in males and increasing trends in females (AAPC, -3.28 to -1.32 for male, 0.63 to 3.96 for female). INTERPRETATION: Most countries had increasing trends in females but decreasing trends in males and in lung cancer incidence and mortality. Tobacco related measures and early cancer detection should be implemented to control the increasing trends of lung cancer in females, and in regions identified as having these trends. Future studies may explore the reasons behind these epidemiological transitions.

Huang, J., et al. (2022). "A Global Trend Analysis of Kidney Cancer Incidence and Mortality and Their Associations with Smoking, Alcohol Consumption, and Metabolic Syndrome." Eur Urol Focus **8**(1): 200-209.

BACKGROUND: Kidney cancer is a major urological disease globally, with more than 400 000 new cases diagnosed every year. OBJECTIVE: To investigate incidence and mortality trends for kidney cancer and their associations with modifiable risk factors for kidney cancer. DESIGN, SETTING, AND PARTICIPANTS: The most up-to-date figures on kidney cancer incidence and mortality were collected from the GLOBOCAN database and the Cancer Incidence in Five Continents (CI5). Data on total alcohol consumption and the prevalence of smoking, overweight, diabetes, and hypertension were extracted from the World Health Organization Global Health Observatory data repository. OUTCOME MEASUREMENTS AND STATISTICAL ANALYSIS: Age-standardized rates (ASRs) for incidence and mortality and their correlations with potential risk factors for kidney cancer were investigated. Multivariable linear regression analysis was also conducted. The 10-yr temporal patterns for incidence are presented as the average annual percent change with 95% confidence interval using joinpoint regression analysis. RESULTS AND LIMITATIONS: Globally, there is wide variation in kidney cancer incidence and mortality. There were positive correlations between rates of smoking, alcohol consumption, and overweight and ASRs of kidney cancer incidence and mortality. Multivariable regression analysis revealed that alcohol consumption and overweight were significant risk factors for kidney cancer incidence, while smoking and alcohol consumption were significant risk factors for kidney cancer mortality. There was an increasing trend for the incidence of kidney cancer globally, with a particularly prominent trend for European countries. Of note, increasing incidence of kidney cancer is evident even for younger individuals aged <50 yr. However, cancer registries vary by country and period and there is a lack of data regarding the severity of risk factors and disease characteristics such as the distribution of histological groups, tumor grading, and staging. CONCLUSIONS: There is an increasing trend for kidney cancer incidence globally, particularly in European countries and the younger population. Modifiable risk factors for kidney cancer incidence and mortality have been identified. The increasing incidence of kidney cancer among younger individuals is worrying and warrants early action on possible preventive measures. PATIENT SUMMARY: The incidence of kidney cancer has been increasing globally, particularly in European countries and the younger population. Risk factors include smoking,

alcohol consumption, overweight, and hypertension, and these factors are all modifiable.

Huang, J., et al. (2022). "Cancer Incidence and Mortality in Asian Countries: A Trend Analysis." Cancer Control **29**: 10732748221095955.

BACKGROUND: This study aimed to evaluate the updated burden and temporal trends of cancer incidence and mortality in Asian countries. METHODOLOGY: The data used in this study were retrieved from the Global Cancer Observatory, Cancer Incidence in Five Continents volumes I-XI, and the World Health Organization mortality database. These data were used to calculate the Average Annual Percentage Change (AAPC), with a 95% confidence interval (CI) by joinpoint regression analysis to determine the epidemiological trend in the past decade. RESULTS: In 2020, the cancer incidence in Asia was 169.1 per 1 00 000, accounting for 49.3% of the global cancer incidence. The most common cancers included lung (13.8%), breast (10.8%) and colorectal (10.6%) cancers. Its mortality was 101.6 per 1 00 000 (58.3% of the global cancer death) with lung (19.2%), liver (10.5%) and stomach (9.9%) cancers being the most common causes of cancer death. The cancer incidence had been increasing in female population, with Korea (AAPC = 5.73, 95% CI [5.30, 6.17], P < .001), Japan (AAPC = 2.67, 95% CI [2.12, 3.23], P < .001) and Kuwait (AAPC = 2.08, 95% CI [.49, 3.69], P = .016) showing the most significant increases in the past decade. The incidence increase was also observed among population aged <40 years old, with Korea (female AAPC = 8.42, 95% CI [7.40, 9.45], P < .001; male AAPC = 5.28, 95% CI [4.23, 6.33], P <.001), China (female AAPC = 2.94, 95% CI [2.07, 3.81], P < .001; male AAPC = 1.37, 95% CI [.57, 2.18], P = .004) and Japan (female AAPC = 2.88, 95% CI [1.88, 3.88], P = .016; male AAPC = 1.59, 95% CI [.40, 2.78], P = .015) showing the most significant increases. However, there was an overall decreasing trend of cancer mortality. CONCLUSIONS: There was a substantial burden of cancer incidence and mortality in Asia. Although there was a decreasing trend in cancer mortality, its incidence had been increasing especially among female and younger populations. Future studies could be done to further investigate the potential reasons for these epidemiologic trends.

Huang, M. M., et al. (2022). "Using Competing Risk of Mortality to Inform the Transition from Prostate Cancer Active Surveillance to Watchful Waiting." Eur Urol Focus **8**(5): 1141-1150.

BACKGROUND: For men on active surveillance (AS) for prostate cancer (PCa), disease progression and age-related changes in health may influence decisions about pursuing curative treatment. OBJECTIVE: To evaluate the predicted PCa and non-PCa mortality at the time of reclassification among men on AS, to identify clinical criteria for considering a transition from AS to watchful waiting (WW). DESIGN, SETTING, AND PARTICIPANTS: Patients enrolled in a large AS program who experienced biopsy grade reclassification (Gleason grade increase) were retrospectively examined. All patients who had complete documentation of medical comorbidities at reclassification were included. OUTCOME MEASUREMENTS AND STATISTICAL ANALYSIS: A validated model was used to assess 10- and 15-yr untreated PCa and non-PCa mortalities based on patient comorbidities and PCa clinical characteristics. We compared the ratio of predicted PCa mortality with predicted non-PCa mortality ("predicted mortality ratio") and divided patients into four risk tiers based on this ratio: (1) tier 1 (ratio: >0.33), (2) tier 2 (ratio 0.33-0.20), (3) tier 3 (ratio 0.20-0.10), and (4) tier 4 (ratio <0.10). RESULTS AND LIMITATIONS: Of the 344 men who were reclassified, 98 (28%) were in risk tier 1, 85 (25%) in tier 2, 93 (27%) in tier 3, and 68 (20%) in tier 4 for 10-yr mortality. Fifteen-year risk tiers were distributed similarly. The 23 (6.7%) men who met the "transition triad" (age >75 yr, Charlson Comorbidity Index >3, and grade group </=2) had a 14-fold higher non-PCa mortality risk and a lower predicted mortality ratio than those who did not (0.07 vs 0.23, p < 0.001). The primary limitations of our study included its retrospective nature and the use of predicted mortalities. CONCLUSIONS: At reclassification, nearly half of patients had a more than five-fold and one in five patients had a more than ten-fold higher risk of non-PCa death than patients having a risk of untreated PCa death. Despite a more significant cancer diagnosis, a transition to WW for older men with multiple comorbidities and grade group <3 PCa should be considered. PATIENT SUMMARY: Men with favorable-risk prostate cancer and life expectancy of >10 yr are often enrolled in active surveillance, which entails delay of curative treatment until there is evidence of more aggressive disease. We examined a group of men on active surveillance who developed more aggressive disease, and found, nevertheless, that the majority of these men continued to have a dramatically higher risk of death from non-prostate cancer causes than from prostate cancer based on a risk prediction tool. For men older than 75 yr, who have multiple medical conditions and who do not have higher-grade cancer, it may be reasonable to reconsider the need for curative treatment given the low risk of death from prostate cancer compared with the risk of death from other causes.

Huang, W., et al. (2021). "Psychological Distress and All-Cause, Cardiovascular Disease, Cancer Mortality

Among Adults with and without Diabetes." Clin Epidemiol **13**: 555-565.

AIM: To examine the association of psychological distress with all-cause, cardiovascular disease (CVD) and cancer mortality in US adults, and verified whether the associations differed between participants with and without diabetes. METHODS: A total of 485,864 adults (446,288 without diabetes and 39,576 with diabetes) who participated in the National Health Interview Survey from 1997 to 2013 were linked to the National Death Index through December 31, 2015. Psychological distress was measured by the Kessler 6 distress scale (K6). Multivariable Cox proportional hazards regression models were performed to estimate hazard ratios (HR) and 95% confidence intervals (95% CI) for the association between psychological distress and mortality. RESULTS: We ascertained 11,746 deaths (mean follow-up, 7. 7 years) among people with diabetes and 51,636 deaths (9.9 years) among those without diabetes. Psychological distress was associated with higher all-cause, CVD, and cancer mortality. Compared to non-diabetic adults without psychological distress, HRs (95% CI) were 1.07 (1.04 to 1.09) for mild, 1.26 (1.22 to 1.30) for moderate and 1.46 (1.38 to 1.55) for severe psychological distress. Compared to the same reference group, in diabetic participants the HRs were 1.39 (1.33 to 1.44) for no psychological distress, 1.59 (1.53 to 1.66) for mild, 1.90 (1.80 to 2.00) for moderate and 1.98 (1.82 to 2.17) for severe psychological distress. Similar associations were also observed for CVD and cancer mortality but with non-statistically significant interaction. CONCLUSION: Psychological distress was associated with higher mortality, particularly in participants with diabetes. Strategies to ameliorate psychological distress may be important to reduce mortality in this population.

Huang, X., et al. (2022). "Age increased the cancer-specific mortality risk of thyroid cancer with lung metastasis." Clin Endocrinol (Oxf) **96**(5): 719-727.

OBJECTIVE: To investigate the relationship between age and cancer-specific mortality in thyroid cancer (TC) with lung-metastasis. PATIENTS AND METHODS: A total of 1418 patients with initial distant metastases from Surveillance, Epidemiology, and End Results databases were investigated. Patients with a median follow-up time of 8 months (interquartile range [IQR]: 2-27] and a median age of 66 years (IQR: 55-76) were divided into five groups by age and the association between age and TC-specific mortality was analysed. RESULTS: The TC-specific mortality rates were 32.78% (118/360), 46.71% (156/334), 53.93% (199/369), 58.96% (158/268) and 82.76% (72/87) in patients aged </=55 years, >55 but </=65 years, >65 but </=75 years, >75 but </=85 years and >85 years. Kaplan-Meier curves showed that TC-specific mortality rate was associated with increased age (p < .001). Compared with patients </=55 years, patients aged >55 but </=65 years, >65 but </=75 years, >75 but </=85 years and >85 years had significantly higher hazard ratios (HRs) of 1.69 (1.26-2.26), 1.97 (1.47-2.64), 2.18 (1.59-2.99) and 3.24 (2.08-5.06) after adjustments for sex, tumour size and radiation therapy (all p < .001). In TC with initial lung-metastasis, compared with patients </=55 years, patients aged >55 but </=65 years, >65 but </=75 years, >75 but </=85 years and >85 years had significantly higher adjusted HRs of 1.68 (1.20-2.36; p = .003), 2.18 (1.57-3.02), 2.16 (1.51-3.08) and 2.91 (1.79-4.75; p < .001). Similar results were obtained in papillary TC. CONCLUSIONS: The TC-specific mortality was increased with age in TC patients with initial lung-metastasis, indicating that further risk stratification based on age was necessary for TC over 55 years with lung-metastasis. Individual treatment strategies maybe recommended for such patients.

Huang, Y., et al. (2021). "Six years of colorectal cancer mortality surveillance in the screening population for a risk stratified screening program." Cancer Epidemiol **73**: 101937.

OBJECTIVE: To evaluate the impact of a colorectal cancer (CRC) risk predicting system on CRC mortality rates. METHOD: An organized population screening program targeted at all the subjects (n = 102,076) at age 40-74 in nine towns of Jiashan county, China was conducted from 2007 to 2012. All of the screening participants were first triaged into high-risk & low-risk groups by a questionnaire and two fecal immunuochemical tests, only the high-risk subjects were subject to colonocopy. The screening participants were surveyed death caused by CRC for a total of six years after the enrollment. The CRC mortality in subgroups of the screening population was analyzed. RESULTS: A total of 82,184 (80.51 % of the targeted population) screening participants were identified. CRC death were recorded for 142 subjects (28.819 per 10(5) person-years). The age-adjusted relative risk(RR) of CRC death in the high-risk subjects (n = 12862, 84.48 per 10(5) person-years) was 3.92 (95 % CI = 2.81-5.49) compared with the low-risk subjects (n = 69322, 18.52 per 10(5) person-years). In the high-risk group, the age-adjusted RR of CRC death for those accepted colonoscopies (51.44 per 10(5) person-years) compared with those refused colonoscopies (187.94 per 10(5) person-years, P < 0.0001) was 0.34 (95 % CI = 0.21-0.56). The first three years after screening has seen the largest difference of CRC death hazard in both comparing groups. CONCLUSION: The high-risk subjects triaged by the risk predicting system have a higher CRC mortality rate than the low-risk subjects,

especially in the first three years after screening. Refusal of colonoscopy is risky behavior for the high-risk subject.

Hue, J. J., et al. (2021). "Mortality and Survival Among Octogenarians with Localized Pancreatic Head Cancer: a National Cancer Database Analysis." J Gastrointest Surg **25**(10): 2582-2592.

BACKGROUND: Pancreatic ductal adenocarcinoma (PDAC) has historically poor outcomes. Difficult decisions must be made by patients and providers, especially in the elderly for whom treatment morbidities may not be tolerable. Herein, we report treatment-dependent outcomes of octogenarians with localized PDAC. METHODS: The National Cancer Database identified patients >/=60 years with localized PDAC of the pancreatic head (2011-2016). Patients were grouped by age (60-79 and >/=80 years) and categorized by treatment regimen: no treatment, chemotherapy, pancreaticoduodenectomy, pancreaticoduodenectomy with perioperative chemotherapy, or pancreaticoduodenectomy with adjuvant chemotherapy. Postoperative outcomes and survival were analyzed. RESULTS: A total of 35,409 patients were included, 8745 (24.7%) of which were >/=80 years. Over 52% of octogenarians did not receive any treatment, compared to 19.1% of younger patients (p<0.001). Patients >/=80 years who underwent a pancreaticoduodenectomy had a significantly greater 90-day mortality rate compared to patients 60-79 years (11.0% vs. 6.7%, p<0.001). Only 42.2% of octogenarians who underwent upfront pancreatectomy received adjuvant chemotherapy. Median survival for octogenarians was 3.3 months without any treatment, 9.7 months with chemotherapy, 12.0 months with pancreaticoduodenectomy, and greater than 20 months with either perioperative or adjuvant chemotherapy in addition to pancreaticoduodenectomy. Age >/=80 was associated with poor survival relative to ages 60-79 when adjusting for treatment regimen (HR=1.19, p<0.001). CONCLUSION: Increasing age is associated with worse overall survival in PDAC, but select octogenarians can achieve reasonable survival with multimodal therapy. Given the poor survival and increased perioperative mortality of octogenarians, patient selection for surgery and consideration of neoadjuvant therapy may be increasingly important.

Hwang, S., et al. (2022). "Association of Zolpidem With Increased Mortality in Patients With Brain Cancer: A Retrospective Cohort Study Based on the National Health Insurance Service Database." J Clin Neurol **18**(1): 65-70.

BACKGROUND AND PURPOSE: Zolpidem is one of the most common hypnotics prescribed to treat insomnia worldwide. However, there are numerous reports of a positive association between zolpidem and mortality, including an association with increased cancer-specific mortality found in a Taiwanese cohort study. This study aimed to determine the association between zolpidem use and brain-cancer-specific mortality in patients with brain cancer. METHODS: This population-based, retrospective cohort study analyzed data in the National Health Insurance Service database. All incident cases of brain cancer at an age of >/=18 years at the time of brain cancer diagnosis over a 15-year period (2003-2017) were included. A multivariate Cox regression analysis after adjustment for covariables was performed to evaluate the associations of zolpidem exposure with brain-cancer-specific and all-cause mortality. RESULTS: This study identified 38,037 incident cases of brain cancer, among whom 11,823 (31.1%) patients were exposed to zolpidem. In the multivariate Cox regression model, the brain-cancer-specific mortality rate was significantly higher in patients who were prescribed zolpidem than in those with no zolpidem prescription (adjusted hazard ratio [HR]=1.14, 95% confidence interval [CI]=1.08-1.21, p<0.001). Zolpidem exposure was significantly associated with increased brain-cancer-specific mortality after adjustment in younger adults (age 18-64 years; adjusted HR=1.37, 95% CI=1.27-1.49) but not in older adults (age >/=65 years; adjusted HR=0.94, 95% CI=0.86-1.02). CONCLUSIONS: Zolpidem exposure was significantly associated with increased brain-cancer-specific mortality in patients with brain cancer aged 18-64 years. Further prospective studies are warranted to understand the mechanism underlying the effect of zolpidem on mortality in patients with brain cancer.

Hwang, S. H., et al. (2021). "A comparison of meta-analysis results with and without adjustment for the healthy worker effect: cancer mortality among workers in the semiconductor industry." Epidemiol Health **43**: e2021057.

OBJECTIVES: This study compared the results of meta-analysis with and without adjustment for the healthy worker effect on the association between working in the semiconductor industry and cancer mortality. METHODS: Six studies that reported standardized mortality ratios (SMRs) for cancers were selected for meta-analysis. Using a random-effects model, the SMR results from each study were combined for all cancers and leukemias to estimate the summary SMRs (95% confidence interval, CI). To adjust for the healthy worker effect, the relative standardized mortality ratio (rSMR=SMRx/SMRnot x) were calculated using observed and expected counts for the specific cause of interest (i.e., all cancers and

leukemias) and the observed and expected counts for all other causes of mortality. Then, the rSMR results were combined to estimate the summary rSMRs (95% CIs). RESULTS: The SMRs for all causes of mortality among semiconductor industry workers ranged from 0.25 to 0.80, which reflects a significant healthy worker effect. A remarkable difference was found between the summary SMRs and the summary rSMRs. The summary SMR for all cancers was 0.70 (95% CI, 0.63 to 0.79) whereas the summary rSMR was 1.38 (95% CI, 1.20 to 1.59). The summary SMR for leukemia was 0.88 (95% CI, 0.72 to 1.07), and the summary rSMR was 1.88 (95% CI, 1.20 to 2.95). CONCLUSIONS: Our results suggest that adjustment for the healthy worker effect (i.e., rSMR) may be useful in meta-analyses of cohort studies reporting SMRs.

Hwee, J. and E. Bougie (2021). "Do cancer incidence and mortality rates differ among ethnicities in Canada?" Health Rep **32**(8): 3-17.

BACKGROUND: Cancer incidence rates have been shown to vary by ethnicity, and the increasing awareness of and interest in reporting ethnic health inequalities have been growing internationally. The objective of this study was to assess cancer incidence and mortality rates by ethnicity in Canada. DATA AND METHODS: The study used the 2006 Canadian Census Health and Environment Cohort, linked to the Canadian Cancer Registry and the Canadian Vital Statistics-Death Database, to determine cancer cases and mortality from 2006 to 2016. Ethnicity was categorized as non-Indigenous North American (NINA); European; Caribbean; Latin, Central and South American (LCSA); African; East Asian; South Asian; and West Central Asian and Middle Eastern. RESULTS: Europeans had the highest standardized incidence rates, while NINA had the highest mortality rates. Rates varied substantially by ethnicity and immigrant status. The top three cancers accounted for 46.5% to 61.9% of all new cancers, while the top three cancer deaths accounted for 36.1% to 61.9% of all deaths. The distribution of cancers within the top 10 cancers and the top 10 cancer deaths also differed; e.g., stomach cancer was found to be more prevalent in the East Asian, LCSA, African and Caribbean groups. Non-immigrant African males had the highest cancer incidence rates, and non-immigrant South Asian females had the highest mortality rates. DISCUSSION: There is considerable variability in cancer incidence and cancer mortality rates by ethnicity, and this study addresses the knowledge gap in Canada in this area. Establishing baseline indicators, such as cancer rates by ethnicity, is essential to understanding the differences within the diverse Canadian population and to informing targeted interventions that may help reduce health inequalities.

Iacoviello, L., et al. (2022). "Low antithrombin levels are associated with low risk of cardiovascular death but are a risk factor for cancer mortality." PLoS One **17**(9): e0271663.

BACKGROUND: Thrombosis is common in subjects suffering from cardiovascular diseases (CVD) and cancer. Hypercoagulation plays a pivotal role in the pathophysiology of thrombosis. Therefore, the inactivation of thrombin, the key enzyme in coagulation, is tightly regulated via antithrombin (AT). AT deficiency is related to thrombosis and cardiovascular death. In this study we investigated the association between AT levels and mortality, in particularly cardiovascular-related and cancer-related death in the general population. METHODS: We studied the association of AT levels and mortality in a prospective cohort sampled from the general Italian population (n = 19,676). AT levels were measured in the baseline samples, and mortality was recorded during a median follow-up period of 8.2 years. Cox regression was performed to investigate the association of all-cause, CVD-related and cancer-related mortality with variations in AT levels. RESULTS: In total, 989 subjects died during follow-up, of which 373 subjects of CVD and 353 of cancer-related causes. Cox analysis revealed that, after adjustment for age, sex, current smoking, BMI, diabetes, hypertension, hypercholesterolemia, history of cardiovascular disease, history of cancer, vitamin K antagonists, antiplatelet medication, heparin and oral contraceptives AT levels were not associated with all-cause mortality (HRQ1vsQ5: 0.92, 95% CI:0.74-1.15). Interestingly, the risk of CVD-related mortality was reduced in subjects with low AT levels compared to subjects with higher AT levels, after adjustment for age and sex and other confounders did not change the association (HRQ1vsQ5: 0.64, 95% CI:0.44-0.91). Moreover, low AT levels were associated with increased cancer mortality in a fully adjusted model (HRQ1vsQ2-5: 1.26, 95% CI:0.88-1.81). CONCLUSIONS: Low AT levels are associated to a lower risk of fatal cardiovascular events in the general population, regardless of age, sex and medication use. In contrast, low AT levels are associated with lower cancer survival. For the first time we show that AT levels lower than the normal range in the general population, even before the development or diagnosis of cancer, are associated with an elevated risk of cancer death.

Ibanez-Sanz, G., et al. (2021). "Positive impact of a faecal-based screening programme on colorectal cancer mortality risk." PLoS One **16**(6): e0253369.

INTRODUCTION: The effectiveness of colorectal cancer (CRC) screening programs is directly related to participation and the number of interval CRCs. The objective was to analyse specific-mortality in a cohort of individuals invited to a CRC screening program according to type of CRC diagnosis (screen-detected cancers, interval cancers, and cancers among the non-uptake group). MATERIAL AND METHODS: Retrospective cohort that included invitees aged 50-69 years of a CRC screening program (target population of 85,000 people) in Catalonia (Spain) from 2000-2015 with mortality follow-up until 2020. A screen-detected CRC was a cancer diagnosed after a positive faecal occult blood test (guaiac or immunochemical); an interval cancer was a cancer diagnosed after a negative test result and before the next invitation to the program (</=24 months); a non-uptake cancer was a cancer in subjects who declined screening. RESULTS: A total of 624 people were diagnosed with CRC (n = 265 screen-detected, n = 103 interval cancers, n = 256 non-uptake). In the multivariate analysis, we observed a 74% increase in mortality rate in the group with interval CRC compared to screen-detected CRC adjusted for age, sex, location and stage (HR: 1.74%, 95% CI:1.08-2.82, P = 0.02). These differences were found even when we restricted for advanced-cancers participants. In the stratified analysis for type of faecal occult blood test, a lower mortality rate was only observed among FIT screen-detected CRCs. CONCLUSION: CRC screening with the FIT was associated with a significant reduction in CRC mortality.

Ibilibor, C., et al. (2021). "The association between sarcopenia and bladder cancer-specific mortality and all-cause mortality after radical cystectomy: A systematic review and meta-analysis." Arab J Urol **19**(1): 98-103.

Objective: To compare cancer-specific mortality (CSM) and all-cause mortality (ACM) between patients with and without sarcopenia who underwent radical cystectomy for bladder cancer. Materials and methods: We performed a systematic review and meta-analysis of original articles published from October 2010 to March 2019 evaluating the effect of sarcopenia on CSM and ACM. We extracted hazard ratios (HRs) and 95% confidence intervals (CIs) for CSM and ACM from the included studies. Heterogeneity amongst studies was measured using the Q-statistic and the I (2) index. Meta-analysis was performed using a random-effects model if heterogeneity was high and fixed-effects models if heterogeneity was low. Results: We identified 145 publications, of which five were included in the meta-analysis. These five studies represented 1447 patients of which 453 were classified as sarcopenic and 534 were non-sarcopenic. CSM and ACM were increased in sarcopenic vs non-sarcopenic patients (HR 1.64, 95% CI 1.30-2.08, P < 0.01 and HR 1.41, 95% CI 1.22-1.62, P < 0.01, respectively). Conclusions: Sarcopenia is significantly associated with increased CSM and ACM in bladder cancer. Identifying patients with sarcopenia will augment preoperative counselling and planning. Further studies are required to evaluate targeted interventions in patients with sarcopenia to improve clinical outcomes. Abbreviations: ACM: all-cause mortality; ASA: American Association of Anesthesiologists; BMI: body mass index; CCI: Charlson Comorbidity Index; CSM: cancer-specific mortality; CSS: cancer-specific survival; ECOG: Eastern Cooperative Oncology Group; HR: hazard ratio; NAC: neoadjuvant chemotherapy; NIH: National Institutes of Health; OS: overall survival; RC: radical cystectomy; RCT: randomised controlled trial; SMI: Skeletal Muscle Index.

Ibrahem, S., et al. (2022). "Trends in colorectal cancer in Iraq over two decades: incidence, mortality, topography and morphology." Ann Saudi Med **42**(4): 252-261.

BACKGROUND: Colorectal cancer (CRC) is mainly a disease of the elderly in the Western world, but its characteristics are changing globally. Iraq does not have a well established CRC screening program. Understanding trends of CRC incidence, fatality and the clinical features of CRC patients is vital to the design of effective public health measures; public awareness, screening, diagnosis and treatment strategies to meet the future demands. OBJECTIVES: Determine trends in demography, incidence proportion, mortality, topography (primary tumor site) and morphology (histology) over two decades. DESIGN: Registry-based study SETTING: Iraqi National Cancer Registry (INCR) database PATIENTS AND METHODS: We collected and analyzed data from CRC patients obtained from the INCR to calculate incidence and mortality proportion per 100 000 population for the period from 2000 to 2019. In addition to estimation, data were examined by anatomic location and morphological type. MAIN OUTCOME MEASURES: Change in the incidence and mortality proportion, topography and morphology of CRC over 20 years. SAMPLE SIZE: 20 880 CRC patients ranging in age from 14-80 years. RESULTS: The overall (males and females) CRC incidence proportion (CIP) increased from 2.28 to 6.18 per 100 000 population in 2000 and 2019, respectively, with an annual percentage change (APC) of 5.11%. The incidence proportion (IP) of CRC in patients from 20 to <50 years rose from 1.46 in 2000 to 4.36 per 100 000 population in 2019, which is an APC of 5.6%. The IP in patients older than 50 years rose from 12.7 to 40.59

per 100 000 population in 2000 and 2019, respectively, with an APC of 5.98%. The percentage of all CRC cases to all total malignancies in Iraq grew from 3.69% in 2000 to 6.5% in 2019. The CRC mortality proportion increased from 1.25 to 1.77 per 100 000 populations in 2010 and 2019, respectively, reflecting an APC of 3.54%. Anatomically, colon (C18) tumor represented 59.2% and 65.7% in 2000 and 2019, respectively. Rectal (C20) tumors were 37.2% in 2000 down to 31.4% in 2019, while rectosigmoid junction tumor (C19) were 3.6% in 2000 dropping to 2% in 2019. CONCLUSIONS: CRC in Iraq is still a disease of the elderly and is rising in incidence and mortality in all age groups. This necessitates reconsidering health policy regarding CRC; public awareness, screening and management strategies to accommodate for these alarming changes. LIMITATIONS: Data about stages, grades and molecular characterisations are not available in the INCR. CONFLICT OF INTEREST: None.

Igissinov, N., et al. (2022). "Trend in Gastric Cancer Mortality in Kazakhstan." Asian Pac J Cancer Prev **23**(11): 3779-3789.

OBJECTIVE: The aim is to study the trends in gastric cancer (GC) mortality in Kazakhstan. METHODS: Data on those who died from GC and on the annual population were obtained from the Bureau of National Statistics of the Agency for Strategic Planning and Reforms of the Republic of Kazakhstan. A retrospective study was carried out for the period 2009-2018 using descriptive and analytical methods of oncoepidemiology. The extensive, crude and age-specific mortality rates are determined according to the generally accepted methodology used in sanitary statistics. RESULTS: GC mortality in Kazakhstan is considered to be decreasing. It was determined that during the studied period 19,672 died of this cancer. The mean of death was 67.8 with 95% CI of 67.6 to 68.0. The highest mortality rates per 100,000 in the entire population were found in the age groups 75-79 years (145.9+/-24.1), 80-84 years (161.0+/-11.0), and 85+ years (116.5+/-16.4). Trends in age-related mortality rates had a pronounced tendency to increase in 70-74 years (T=+4.3%, R2=0.1924) and to decrease in the age of up to 30 (T=-8.7%, R2=0.2426). The average annual standardized mortality rate was 13.2 per 100,000, and in trends tended to decrease (T=-5.8%; R2=0.9763). In all regions, there is a decrease in mortality, except for the city of Astana. During categorization mortality rates were determined on the basis of standardized indicators: low - up to 12.9, average - from 12.9 to 15.1, high - above 15.1 per 100,000 for the entire population. CONCLUSION: The mortality rates from GC tend to decrease, while the downward trends and the degree of their approximation are expressed in almost all regions. The study of regional mortality has theoretical and practical significance for monitoring and evaluating the effectiveness of early detection and treatment. Health authorities should take into account the results obtained when organizing antitumor measures.

Ignjatovic, A., et al. (2022). "Cancer of unknown primary - incidence, mortality trend, and mortality-to-incidence ratio is associated with human development index in Central Serbia, 1999-2018: Evidence from the national cancer registry." Eur J Cancer Care (Engl) **31**(1): e13526.

OBJECTIVES: The aim was to estimate the trend of incidence, mortality and mortality-to-incidence ratio (MIR) in Central Serbia in 1999-2018 and its possible association with the human development index (HDI). METHODS: In this study, cancer of unknown primary (CUP) was included as C77-C80 codes. Trend analysis was performed in the Joinpoint Regression Programme version 4.8.0.1. HDI combines life expectancy, educational attainment and gross national income. HDI values for Serbia are extracted from the global bank site. RESULTS: Joinpoint regression analysis of the age-standardised incidence rate of CUP showed a significantly increasing trend with annual percent change (APC) of 8.5% (95% confidence interval [CI] 3.0-14.3%) in males and 7.8% (95%CI 2.7-13.2) in females. The age-standardised mortality rate of CUP showed a significantly decreasing trend with APC of -1.7% (95%CI -2.8 to -0.5%) in males and -1.4% (95%CI -2.7 to -0.1%) in females. MIR showed a significantly decreasing trend with APC of -9.3% (95%CI -14.6 - -3.6%) in males and -7.1% (95%CI -10.5% to -4.2%) in females. The linear regression showed significant inverse association among HDI and the MIR of CUP in males ($r(2) = 0.464$, $p = 0.002$) and in females ($r(2) = 0.612$, $p < 0.001$). CONCLUSIONS: Decline of MIR was associated with HDI, suggesting that CUP prognosis follows socio-economic status.

Ikuemonisan, J., et al. (2021). "Association between preoperative prostate-specific antigen levels and mortality in high- and intermediate-grade prostate cancer patients who received radical prostatectomy: Findings from the SEER database." Prostate Int **9**(2): 72-77.

BACKGROUND: The degree of expression of prostate-specific antigen (PSA) has been applied for the purpose of screening and monitoring the progression of prostate cancer. The goal of this study was to evaluate the association between preoperative PSA levels and mortality outcomes in men with high- and intermediate-grade prostate cancer who received radical prostatectomy. METHODS: The 2004-2014 files of the Surveillance, Epidemiology, and End Result

database were analyzed. A total of 97,357 patients with non-metastatic high- and intermediate-grade adenocarcinoma of the prostate who received radical prostatectomy were identified. Using Kaplan-Meier estimates and multivariable Cox proportional hazard models, the relationship between preoperative PSA values and cancer-specific mortality outcomes in men with high- and intermediate-grade prostate cancer who received radical prostatectomy was tested. RESULTS: Of 97,357 patients with high- and intermediate-grade prostate cancer who received radical prostatectomy from 2001 to 2014, there were 983 cancer-specific deaths, and the average follow-up time for the cohort was 85.0 (34.6) months. Preoperative PSA values > 10 ng/ml were associated with greater risk of cancer-specific mortality (hazard ratio 2.3, P < 0.0001) when compared to the referent/normal values for preoperative PSA (<4 ng/ml). Individuals with preoperative PSA values 4-10 ng/ml had lower risk of prostate cancer-specific mortality (hazard ratio 0.80, P = 0.03) when compared to individuals with normal preoperative PSA values. CONCLUSIONS: Individuals with preoperative PSA values 4-10 ng/ml had 20% lower risk of prostate cancer-specific mortality when compared to individuals with preoperative PSA values of <4 ng/dl. The findings from this study suggest that low or normal preoperative PSA values may not always mean that prostate cancer is indolent, and more work needs to be done to better classify risk in men with prostate cancer.

Ilic, I. and M. Ilic (2022). "International patterns in incidence and mortality trends of pancreatic cancer in the last three decades: A joinpoint regression analysis." World J Gastroenterol **28**(32): 4698-4715.

BACKGROUND: Pancreatic cancer, as the one of most fatal malignancies, remains a critical issue in the global burden of disease. AIM: To estimate trends in pancreatic cancer incidence and mortality worldwide in the last three decades. METHODS: A descriptive epidemiological study was done. Pancreatic cancer incidence and mortality data were obtained from the database of the World Health Organization. Analysis of pancreatic cancer incidence and mortality during 2020 was performed. The age-standardized rates (ASRs, expressed per 100000) were presented. To estimate trends of incidence and mortality of pancreatic cancer, joinpoint regression analysis was used: the average annual percent change (AAPC) with the corresponding 95% confidence interval (95%CI) was calculated. Additionally, analysis was performed by sex and age. In this paper, the trend analysis included only countries with high and medium data quality. RESULTS: A total of 495773 (262865 male and 232908 female) new cases and 466003 (246840 male and 219163 female) deaths from pancreatic cancer were reported worldwide in 2020. In both sexes, most of the new cases (191348; 38.6% of the total) and deaths (182074; 39.1% of the total) occurred in the Western Pacific Region. In both sexes, the highest ASRs were found in the European Region, while the lowest rates were reported in the South-East Asia Region. The general pattern of rising pancreatic cancer incidence and mortality was seen across countries worldwide in observed period. Out of all countries with an increase in pancreatic cancer incidence, females in France and India showed the most marked rise in incidence rates (AAPC = +3.9% and AAPC = +3.7%, respectively). Decreasing incidence trends for pancreatic cancer were observed in some countries, but without significance. Out of all countries with an increase in pancreatic cancer mortality rates, Turkmenistan showed the most marked rise both in males (AAPC = +10.0%, 95%CI: 7.4-12.5) and females (AAPC = +6.4%, 95%CI: 3.5-9.5). The mortality trends of pancreatic cancer were decreasing in both sexes only in Canada and Mexico. CONCLUSION: Further research is needed to explain the cause of large international differences in incidence and mortality trends of pancreatic cancer in last three decades.

Jacobson, F. L., et al. (2021). "Preserving NLST mortality benefits and acceptable morbidity for lung cancer surgery in a community hospital." J Surg Oncol **124**(1): 124-134.

BACKGROUND AND OBJECTIVES: The aim of this study was to demonstrate whether academic thoracic surgeons could achieve morbidity and mortality rates in community hospitals equivalent to those seen in National Lung Screening Trial (NLST). METHODS: This was a retrospective review of community hospital lung cancer procedures for clinical Stage I-III non-small-cell lung cancers from 2007 through 2014. Variables include age, comorbidities, computed tomography (CT) characterization, and operative techniques. RESULTS: There were 177 patients who had lung cancers removed by a minimally invasive approach (79%), including lobectomy in 127 (72%), segmentectomy in 4 (2%), and wedge-resections in 46 (26%). The median patient age was 71 years (interquartile range [IQR], 63-76). The cohort was primarily female (58%), clinical Stage I (82%), with a median tumor size of 2.3 cm (IQR, 1.5-3.3). The median length of stay was 6 days (range: 1-35). Complications were experienced by 78 (44.1%) patients, most commonly atrial fibrillation in 20 (11.3%) followed by air-leak in 19 (10.7%). There were no in-hospital deaths. Tumor location and extent of resection were associated with complications, while larger tumor size, margin contour, and resection method were associated with air-leak (all p < 0.05).

Higher clinical stage and larger tumor size were associated with occult Stage III disease (both $p < 0.05$). CONCLUSIONS: The low morbidity and mortality rates from the NLST were achievable in a community setting for early-stage lung cancer. Characterization of cancers using CT imaging identified factors most commonly associated with postoperative complications and the presence of occult Stage III disease.

Jakobsen, E., et al. (2021). "Forecasting lung cancer incidence, mortality, and prevalence to year 2030." BMC Cancer **21**(1): 985.

BACKGROUND: Lung cancer incidence and prevalence is increasing worldwide and there is a focus on prevention, early detection, and development of new treatments which will impact the epidemiological patterns of lung cancer. The clinical characteristics and the trends in incidence, mortality, and prevalence of lung cancer in Denmark from 2006 through 2015 are described and a model for predicting the future epidemiological profile of lung cancer through 2030 is introduced. METHODS: The study population comprised all cases of lung cancer, registered in the Danish Cancer Registry, who were alive on January 1, 2006 or had a first-time ever diagnosis of lung cancer during 2006 through 2015. Information on morphology, stage of the disease, comorbidity and survival was obtained from other Danish health registers. Based on NORDCAN data and estimated patient mortality rates as well as prevalence proportions for the period 2006 through 2015, future case numbers of annual incidence, deaths, and resulting prevalence were projected. RESULTS: A total of 44.291 patients were included in the study. A shift towards more patients diagnosed with lower stages and with adenocarcinoma was observed. The incidence increased and the patient mortality rate decreased significantly, with a doubling of the prevalence during the observation period. We project that the numbers of prevalent cases of lung cancer in Denmark most likely will increase from about 10,000 at the end of 2015 to about 23,000 at the end of 2030. CONCLUSIONS: Our findings support that lung cancer is being diagnosed at an earlier stage, that incidence will stop increasing, that mortality will decrease further, and that the prevalence will continue to increase substantially. Projections of cancer incidence, mortality, and prevalence are important for planning health services and should be updated at regular intervals.

Jamal, S., et al. (2021). "Cancer in First Nations people in Ontario, Canada: Incidence and mortality, 1991 to 2010." Health Rep **32**(6): 14-28.

BACKGROUND: This study aims to measure cancer incidence and mortality rates of Registered First Nations people in Ontario and compare them with those of other people in Ontario from 1991 to 2010. DATA AND METHODS: The federal Indian Register, the Ontario Cancer Registry and the Registered Persons Database were linked to develop a cohort of First Nations people diagnosed with cancer in Ontario. Sex- and site-specific age-standardized cancer incidence and mortality rates, and selected trends over time, were calculated. Rate ratios (RRs) were used to compare rates in First Nations peoples with those of other people in Ontario. RESULTS: The First Nations cohort comprised 194,392 people, with 6,859 cancer diagnoses. First Nations people had higher rates for certain cancers than others in Ontario: lung (males RR 1.19; females RR 1.47), colorectal (males RR 1.36; females RR 1.34) and kidney (males RR1.95; females RR 2.23). While lung cancer rates rose in First Nations females (annual percent change [APC] +2.67), they fell at a similar rate (APC -2.28) in males. Cervical cancer rates fell (APC -9.53) and approached the rate among other females in Ontario. Kidney cancer rates increased in First Nations people. DISCUSSION: First Nations people in Ontario have higher incidence and mortality for certain cancers compared with other people in Ontario. However, the declines in cervical cancer rates in First Nations females and lung cancer rates in First Nations males illustrate the likely impact of Pap test uptake and smoking cessation programs. Community-led efforts to develop culturally appropriate prevention and screening programs are essential to further reduce cancer rates in First Nations people.

Jang, D., et al. (2020). "Smoking status before and after colorectal cancer diagnosis and mortality in Korean men: A population-based cohort study." Cancer Med **9**(24): 9641-9648.

BACKGROUND: Smoking is a well-known risk factor for colorectal cancer incidence; however, the effect of smoking before and after cancer diagnosis on mortality has not been addressed well. Thus, we aimed to evaluate the association of prediagnosis and postdiagnosis smoking status and mortality among colorectal cancer patients. METHODS: A retrospective cohort consisted of 37,079 male colorectal cancer patients. Smoking status was defined from information within 2 years of colorectal cancer diagnosis for prediagnosis and at least 1 year later for postdiagnosis. The prediagnostic and postdiagnostic smoking status were categorized into four groups (nonsmoker/nonsmoker, nonsmoker/smoker, smoker/nonsmoker, and smoker/smoker). Hazard ratios (HRs) and 95% confidence intervals (CIs) were estimated using the Cox proportional hazard model. RESULTS: During a median of 6.3 years of follow-up, a total of 3980 deaths and 2137 deaths from colorectal cancer occurred. The number of prediagnosis smokers were 11,100 and 62.4% of them quitted smoking after

the diagnosis. Significantly elevated mortality rate in prediagnosis smokers was observed regardless of postdiagnosis smoking status (smoker/nonsmoker [HR, 1.30; 95% CI, 1.20-1.41] and smoker/smoker [HR, 1.21; 95% CI, 1.09-1.34]). Among patients treated with surgical operation only, those who quit smoking after diagnosis showed lower mortality rates compared to continual smokers (HR, 0.80; 95% CI, 0.67-0.96). CONCLUSIONS: Smoking before cancer diagnosis rather than postdiagnosis has stronger impact on prognosis colorectal cancer patients, and quitting smoking may improve survival, especially among early stage colorectal cancer patients.

Jani, C., et al. (2021). "Trends of HIV-Related Cancer Mortality between 2001 and 2018: An Observational Analysis." Trop Med Infect Dis **6**(4).

The burden of AIDS-defining cancers has remained relatively steady for the past two decades, whilst the burden of non-AIDS-defining cancer has increased. Here, we conduct a study to describe mortality trends attributed to HIV-associated cancers in 31 countries. We extracted HIV-related cancer mortality data from 2001 to 2018 from the World Health Organization Mortality Database. We computed age-standardized death rates (ASDRs) per 100,000 population using the World Standard Population. Data were visualized using Locally Weighted Scatterplot Smoothing (LOWESS). Data for females were available for 25 countries. Overall, there has been a decrease in mortality attributed to HIV-associated cancers among most of the countries. In total, 18 out of 31 countries (58.0%) and 14 out of 25 countries (56.0%) showed decreases in male and female mortality, respectively. An increasing mortality trend was observed in many developing countries, such as Malaysia and Thailand, and some developed countries, such as the United Kingdom. Malaysia had the greatest increase in male mortality (+495.0%), and Canada had the greatest decrease (-88.5%). Thailand had the greatest increase in female mortality (+540.0%), and Germany had the greatest decrease (-86.0%). At the endpoint year, South Africa had the highest ASDRs for both males (16.8/100,000) and females (19.2/100,000). The lowest was in Japan for males (0.07/100,000) and Egypt for females (0.028/100,000).

Jani, C., et al. (2021). "Lung cancer mortality in Europe and the USA between 2000 and 2017: an observational analysis." ERJ Open Res **7**(4).

BACKGROUND: The lung is the most common site for cancer and has the highest worldwide cancer-related mortality. Our study reports and compares trends in lung cancer mortality in the USA and 26 European countries. STUDY DESIGN AND METHODS: Lung cancer mortality data were extracted for males and females for each of the years 2000-2017 from the World Health Organization (WHO) Mortality and the Centers for Disease Control and Prevention (CDC) WONDER databases. Lung cancer mortality trends were compared using Joinpoint regression analysis, and male-to-female mortality ratios were calculated. RESULTS: Down-trending lung cancer mortality rates were observed in males in all countries except Cyprus and Portugal between 2000 and 2017. In females, increasing mortality rates were observed in 22 of the 27 countries analysed. Latvia had the highest estimated annual percentage change (EAPC) in male mortality (-9.6%) between 2013 and 2015. In the USA, EAPCs were -5.1% for males and -4.2% for females between 2014 and 2017. All countries had an overall decrease in the ratio of male-to-female lung cancer mortality. The most recent observation of median male-to-female mortality was 2.26 (IQR 1.92-4.05). The countries with the greatest current sex disparity in lung cancer mortality were Lithuania (5.51) and Latvia (5.00). CONCLUSION: Between 2000 and 2017, lung cancer mortality rates were decreasing for males in Europe and the USA, whereas increasing lung cancer mortality rates were generally observed in females. There is a persistent but decreasing sex-mortality gap, with men having persistently greater lung cancer mortality but with rates decreasing faster than women.

Jani, C., et al. (2021). "Trends in Breast Cancer Mortality Between 2001 and 2017: An Observational Study in the European Union and the United Kingdom." JCO Glob Oncol **7**: 1682-1693.

PURPOSE: Breast cancer is the most common cancer in women worldwide, representing 25.4% of the newly diagnosed cases in 2018. The past two decades have seen advancements in screening technologies, guidelines, and newer modalities of treatment. Our study reports and compares trends in breast cancer mortality in the European Union and the United Kingdom. MATERIALS AND METHODS: We used the WHO Mortality Database. We extracted breast cancer mortality data from 2001 to 2017 on the basis of the International Classification of Diseases, 10th revision system. Crude mortality rates were dichotomized by sex and reported by year. We computed age-standardized death rates (ASDRs) per 100,000 population using the world standard population. Breast cancer mortality trends were compared using joinpoint regression analysis. RESULTS: We analyzed data from 24 EU countries, including the United Kingdom. For women, breast cancer mortality was observed to be downtrending in all countries except Croatia, France, and Poland. For the most recent female data, the highest ASDR for breast cancer was identified in Croatia (19.29 per 100,000), and the lowest ASDR was noted in Spain

(12.8 per 100,000). Denmark had the highest change in ASDR and the highest estimated annual percentage change of -3.2%. For men, breast cancer mortality decreased in 18 countries, with the largest relative reduction observed in Denmark with an estimated annual percentage change of -27.5%. For the most recent male data, the highest ASDR for breast cancer was identified in Latvia (0.54 per 100,000). CONCLUSION: Breast cancer mortality rates have down trended in most EU countries between 2001 and 2017 for both men and women. Given the observational nature of this study, causality to the observed trends cannot be reliably ascribed. However, possible contributing factors should be considered and subject to further study.

Jankhotkaew, J., et al. (2020). "Associations between alcohol consumption trajectory and deaths due to cancer, cardiovascular diseases and all-cause mortality: a 30-year follow-up cohort study in Thailand." BMJ Open **10**(12): e038198.

OBJECTIVES: This study examined the association between alcohol consumption trajectory and deaths due to cancer, cardiovascular diseases (CVDs) and all-cause mortality in Thailand. DESIGN: Data were obtained from a Thai prospective cohort study with more than 30 years of follow-up (n=1961). SETTING: All participants resided in Bangkok and its vicinity. PARTICIPANTS: Employees from the Electricity Generating Authority of Thailand aged between 35 and 54 years old were randomly selected. MAIN OUTCOME MEASURES: Exposure was alcohol consumption trajectory over the study period from 1985 to 2012. The main outcomes were all-cause mortality, and deaths due to cancer and CVDs recorded in national vital registries between 2002 and 2015. Cox's proportional hazard regression was used to determine the associations between alcohol consumption trajectory and each outcome adjusting for sample characteristics, health behaviours and health conditions. RESULTS: From a total of 59 312 person years, 276 deaths were observed. Compared with drinkers who drank occasionally or most occasional over their lifetime, consistent regular or mostly consistent-regular drinkers had higher rates of all-cause mortality (HR: 1.53; 95% CI 1.09 to 2.16) and cancer mortality (HR: 2.05; 95% CI 1.13 to 3.74). The study did not find a significant association between trajectory of alcohol consumption and deaths due to CVDs. CONCLUSIONS: Regular drinking of alcohol increased risk for all-cause and cancer mortality. Effective interventions should be implemented to reduce number of regular drinkers in order to saves life of individuals.

Kaplan, K., et al. (2022). "The effect of D3 dissection on postoperative morbidity and early mortality in gastric cancer patients who underwent curative total gastrectomy." Ann Ital Chir **11**.

AIM: The present study presents the factors associated with early complications and mortality in patients undergoing total gastrectomy. MATERIAL AND METHOD: The study included patients who underwent curative total gastrectomy for gastric adenocarcinoma between January 2001 and December 2016 in the General Surgery Department of the Cukurova University Medical Faculty Hospital. The patients were divided into D1, D2, and D3 groups depending on the lymph node dissection width, and the demographic and clinical data and mortality were compared. In addition, mortality-associated factors were analyzed. RESULTS: The study sample included 148 (62.7%) males and 88 (37.3%) females, with a mean age of 65.5+/-11.4 years. There were 87 patients in the D1 group, 117 in the D2 group, and 23 in the D3 group. As expected, the duration of the operation was longer in the D2 and D3 groups (179 vs. 224 vs. 252; $p<0.001$), and these groups had also higher numbers of lymph nodes dissected (8 vs. 20 vs. 32; $p<0.001$) and metastatic lymph nodes (2.6 vs. 7.5 vs. 9.2; $p<0.001$). The analysis of the operation type in terms of complications revealed a significant relationship only with stump blowout, which was significantly more common after D3 dissection than following D2 and D1 dissections (p:0.01). The male gender (87.5 vs 60.9 p:0.03) was more associated with mortality. CONCLUSION: D1, D2 and D3 Lymph node dissection in gastric cancer surgery can be safely performed with low mortality and morbidity rates by surgeons with sufficient technical knowledge, and in centers with sufficient hospital volume. KEY WORDS: Complications, Gastric Cancer, Mortality, Lymph Node Dissection.

Kappen, S., et al. (2021). "Differences in Prostate Cancer Incidence and Mortality in Lower Saxony (Germany) and Groningen Province (Netherlands): Potential Impact of Prostate-Specific Antigen Testing." Front Oncol **11**: 681006.

BACKGROUND: Prostate cancer (PCa) is the most frequent cancer among men in Europe. Differences in PCa incidence around the world can be partly explained by variations in recommendations for prostate-specific antigen (PSA), particularly for early detection. For example, the PSA testing policy is more conservative in the Netherlands than in Germany. To better understand the relationship between PSA testing recommendations and PCa incidence, stage distribution, and mortality, we compared these variables over time between Lower Saxony in northwestern Germany and the neighboring province of

Groningen in the Netherlands. METHODS: Population data, tumor stage- and age group-specific PCa incidence (ICD-10 C61) and mortality rates for Lower Saxony and Groningen were obtained from the Lower Saxony Epidemiological Cancer Registry, the Netherlands Comprehensive Cancer Organization, and Statistics Netherlands for 2003-2012. Incidence and mortality rates per 100,000 person-years were age-standardized (ASR, old European standard). Trends in age-standardized incidence rates (ASIR) and mortality rates (ASMR) for specific age groups were assessed using joinpoint regression. RESULTS: The mean annual PCa ASIR between 2003 and 2012 was on average 19.9% higher in Lower Saxony than in Groningen (120.5 vs. 100.5 per 100,000), while the mean annual ASMR was on average 24.3% lower in Lower Saxony than in Groningen (21.5 vs. 28.4 per 100,000). Between 2003 and 2012, the average annual percentage change (AAPC) in PCa incidence rates did not change significantly in either Lower Saxony (-1.8%, 95% CI -3.5, 0.0) or Groningen (0.2%, 95% CI -5.0, 5.7). In contrast, the AAPC in mortality rate decreased significantly during the same time period in Lower Saxony (-2.5%, 95% CI -3.0, -2.0) but not in Groningen (0.1%, 95% CI -2.4, 2.6). CONCLUSIONS: Higher PCa incidence and lower PCa-related mortality was detected in Lower Saxony than in Groningen. Although recommendations on PSA testing may play a role, the assessed data could not offer obvious explanations to the observed differences. Therefore, further investigations including data on the actual use of PSA testing, other influences (e.g., dietary and ethnic factors), and better data quality are needed to explain differences between the regions.

Karahan, I. and S. Yalcin (2020). "Is C-Reactive Protein/Albumin Ratio of Advanced-Stage Non-small Cell Lung Cancer Patients Able to Predict Mortality in the Admission for Palliative Care?" Indian J Palliat Care **26**(3): 365-368.

CONTEXT: Lung cancer is frequent and mortal cancer. The predicting mortality may be helpful for cancer management. AIM: The purpose of the study was to evaluate the role of baseline C-reactive protein (CRP)/albumin ratio (CAR) in relation to hospital mortality, the setting of advanced stage non-small cell lung cancer (NSCLC). MATERIALS AND METHODS: The present study is a retrospective analysis and included 77 adult patients with Stage IV NSCLC who were hospitalized for supportive care. All patients are divided into two groups as survivors and nonsurvivors. CAR on the admission was compared between groups. The correlation between CAR and the death time was investigated. The cutoff level of CAR was calculated, and patients with a high level were described in two groups. RESULTS: For all participants, the mean age was 63.0 +/- 9.9 years, and the median values of CRP and albumin levels were 15.3 mg/dl (1-51.5) and 5.7 g/dl (0.02-22.7), respectively. CAR was significantly lower in the survivor group. By receiver operation curve analysis, the cutoff levels of CRP and CAR were determined as 10.8 and 3.5, respectively. The odds ratio of mortality was 3.85 (1.49-9.94 95% confidence interval [CI], P = 0.006) for higher than cutoff levels of CAR. The odds ratio was 3.38 (1.32-8.65 95% CI, P = 0.01) for higher CRP levels. There was a significant but weak negative correlation between the time of death and both CRP and CAR in the nonsurvivor group (r = -0.46, P = 0.002; r = -0.48, P = 0.001, respectively). CONCLUSION: The present study showed that CAR was significantly increased in nonsurvivors. CAR may be a cheap, easy, and effective tool for predicting the death and its time of hospitalized NSCLC patients.

Karia, P. S., et al. (2022). "Racial and ethnic differences in type II endometrial cancer mortality outcomes: The contribution of sociodemographic, clinicopathologic, and treatment factors." Gynecol Oncol **168**: 119-126.

OBJECTIVE: The burden of type II endometrial cancer (EC) is rising dramatically in the U.S. Although type II EC disproportionately affects Black women, the magnitude of racial/ethnic differences in type II EC mortality outcomes and factors underlying these differences remain understudied. We examined racial/ethnic differences in cancer-specific and overall mortality in women with type II EC and quantified the extent to which mortality differences are mediated by sociodemographic, clinicopathologic, and treatment factors. METHODS: 14,710 women >/=18 years with type II EC from 2007 to 2016 were identified from the Surveillance, Epidemiology, and End Results database. The association between race/ethnicity (non-Hispanic White [NHW], non-Hispanic Black [NHB], Hispanic, and non-Hispanic Asian/Pacific Islander [NHAPI]) and cancer-specific and overall mortality was examined. Mediation analysis was used to identify factors underlying differences in mortality outcomes. RESULTS: NHB women had a higher risk of cancer-specific mortality than NHW women (hazard ratio [HR]: 1.22, 95% CI: 1.12-1.33), whereas NHAPI (HR: 0.88, 95% CI: 0.78-0.99) and Hispanic women (HR: 0.91, 95% CI: 0.81-1.01) had a lower risk of cancer-specific mortality than NHW women. Differences in clinicopathologic (stage, grade, histologic subtype), sociodemographic (insurance type, geographic region and location, neighborhood socioeconomic status), and treatment factors (treatment type, lymphadenectomy) explained 43.5%, 8.1%, and 7.3% of the difference in cancer-specific mortality between NHB and NHW

women, respectively. Similar results were noted for overall mortality. CONCLUSIONS: Multidisciplinary and multilevel approaches that integrate and address social and biological factors are needed to reduce the disproportionate burden of type II EC mortality in NHB women.

Karia, P. S., et al. (2022). "Cancer-Specific Mortality in Asian American Women Diagnosed with Gynecologic Cancer: A Nationwide Population-Based Analysis." Cancer Epidemiol Biomarkers Prev **31**(3): 578-587.

BACKGROUND: Cancer is the leading cause of death in Asian Americans (AA), the fastest-growing U.S. population group. Despite heterogeneity in socioeconomic status and health behaviors by ethnicity, few studies have assessed cancer outcomes across AA ethnic groups. We examined differences in gynecologic cancer mortality between AA ethnic groups and non-Hispanic Whites (NHW). METHODS: Using the Surveillance, Epidemiology, and End Results database, we identified ovarian (n = 69,113), uterine (n = 157,340), and cervical cancer cases (n = 41,460) diagnosed from 1991-2016. Competing risk regression was used to compare cancer-specific mortality for AAs by ethnicity, using NHW as the reference population. RESULTS: In adjusted analyses, AAs had a lower risk of ovarian [HR, 0.90; 95% confidence interval (CI), 0.86-0.94] and cervical cancer death (HR, 0.80; 95% CI, 0.75-0.87) than NHWs, with stronger associations among those >/=50 years at diagnosis [(HRovary, 0.87; 95% CI, 0.82-0.92); (HRcervix, 0.74; 95% CI, 0.67-0.81)]. No overall difference was noted for uterine cancer death (HR, 1.03; 95% CI, 0.97-1.10); however, AAs <50 years at diagnosis had a higher risk of uterine cancer death than NHWs (HR, 1.26; 95% CI, 1.08-1.46). Patterns of cancer mortality were heterogeneous, with Filipino and Chinese women at the highest risk of uterine cancer death and Indian/Pakistani women at the lowest risk of ovarian and cervical cancer death. CONCLUSIONS: There are significant differences in gynecologic cancer mortality between AAs and NHWs, with heterogeneity by AA ethnicity. IMPACT: Disaggregated analysis of AA is needed to better understand the burden of gynecologic cancer and identify high-risk groups for cancer prevention efforts.

Karlin, N. J., et al. (2020). "Assessing the relationship between institutional cancer and diabetes mortality rates using National Death Index data." Future Sci OA **6**(10): FSO633.

AIM: To evaluate overall survival (OS), glycemic control in cancer patients with and without diabetes mellitus (DM). PATIENTS & METHODS: Patients (2010-2015) with newly diagnosed prostate, breast, lung, colorectal and pancreatic cancers were identified in institutional cancer registry. Data linked to National Death Index for vital status. 5-year OS estimated; glucose and hemoglobin A(1c) assessed during year postdiagnosis. RESULTS: We identified 1404 patients (non-DM, n = 936; DM, n = 468). DM cohort had 168 deaths (36%); non-DM, 267 (29%). 5-year OS estimated at 58% (95% CI: 53-64%) for DM and 67% (95% CI: 64-71%) for controls; for matched pairs, hazard ratio: 1.35 (95% CI: 1.02-1.79). Cancer did not harm glycemic control. CONCLUSION: OS among cancer patients with DM was lower than without DM.

Karlsson, A., et al. (2021). "Impact of deep learning-determined smoking status on mortality of cancer patients: never too late to quit." ESMO Open **6**(3): 100175.

BACKGROUND: Persistent smoking after cancer diagnosis is associated with increased overall mortality (OM) and cancer mortality (CM). According to the 2020 Surgeon General's report, smoking cessation may reduce CM but supporting evidence is not wide. Use of deep learning-based modeling that enables universal natural language processing of medical narratives to acquire population-based real-life smoking data may help overcome the challenge. We assessed the effect of smoking status and within-1-year smoking cessation on CM by an in-house adapted freely available language processing algorithm. MATERIALS AND METHODS: This cross-sectional real-world study included 29 823 patients diagnosed with cancer in 2009-2018 in Southwest Finland. The medical narrative, International Classification of Diseases-10th edition codes, histology, cancer treatment records, and death certificates were combined. Over 162 000 sentences describing tobacco smoking behavior were analyzed with ULMFiT and BERT algorithms. RESULTS: The language model classified the smoking status of 23 031 patients. Recent quitters had reduced CM [hazard ratio (HR) 0.80 (0.74-0.87)] and OM [HR 0.78 (0.72-0.84)] compared to persistent smokers. Compared to never smokers, persistent smokers had increased CM in head and neck, gastro-esophageal, pancreatic, lung, prostate, and breast cancer and Hodgkin's lymphoma, irrespective of age, comorbidities, performance status, or presence of metastatic disease. Increased CM was also observed in smokers with colorectal cancer, men with melanoma or bladder cancer, and lymphoid and myeloid leukemia, but no longer independently of the abovementioned covariates. Specificity and sensitivity were 96%/96%, 98%/68%, and 88%/99% for never, former, and current smokers, respectively, being essentially the same with both models. CONCLUSIONS: Deep learning can be used to classify large amounts of smoking data from the medical narrative with good accuracy. The results

highlight the detrimental effects of persistent smoking in oncologic patients and emphasize that smoking cessation should always be an essential element of patient counseling.

Karttunen, E., et al. (2022). "Incidence, mortality and relative survival of patients with cancer of the bladder and upper urothelial tract in the Nordic countries between 1990 and 2019." Scand J Urol: 1-7.

PURPOSE: To understand the potential impact of new treatment options for urinary tract cancer, recent population trends in incidence, mortality and survival should be elucidated. This study estimated changes in the incidence, mortality and relative survival of urinary tract cancer in the Nordic countries (Denmark, Finland, Iceland, Norway and Sweden) between 1990 and 2019. METHODS: Annual counts of incident cases and deaths due to urinary tract cancer (International Classification of Diseases, Tenth Revision, Clinical Modification codes C65-C68, D09.0-D09.1, D30.1-D30.9 and D41.1-D41.9) in Nordic countries were retrieved in 5-year age categories by sex during the study period. Country-specific time trends (annual rate ratios [RRs]) were estimated using Poisson regression, and RRs were compared between sexes. RESULTS: The incidence rate of bladder and upper urothelial tract cancer was >3-times lower in women than men in all countries across all age groups (incidence RR for women to men ranging from 0.219 [95% CI = 0.213-0.224] in Finland to 0.291 [95% CI = 0.286-0.296] in Denmark). Incidence rates were lowest in Finland and highest in Norway and Denmark. Age-adjusted mortality decreased in Finland, Denmark and Norway and in Swedish men, with the greatest decrease seen in Danish men (annual RR = 0.976; 95% CI = 0.975-0.978). In all countries and age groups, women had a lower relative survival rate than men. CONCLUSION: Between 1990 and 2019, the incidence of urinary tract cancer was stable in the Nordic countries, while mortality rates declined and relative survival increased. This could be due to earlier diagnosis and better treatment.

Katanoda, K., et al. (2021). "Updated Trends in Cancer in Japan: Incidence in 1985-2015 and Mortality in 1958-2018-A Sign of Decrease in Cancer Incidence." J Epidemiol **31**(7): 426-450.

BACKGROUND: Unlike many North American and European countries, Japan has observed a continuous increase in cancer incidence over the last few decades. We examined the most recent trends in population-based cancer incidence and mortality in Japan. METHODS: National cancer mortality data between 1958 and 2018 were obtained from published vital statistics. Cancer incidence data between 1985 and 2015 were obtained from high-quality population-based cancer registries maintained by three prefectures (Yamagata, Fukui, and Nagasaki). Trends in age-standardized rates (ASR) were examined using Joinpoint regression analysis. RESULTS: For males, all-cancer incidence increased between 1985 and 1996 (annual percent change [APC] +1.1%; 95% confidence interval [CI], 0.7-1.5%), increased again in 2000-2010 (+1.3%; 95% CI, 0.9-1.8%), and then decreased until 2015 (-1.4%; 95% CI, -2.5 to -0.3%). For females, all-cancer incidence increased until 2010 (+0.8%; 95% CI, 0.6-0.9% in 1985-2004 and +2.4%; 95% CI, 1.3-3.4% in 2004-2010), and stabilized thereafter until 2015. The post-2000 increase was mainly attributable to prostate in males and breast in females, which slowed or levelled during the first decade of the 2000s. After a sustained increase, all-cancer mortality for males decreased in 1996-2013 (-1.6%; 95% CI, -1.6 to -1.5%) and accelerated thereafter until 2018 (-2.5%; 95% CI, -2.9 to -2.0%). All-cancer mortality for females decreased intermittently throughout the observation period, with the most recent APC of -1.0% (95% CI, -1.1 to -0.9%) in 2003-2018. The recent decreases in mortality in both sexes, and in incidence in males, were mainly attributable to stomach, liver, and male lung cancers. CONCLUSION: The ASR of all-cancer incidence began decreasing significantly in males and levelled off in females in 2010.

Katanoda, K., et al. (2021). "International comparison of trends in cancer mortality: Japan has fallen behind in screening-related cancers." Jpn J Clin Oncol **51**(11): 1680-1686.

While the age-standardized mortality rate in Japan is decreasing for all cancers as a whole, this is not the case for some major site-specific cancers. We descriptively compared trends in all-cancer and site-specific cancer mortality in Japan and selected countries. Data on age-standardized cancer mortality rates in six countries (Japan, the USA, the UK, Canada, Australia and the Republic of Korea) in 1980-2016 were obtained from the World Health Organization mortality database. While stomach and liver cancer mortality rates in Japan and Korea were initially much higher than those in non-Asian countries, they have rapidly decreased over the long term. By contrast, colorectal, pancreatic and cervical cancer mortality rates in Japan, which were initially lower than those in other countries, have increased such that they are now similar or higher than the rates in non-Asian countries. For male lung cancer, Japan's initially lower mortality rate is now comparable to that in non-Asian countries as a result of slower decline. Meanwhile, the mortality rate of female breast cancer in Japan and Korea has increased and is nearing the rates observed in non-Asian countries, which by contrast have shown a steady decrease. Thus, while Japan has been successful

in reducing the burden of stomach and liver cancers, it is falling behind in reducing the mortality rate of screening-related cancers such as colorectal, female breast and cervical cancers. Control measures for these cancers need to be strengthened.

Katsura, N., et al. (2021). "Extracellular water to total body water ratio may mediate the association between phase angle and mortality in patients with cancer cachexia: A single-center, retrospective study." Clin Nutr ESPEN **46**: 193-199.

BACKGROUND & AIMS: Recently, prognostic factors for cancer cachexia patients have been reported. We hypothesized that phase angle (PhA), which is measured by bioelectrical impedance analysis (BIA), might be a promising marker for assessing the nutritional status and prognosis of cancer patients. This study aimed to evaluate the predictive utility of PhA, which is mediated by several BIA factors and other anthropometric parameters, such as calf circumference, for the prognosis of cancer cachexia patients. METHODS: Consecutive patients (114, both outpatients and inpatients) with an unselected stage of cancer cachexia were recruited between July 2018 and December 2019 in Fujita Health University Hospital for this retrospective cohort study. Their mean age was 74.0 years (standard deviation, 8.5); among the total, 70 were men and 44 women. A time-dependent Cox proportional-hazards regression analysis (adjusted for age and sex) was performed to assess the following: 1) the association between potential mediators and mortality; 2) the association between five PhAs and statistically significant mediators from 1); and 3) the association between the five PhAs and mortality. Finally, Kaplan-Meier survival curves were constructed and compared between the two groups based on the patients' median baseline ratio of extracellular water (ECW) to total body water (TBW) using a log-rank test. RESULTS: The ECW/TBW ratio (hazard ratio [HR] per 1-interquartile range [IQR] increase: 2.87; 95% confidence interval [CI]: 1.46, 5.46; $p < 0.001$) and skeletal muscle mass index (HR per 1-IQR increase: 0.67; 95% CI: 0.51, 0.89; $p = 0.001$) were associated with mortality. All five PhAs were associated with the ECW/TBW ratio ($p < 0.001$). Before adjustment for the ECW/TBW ratio, all five PhAs were associated with mortality ($p < 0.001$); only the association of the PhAs of the left arm and the trunk retained the statistical significance after adjusting for confounders ($p < 0.05$). The median survival times in the low (370 days; 95% CI: 168, not calculated) and high ECW/TBW groups (101 days; 95% CI: 61, 219) differed significantly ($p < 0.001$). CONCLUSIONS: The association between PhA and mortality in cancer cachexia patients was largely mediated by the ECW/TBW ratio. We believe that adjusting PhA for the ECW/TBW ratio may improve the prognostication of cancer patients with cachexia, ultimately improving their palliative care.

Katzmarzyk, P. T., et al. (2022). "Association of Abdominal Visceral Adiposity and Total Fat Mass with Cancer Incidence and Mortality in White and Black Adults." Cancer Epidemiol Biomarkers Prev **31**(8): 1532-1538.

BACKGROUND: Race modifies the association between anthropometric measures of obesity and cancer risk. However, the degree to which abdominal visceral adipose tissue (VAT) and total fat mass (FM) are associated with cancer risk is not known. METHODS: The sample included 3,017 White and 1,347 Black adults who were assessed between 1995 and 2016 and followed for outcome assessment through 2017. Abdominal VAT and FM were measured using imaging techniques. The co-primary endpoints were diagnosis of histologically confirmed invasive cancer (excluding nonmelanoma skin cancer) or death from cancer. Multivariable Cox proportional hazards models quantified the HR of incident cancer and cancer mortality. RESULTS: There were 353 incident cancer cases and 75 cancer deaths in an average of 12.9 years of follow-up. Both VAT [HR, 1.21; 95% confidence interval (CI), 1.09-1.36] and FM (HR, 1.25; 95% CI, 1.10-1.43) were significantly associated with incident cancer, while VAT (HR, 1.28; 95% CI, 1.01-1.61) was significantly associated with cancer mortality after adjustment for several covariates. VAT remained significantly associated with cancer incidence (HR, 1.22; 95% CI, 1.03-1.46) after additional inclusion of FM in the multivariable model, but not vice versa. There were no significant sex- or race-interactions. CONCLUSIONS: VAT was associated with risk of cancer and cancer mortality in this cohort, and the associations did not differ by sex or race. The association between VAT and incident cancer was largely independent of total FM. IMPACT: Our results suggest that utility of anthropometry in assessing obesity-related cancer risk may need to be further refined by including more direct measures of adiposity.

Kaur, H., et al. (2021). "Impact of Underlying Comorbidities on Mortality in SARS-COV-2 Infected Cancer Patients: A Systematic Review and Meta-Analysis." Asian Pac J Cancer Prev **22**(5): 1333-1349.

BACKGROUND: The evidence has shown that SARS CoV-2 infected patients with comorbidities are more likely to have severe disease sequel and mortality. In SARS-CoV-2 infected cancer patients risks associated with other underlying comorbidities might vary from those in non-cancer SARS CoV-2 infected patients. The relative impact of different underlying health conditions among patients with

cancer and SARS CoV-2 infection remains yet to be explored. This systematic review aims to explore the prevalence of comorbidities among cancer patients with SARS CoV-2 infection and their impact on mortality. METHODS: Online databases PubMed, Embase, Scopus and Web of science were searched for articles published between 9th July 2019 to July 8th 2020.Studies of cancer patients (>18 years) with diagnosis of SARS CoV-2 infection, published in English were included. A random-effects modelling for the meta-analyses was applied to assess the pooled prevalence and odds ratio for mortality due to comorbidities in SARS CoV-2 infected cancer patients. RESULTS: Total 31studies with 4086 SARS-CoV-2 infectedcancer patientsmet the inclusion criteria. Most prevalent co-morbidities in cancer patients with SARS CoV-2 infection were hypertension [42.3% (95%CI:37.5- 47.0)], diabetes [17.8% (95% CI: 15.3-20.4)] and cardiovascular diseases [16.7% (95%CI:12.9-20.4)].The risk of mortality (pOR) was significantly higher in individuals with hypertension[1.6(95%CI 1.24-2.00)], cardiovascular diseases [2.2 (95%CI 1.49- 3.27)], chronic obstructive pulmonary diseases [1.4(95% CI 1.05-2.00)] and diabetes [1.35(95%CI 1.06-1.73)]. CONCLUSION: Our results indicates that the mortality in SARS-CoV-2 infected cancer patients is affected by preexisting non-cancer comorbidities. By identifying the comorbidities predictive for mortality, clinicians can better stratify the risk of cancer patients presenting with SARS-COV-2, on their initial contact with health services.
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Kavaliauskas, P., et al. (2022). "Trends in Pancreatic Cancer Incidence and Mortality in Lithuania, 1998-2015." Int J Environ Res Public Health **19**(2).

BACKGROUND: Pancreatic cancer is one of the deadliest cancers worldwide, and its incidence is increasing. The aim of this study was to examine the time trends in the incidence and mortality rates of pancreatic cancer for the period of 1998-2015 for the first time in Lithuania by sex, age, subsite, and stage. METHODS: This study was based on all cases (deaths) of pancreatic cancer diagnosed between 1998 and 2015. Age-standardized incidence (mortality) rates and group-specific rates were calculated for each sex using the direct method (European Standard). TNM classification-based information reported to the cancer registry was grouped into three categories: (1) localized cancer: T1-3/N0/M0; (2) cancer with regional metastasis: any 1-3/N+/M0; (3) advanced cancer: any T/any N/M+. Joinpoint regression was used to provide annual percentage changes (APCs) and to detect points in time where statistically significant changes in the trends occurred. RESULTS: Overall, 8514 pancreatic cancer cases (4364 in men and 3150 in women) were diagnosed and 7684 persons died from cancer of the pancreas. Pancreatic cancer incidence rates were considerably lower for women than for men, with a female:male ratio of 1:2. Incidence rates changed during the study period from 14.2 in 1998 to 15.0/100,000 in the year 2015 in men, and from 6.7 to 9.8/100,000 in women. Incidence rates over the study period were stable for men (APC = 0.1%) and increasing for women by 1.1% per year. Similarly, mortality rates increased in women by 0.9% per year, and were stable in men. During the study period, incidence and mortality rates of pancreatic cancer were close. For the entire study period, rates increased significantly in the 50-74 years age group; only cancer of the head of pancreas showed a decline by 0.9%, while tail and not-specified pancreatic cancer incidence increased by 11.4% and 4.51%, respectively. CONCLUSIONS: The increasing pancreatic cancer incidence trend in the Lithuanian population may be related to the prevalence of its main risk factors (smoking, obesity, physical inactivity, diet, and diabetes).

Kawa, S. M., et al. (2020). "What is the risk of prostate cancer mortality following negative systematic TRUS-guided biopsies? A systematic review." BMJ Open **10**(12): e040965.

OBJECTIVE: To investigate the risk of prostate cancer-specific mortality (PCSM) following initial negative systematic transrectal ultrasound-guided (TRUS) prostate biopsies. DESIGN: Systematic review. DATA SOURCES: PubMed and Embase were searched using a string combination with keywords/Medical Subject Headings terms and free text in the search builder. Date of search was 13 April 2020. STUDY SELECTION: Studies addressing PCSM following initial negative TRUS biopsies. Randomised controlled trials and population-based studies including men with initial negative TRUS biopsies reported in English from 1990 until present were included. DATA EXTRACTION: Data extraction was done using a predefined form by two authors independently and compared with confirm data; risk of bias was assessed using the Newcastle-Ottawa Scale for cohort studies when applicable. RESULTS: Four eligible studies were identified. Outcomes were reported differently in the studies as both cumulative incidence and Kaplan-Meier estimates have been used. Regardless of the study differences, all studies reported low estimated incidence of PCSM of 1.8%-5.2% in men with negative TRUS biopsies during the following 10-20 years. Main limitation in all studies was limited follow-up. CONCLUSION: Only a few studies have investigated the risk of PCSM following initial negative biopsies and all studies included patients before the era of MRI of the prostate. However, the studies point to the fact that the risk of PCSM is low

following initial negative TRUS biopsies, and that the level of prostate-specific antigen before biopsies holds prognostic information. This may be considered when advising patients about the need for further diagnostic evaluation. PROSPERO REGISTRATION NUMBER: CRD42019134548.

Kawa, S. M., et al. (2022). "A Nationwide Analysis of Risk of Prostate Cancer Diagnosis and Mortality following an Initial Negative Transrectal Ultrasound Biopsy with Long-Term Followup." J Urol **208**(1): 100-108.

PURPOSE: Magnetic resonance imaging (MRI) targeted prostate biopsy has been shown to find many high-grade prostate cancers in men with concurrent negative transrectal ultrasound (TRUS) systematic biopsy. The oncologic risk of such tumors can be explored by looking at long-term outcomes of men with negative TRUS biopsy followed without MRI. The aim was to analyze the mortality after initial and second negative TRUS biopsy. MATERIALS AND METHODS: All men who underwent initial TRUS biopsies between January 1, 1995 and December 31, 2016 in Denmark were included. A total of 37,214 men had a negative initial TRUS biopsy and 6,389 underwent a re-biopsy. Risk of cause-specific mortality was analyzed with competing risks. Diagnosis of Gleason score >/=7 prostate cancer following negative biopsies was analyzed with multivariable logistic regression including time to re-biopsy, prostate specific antigen (PSA), age and digital rectal examination. RESULTS: The 15-year prostate cancer-specific mortality was 1.9% (95% CI: 1.7-2.1). Prostate cancer-specific mortality was 1.3% (95% CI: 0.9-1.6) and 4.6% (95% CI: 3.4-5.8) for men with PSA <10 and >20 ng/ml, respectively. Of the TRUS re-biopsies 12% were Gleason score >/=7 and risk of Gleason score >/=7 increased with longer time to re-biopsy (p <0.001). Mortality after re-biopsy was similar to after initial biopsy. CONCLUSIONS: Men with negative TRUS biopsies have a very low prostate cancer-specific mortality, especially with PSA <10 ng/ml. This raises serious questions about the routine use of MRI targeting for initial prostate biopsy and suggests that MRI targeting should only be recommended for men with PSA >10 ng/ml after negative biopsy.

Kawamura, H., et al. (2021). "Impact of Primary Tumor Resection on Mortality in Patients with Stage IV Colorectal Cancer with Unresectable Metastases: A Multicenter Retrospective Cohort Study." World J Surg **45**(10): 3230-3239.

BACKGROUND: Primary tumor resection (PTR) before commencing systemic chemotherapy in patients with stage IV colorectal cancer and unresectable metastases (mCRC) remains controversial. This study aimed to assess whether PTR before systemic chemotherapy is associated with mortality in mCRC patients, after adjusting for confounding factors, such as the severity of the primary tumor and metastatic lesions. METHODS: We analyzed hospital-based cancer registries from nine designated cancer hospitals in Fukushima Prefecture, Japan. Patients were divided into two groups (PTR and non-PTR), based on whether PTR was performed as initial therapy for mCRC or not. The primary outcome was all-cause mortality. Kaplan-Meier survival analysis was performed, and survival estimates were compared using the log-rank test. Adjusted hazard ratios were calculated using Cox regression to adjust for confounding factors. All tests were two-sided; P-values < 0.05 were considered statistically significant. RESULTS: Between 2008 and 2015, 616 mCRC patients were included (PTR: 414 [67.2%]; non-PTR: 202 [32.8%]). The median follow-up time was 18.0 (interquartile range [IQR]: 8.4-29.7) months, and 492 patients (79.9%) died during the study period. Median overall survival in the PTR and non-PTR groups was 23.9 (IQR: 12.2-39.9) and 12.3 (IQR: 6.2-23.8) months, respectively (P < 0.001, log-rank test). PTR was significantly associated with improved overall survival (adjusted hazard ratio: 0.51; 95% confidence interval: 0.42-0.64, P < 0.001). CONCLUSIONS: PTR before systemic chemotherapy in patients with mCRC was associated with improved survival.

Kazemi, A., et al. (2021). "The relationship between major food sources of fructose and cardiovascular disease, cancer, and all-cause mortality: a systematic review and dose-response meta-analysis of cohort studies." Crit Rev Food Sci Nutr: 1-14.

We aimed to summarize the associations between food sources of fructose and cardiovascular diseases (CVD), cancer, and all-cause mortality risk using a systematic review and meta-analysis. We searched PubMed, Scopus, and Web of Science up to November 2020. We included cohort studies that investigated the relationship between mortality risk (all-cause, CVD, specific CVD, and total and site-specific cancers) and intake of >/=1 food source of fructose (fruit, fruit juice, breakfast cereals, sugar-sweetened beverages (SSBs), sweets, and yogurt) in general adult population. Summary hazard ratios and 95% CIs were estimated using a random-effects model for linear and nonlinear relationships. Findings indicated that each 100 g/d increase in fruit intake was associated with 8-13% lower risk of CVDs, stroke, gastrointestinal, and lung cancer mortality. For all-cause mortality, there was a beneficial relationship up to 200 g/d fruit, and then plateaued. For ischemic heart disease and cancer mortality, there was a beneficial relationship up to 300 g/d followed by a slight increase.

Ingestion of breakfast cereals and sweets was also associated with lower risk of all-cause mortality. For yogurt, a non-linear marginal decrease in all-cause mortality was found. Ingestion of each 200 g/d yogurt was associated with a 14% lower risk of CVD mortality. Every 60 g/d increase in sweet intake was linked to a 5% lower risk of all-cause mortality. Contrariwise, every 250 g/d increase in SSBs intake was associated with 7-10% higher risk of all-cause and CVD mortality. In conclusion, beneficial associations were found between fruit, breakfast cereals, sweets, and yogurt with all-cause and/or CVD mortality risk. Fruit intake had also an inverse link with cancer mortality. Conversely, SSBs had a harmful relationship with all-cause and CVD mortality.Registry number: CRD42019144956.

Kehm, R. D., et al. (2022). "Mortality after the 9/11 terrorist attacks among world trade center health registry enrollees with cancer." Cancer Med.

BACKGROUND: While several studies have reported the association between 9/11 exposure and cancer risk, cancer survival has not been well studied in the World Trade Center (WTC) exposed population. We examined associations of 9/11-related exposures with mortality in WTC Health Registry enrollees diagnosed with cancer before and after 9/11/2001. PATIENTS AND METHODS: This is a longitudinal cohort study of 5061 enrollees with a first-ever primary invasive cancer diagnosis between 1995 and 2015 and followed through 2016. Based on the timing of first cancer diagnosis, pre-9/11 (n = 634) and post-9/11 (n = 4427) cancer groups were examined separately. 9/11-related exposures included witnessing traumatic events, injury on 9/11, and 9/11-related post-traumatic stress disorder (PTSD). Associations of exposures with all-cause mortality were examined using Cox proportional hazards regression. In the post-9/11 group, cancer-specific mortality was evaluated by enrollee group (WTC rescue/recovery workers vs. non-workers) using Fine and Gray's proportional sub-distribution hazard models, adjusting for baseline covariates, tumor characteristics, and treatment. RESULTS: In the pre-9/11 group, 9/11-related exposures were not associated with all-cause mortality. In the post-9/11 group, increased risk of all-cause mortality was associated with PTSD (adjusted HR = 1.35; 95% CI = 1.11-1.65), but not with injury or witnessing traumatic events. Cancer-specific mortality was not statistically significantly associated with 9/11-related exposures. In rescue/recovery workers, increased non-cancer mortality risk was associated with PTSD (aHR = 2.13, 95% CI = 1.13-4.00) and witnessing >/=3 traumatic events (aHR = 2.00, 95% CI = 1.13-3.55). CONCLUSIONS: We did not observe associations between 9/11-related exposures and cancer-specific mortality. Similar to findings in the non-cancer WTC exposed population, PTSD was associated with increased risk of all-cause mortality in cancer patients.

Kelly-Reif, K., et al. (2020). "Radon and cancer mortality among underground uranium miners in the Pribram region of the Czech Republic." Am J Ind Med **63**(10): 859-867.

BACKGROUND: This study aims to estimate the association between radon and site-specific cancer mortality among a large contemporary cohort of male uranium miners. METHODS: Annual occupational radon exposure was estimated based on a worker's duration of underground mining in a year and estimates of potential alpha energy of radon progeny in their location of work. Cancer mortality over the period 1977-1992 was ascertained for a cohort of 16 434 male underground uranium miners employed in the Czech Republic between 1946 and 1992. Poisson regression was used to estimate relationships between cumulative radiation exposure (in working level months [WLM]) and site-specific cancer mortality. RESULTS: Radon is positively associated with lung cancer mortality (excess relative rate [ERR] per 100 WLM = 0.2; 95% confidence interval [CI]: 0.10, 0.37). The best fit of the dose-response relationship between radon and lung cancer mortality was linear and estimates of radon-lung cancer associations varied by windows of time-since-exposure. Positive associations between radon and several types of cancer other than lung cancer were identified, notably chronic lymphocytic leukemia (CLL) (ERR/100 WLM = 0.24; 95% CI: [not determined [ND], 5.10]) and extrathoracic cancer (ERR/100 WLM = 0.12; 95% CI: [ND, 0.69]). We observed no associations between radon and stomach cancer, nor between radon and several hematopoietic cancer subtypes. CONCLUSIONS: This study confirms the established radon-lung cancer association and suggests that radon may also be associated with other types of cancer mortality. Further investigations of extrathoracic and CLL cancer, with the aim of obtaining more precise estimates, are warranted to understand associations between radon and cancers other than lung.

Kelty, E., et al. (2021). "Cancer diagnosis and mortality in patients with ankylosing spondylitis: A Western Australian retrospective cohort study." Int J Rheum Dis **24**(2): 216-222.

AIM: Ankylosing spondylitis (AS) has been associated with a modest increase in the risk of cancer. However, little is known as to how AS influences risk of mortality following cancer diagnosis. This study compared the risk of cancer and subsequent mortality in patients with AS compared with a non-AS population group. METHODS: Patients diagnosed with

AS in Western Australia (WA) between 1980 and 2014 were identified from the WA Rheumatic Disease Epidemiological Register (N = 2152; 31 099 patient-years). A non-AS comparison group (N = 10 760; 165 609 patient-years) was selected from hospital records, matched 1:5 on age, Aboriginality, and gender. Data on cancer diagnosis, comorbidities and mortality were extracted from state cancer, hospital, and mortality registers. The relative risk of cancer (overall and by type) and mortality following cancer diagnosis between AS and non-AS comparators was compared using Cox proportional hazard models, adjusting for risk factors and comorbidities. RESULTS: Ankylosing spondylitis patients had a 15% increase in the crude risk of cancer (hazard ratio [HR]: 1.15, 95% CI: 1.02-1.30). However, this association was attenuated following adjustment for smoking and common comorbidities (adjusted HR: 1.08, 95% CI: 0.95-1.22). Following a cancer diagnosis, patients with AS had an increased risk of 5-year mortality in the unadjusted (HR: 1.24, 95% CI: 1.03-1.49) and the adjusted models (adjusted HR: 1.37, 95% CI: 1.13-1.66). CONCLUSION: Ankylosing spondylitis was not associated with an increased risk of cancer diagnosis. Following a cancer diagnosis, AS was associated with an increased risk of 5-year mortality.

Kendzerska, T., et al. (2022). "Polysomnographic Markers of Obstructive Sleep Apnea Severity and Cancer-related Mortality: A Large Retrospective Multicenter Clinical Cohort Study." Ann Am Thorac Soc **19**(5): 807-818.

Rationale: The evidence for an association between cancer survival and obstructive sleep apnea (OSA) remains underexplored. Objectives: To evaluate an association between markers of OSA severity (respiratory disturbances, hypoxemia, and sleep fragmentation) and cancer-related mortality in individuals with previously diagnosed cancer. Methods: We conducted a multicenter retrospective cohort study using linked clinical and provincial health administrative data on consecutive adults who underwent a diagnostic sleep study between 1994 and 2017 in four Canadian academic hospitals and were previously diagnosed with cancer through the Ontario Cancer Registry. Multivariable cause-specific Cox regressions were used to address the research objective. Results: We included 2,222 subjects. Over a median follow-up time of 5.6 years (interquartile range [IQR], 2.7-9.1 years), 261/2,222 (11.7%) individuals with prevalent cancer died from cancer-related causes, which accounted for 44.2% (261/590) of all-cause death. Controlling for age, sex, alcohol use disorder, prior heart failure, chronic obstructive pulmonary disease, hypertension, diabetes, treatment for OSA, clinic site, year of the sleep study, and time since the cancer diagnosis, measures of hypoxemia and sleep fragmentation, but not apnea-hypopnea index, were significantly associated with the cancer-specific mortality: percentage of time spent with arterial oxygen saturation (Sa(O(2))) < 90% (hazard ratio [HR] per 5% increase, 1.05; 95% confidence interval, 1.01-1.09); mean Sa(O(2)) (HR per 3% increase, 0.79; 0.68-0.92); and percentage of stage 1 sleep (HR per 16% increase, 1.27; 1.07-1.51). Conclusions: In a large clinical cohort of adults with suspected OSA and previously diagnosed cancer, measures of nocturnal hypoxemia and sleep fragmentation as markers of OSA severity were significantly associated with cancer-related mortality, suggesting the need for more targeted risk awareness.

Ker, Y. F., et al. (2021). "Application of Standardized Proportional Mortality Ratio to the Assessment of Health Risk in Relatively Healthy Populations: Using a Study of Cancer Risk in Telecommunication Workers with Excess Exposure to Acid Mists as an Example." Int J Environ Res Public Health **18**(18).

When a study population is relatively healthy, such as an occupational population, epidemiological studies are likely to underestimate risk. We used a case study on the cancer risk of workers with exposure to acid mists, a well-documented carcinogen, to demonstrate that using proportional mortality ratios (PMRs) is more appropriate than mortality ratios in assessing risk in terms of mortality. The study included 10,229 employees of a telecommunication company who worked in buildings with battery rooms. In these buildings, the battery rooms had the highest levels of sulfuric acid in the air (geometric mean = 10.7 mug/m(3)). With the general population in Taiwan as a reference, a decreased standardized mortality ratio (0.42, $p < 0.01$) from all causes combined, between 1 January 1985 and 31 December 1996, was observed, indicating a healthy worker effect. When we reanalyzed the data using standardized PMR, elevated risks were observed for all cancers combined (1.46, $p = 0.01$) and cancers of the digestive organs and peritoneum (1.61, $p = 0.02$), especially stomach cancer (2.94, $p = 0.01$). The results showed that PMR can detect increases in mortality when a study population is generally healthier than the comparison population and call for further studies on the possible carcinogenic effects of low-level acid mist exposures on the stomach.

Kerr, A. J., et al. (2022). "Adjuvant and neoadjuvant breast cancer treatments: A systematic review of their effects on mortality." Cancer Treat Rev **105**: 102375.

BACKGROUND: Adjuvant and neoadjuvant breast cancer treatments can reduce breast cancer mortality but may increase mortality from other causes.

Information regarding treatment benefits and risks is scattered widely through the literature. To inform clinical practice we collated and reviewed the highest quality evidence. METHODS: Guidelines were searched to identify adjuvant or neoadjuvant treatment options recommended in early invasive breast cancer. For each option, systematic literature searches identified the highest-ranking evidence. For radiotherapy risks, searches for dose-response relationships and modern organ doses were also undertaken. RESULTS: Treatment options recommended in the USA and elsewhere included chemotherapy (anthracycline, taxane, platinum, capecitabine), anti-human epidermal growth factor 2 therapy (trastuzumab, pertuzumab, trastuzumab emtansine, neratinib), endocrine therapy (tamoxifen, aromatase inhibitor, ovarian ablation/suppression) and bisphosphonates. Radiotherapy options were after breast conserving surgery (whole breast, partial breast, tumour bed boost, regional nodes) and after mastectomy (chest wall, regional nodes). Treatment options were supported by randomised evidence, including > 10,000 women for eight treatment comparisons, 1,000-10,000 for fifteen and < 1,000 for one. Most treatment comparisons reduced breast cancer mortality or recurrence by 10-25%, with no increase in non-breast-cancer death. Anthracycline chemotherapy and radiotherapy increased overall non-breast-cancer mortality. Anthracycline risk was from heart disease and leukaemia. Radiation-risks were mainly from heart disease, lung cancer and oesophageal cancer, and increased with increasing heart, lung and oesophagus radiation doses respectively. Taxanes increased leukaemia risk. CONCLUSIONS: These benefits and risks inform treatment decisions for individuals and recommendations for groups of women.

Ketelaers, S. H. J., et al. (2021). "Age-related differences in morbidity and mortality after surgery for primary clinical T4 and locally recurrent rectal cancer." Colorectal Dis **23**(5): 1141-1152.

AIM: Outcomes in elderly patients (>/=75 years) with non-advanced colorectal cancer have improved. It is unclear whether this is also true for elderly patients with clinical T4 rectal cancer (cT4RC) or locally recurrent rectal cancer (LRRC). We aimed to compare age-related differences in morbidity and mortality after curative treatment for cT4RC and LRRC. METHODS: All cT4RC and LRRC patients without distant metastasis who underwent curative surgery between 2005 and 2017 in the Catharina Hospital (Eindhoven, The Netherlands) were included. Morbidity and mortality were evaluated based on age (<75 and >/=75 years) and date of surgery (2005-2011 and 2012-2017). RESULTS: Overall, 72 of 474 (15.2%) cT4RC and 53 of 293 (18.1%) LRRC patients were >/=75 years. No significant differences in the incidence of Clavien-Dindo I-IV complications were observed between age groups. However, in elderly cT4RC patients, cerebrovascular accidents occurred more frequently (4.2% vs. 0.5%, P = 0.03). Between 2005-2011 and 2012-2017, 30-day mortality improved from 7.5% to 3.1% and from 10.0% to 0.0% in elderly cT4RC and LRRC patients, respectively. The 1-year mortality during 2012-2017 was worse in elderly than in younger patients (28.1% vs. 6.2%, P = 0.001 for cT4RC and 27.3% vs. 13.8%, P = 0.06 for LRRC). In elderly cT4RC and LRRC patients, 44.4% and 46.2% died due to non-cancer-related causes, while only 27.8% and 23.1% died due to disease recurrence, respectively. CONCLUSION: Although the 30-day mortality in elderly cT4RC and LRRC patients improved after curative treatment, the 1-year mortality in elderly patients continued to be high, which requires more awareness for the elderly after hospitalization.

Keum, N., et al. (2022). "Vitamin D supplementation and total cancer incidence and mortality by daily vs. infrequent large-bolus dosing strategies: a meta-analysis of randomised controlled trials." Br J Cancer **127**(5): 872-878.

BACKGROUND: Efficacy of vitamin D supplementation may vary by dosing strategies and adiposity. To address such heterogeneity, we performed a meta-analysis of randomised controlled trials of vitamin D supplementation and total cancer outcomes. METHODS: PubMed and Embase were searched through January 2022. Summary relative risk (SRR) and 95% confidence interval (CI) were estimated using the DerSimonian-Laird random-effects model. RESULTS: For total cancer incidence (12 trials), the SRR for vitamin D supplementation vs. control group was 0.99 (95% CI, 0.94-1.03; P = 0.54; I(2) = 0%). No significant association was observed regardless of whether the supplement was given daily or infrequently in a large-bolus. Yet, among trials testing daily supplementation, a significant inverse association was observed among normal-weight individuals (SRR, 0.76; 95% CI, 0.64-0.90; P = 0.001, I(2) = 0%), but not among overweight or obese individuals (P(heterogeneity) = 0.02). For total cancer mortality (six trials), the SRR was 0.92 (95% CI, 0.82-1.03; P = 0.17; I(2) = 33%). A significant inverse association emerged (SRR, 0.87; 95% CI, 0.78-0.96; P = 0.007; I(2) = 0%) among studies testing daily supplementations but not among studies that testing infrequent large-bolus supplementations (P(heterogeneity) = 0.09). CONCLUSIONS: For vitamin D supplementation, daily dosing, but not infrequent large-bolus dosing, reduced total cancer mortality. For total cancer incidence, bolus dosing did

not reduce the risk and the benefits of daily dosing were limited to normal-weight individuals.

Keys, M. T., et al. (2021). "Population-based organized screening by faecal immunochemical testing and colorectal cancer mortality: a natural experiment." Int J Epidemiol **50**(1): 143-155.

BACKGROUND: Population-based organized screening programmes for colorectal cancer (CRC) are underway worldwide, with many based on the faecal immunochemical test (FIT). No clinical trials assessing FIT compared with no screening are planned, and few studies have assessed the population impact of such programmes. METHODS: Before 2010, 11 out of 50 Spanish provinces initiated population-based organized screening programmes with FIT for an average-risk population aged 50-69 years. We used a quasi-experimental design across Spanish provinces between 1999 and 2016 to evaluate their impact on population age-standardized mortality and incidence rates due to CRC. Difference-in-differences and synthetic control analyses were performed to test for validation of statistical assumptions and to assess the dynamics of screening-associated changes in outcomes over time. RESULTS: No differences in outcome trends between exposed (n = 11) and control (n = 36) provinces were observed for up to 7 years preceding the implementation of screening. Relative to controls, exposed provinces experienced a mean increase in age-standardized incidence of 10.08% [95% confidence interval (CI) (5.09, 15.07)] 2 years after implementation, followed by a reduction in age-standardized mortality rates due to CRC of 8.82% [95% CI (3.77, 13.86)] after 7 years. Results were similar for both women and men. No associated changes were observed in adjacent age bands not targeted by screening, nor for 10 other major causes of death in the exposed provinces. CONCLUSIONS: FIT-based organized screening in Spain was associated with reductions in population colorectal cancer mortality. Further research is warranted in order to assess the replicability and external validity of our findings, and on gender-specific use of FIT in organized screening.

Khadhra, H. B., et al. (2021). "Relationship between socioeconomic status and prostate cancer (incidence, aggressiveness, treatment with curative intent, and mortality): a spatial analysis using population-based cancer registry data." Rev Epidemiol Sante Publique **69**(6): 329-336.

BACKGROUND: Morbidity and mortality associated with prostate cancer in a given geographic area might be related to the level of socioeconomic deprivation. The Somme area (a region of northern France) is considered economically disadvantaged, with major territorial disparities. The aim of this study was to assess the impact of the socioeconomic level on prostate cancer, using data from a population-based cancer registry. METHODS: The source of data on cases of prostate cancer between 2006 and 2010 was the Somme cancer registry (Amiens, France). Socioeconomic status was measured according to the European Deprivation Index (EDI), which was used to classify each geographical "IRIS" unit (the smallest sub-municipal geographical entity for which French census data are available) according to its level of social deprivation. For spatial analysis, we considered a hierarchical generalized linear model. RESULTS: In the spatial analysis, prostate cancer incidence was higher in the less disadvantaged areas and treatment frequency with curative intent was lower in the most disadvantaged areas. Cancer aggressiveness and mortality were higher in the most disadvantaged areas: relative risk (RR) = 1.36; 95% CI: [1.09; 1.73] and RR=3.09 [1.70; 5.59], respectively. CONCLUSION: Our results evidenced a significant association between socioeconomic deprivation and prostate cancer, with worse outcomes among men with the lowest socioeconomic status.

Khan, S. U., et al. (2022). "A comparative analysis of premature heart disease- and cancer-related mortality in women in the USA, 1999-2018." Eur Heart J Qual Care Clin Outcomes **8**(3): 315-323.

AIMS: To compare premature heart disease- and cancer-related deaths in women in the USA. METHODS AND RESULTS: We analysed the US national database of death certificates of women aged <65 from the Centers for Disease Control and Prevention Wide-ranging Online Data for Epidemiologic Research database between 1999 and 2018. We measured annual percentage changes (APCs) in age-adjusted mortality rates (AAMRs) and years of potential life lost per 100 000 persons due to heart disease and cancer. Overall, cancer was a more prevalent cause of premature death compared with heart disease. Between 1999 and 2018, the AAMRs decreased for both cancer (61.9/100 000 to 45.6/100 000) and heart disease (29.2/100 000 to 22.6/100 000). However, while APC in AAMR for cancer declined consistently over time, after an initial decline, APC in AAMR for heart disease increased between 2010 and 2018 [0.53 95% confidence interval (0.18-0.89)], with a significant rise in Midwest, medium/small metros, and rural areas after 2008. Compared with cancer, APC in AAMR for heart disease increased in women aged 25-34 years [2.24 (0.30-4.22); 2013-18) and 55-64 years [0.46 (0.13-0.80); 2009-13], as well as Non-Hispanic (NH) Whites [APC, 0.79 (0.46-1.13); 2009-18] and NH American Indian/Alaskan Native [2.71 (0.59-4.87); 2011-2018]. Consequently, the mortality gap between cancer and heart disease has narrowed

from an AAMR of 32.7/100 000 to 23.0/100 000. CONCLUSIONS: The mortality gap between cancer and heart disease is decreasing among women <65 years. Intensive cardiovascular health interventions are required focusing on vulnerable young demographic subgroups and underserved regional areas to meet the American Heart Association's Impact Goal and Million Hearts Initiative.

Kim, H. and E. Giovannucci (2020). "Vitamin D Status and Cancer Incidence, Survival, and Mortality." Adv Exp Med Biol **1268**: 39-52.

Over the last several decades, extensive research on vitamin D and its role on cancer incidence, cancer survival (survival or mortality from cancer among individuals diagnosed with cancer), and cancer mortality (fatal cases occurring during the study period in an initially cancer-free population) has been conducted. A variety of study designs were implemented to explore vitamin D status, assessed by measuring sun exposure, vitamin D intake, and circulating 25-hydroxyvitamin D (25(OH)D) concentration. Although not many randomized controlled trials have examined the relationship between vitamin D and cancer incidence, observational studies have consistently shown a protective association between vitamin D and cancer incidence, especially for colorectal cancer. In addition, randomized controlled trials and most observational studies suggested that vitamin D plays a role in reducing cancer mortality. The potential benefit of vitamin D on cancer mortality may operate during the pre-diagnostic stages by affecting late-stage tumor progression and metastatic seeding, during the treatment phase by complementing or enhancing effects of therapies, or during the post-diagnostic stages. However, further studies are needed to confirm these conclusions, establish the optimal dosage and timing of vitamin D intakes for the most benefit, find which cancer types are affected, and understand the underlying mechanisms.

Kim, J., et al. (2021). "Metformin use in cancer survivors with diabetes reduces all-cause mortality, based on the Korean National Health Insurance Service between 2002 and 2015." Medicine (Baltimore) **100**(11): e25045.

Malignant neoplasms are the leading cause of death in Korea. We aimed to examine if metformin use in cancer survivors reduces all-cause mortality. This study was retrospectively designed based on data from the Korean National Health Insurance Service-National Health Screening Cohort (HEALS) between 2002 and 2015. The Kaplan-Meier estimator and log-rank test was performed to estimate the survival function according to metformin usage (3721 metformin non-users with diabetes, 5580 metformin users with diabetes, and 24,483 non-diabetic individuals). Adjusted hazard ratios (HRs) and 95% confidence intervals (CIs) for all-cause mortality were calculated using Cox proportional hazards regression models.The median follow-up duration was 4.2 years. The HRs (95% CIs) for all-cause mortality of metformin users and the non-diabetic group were 0.762 (0.683-0.850) and 1.055 (0.966-1.152) in men and 0.805 (0.649-0.999), and 1.049 (0.873-1.260) in women, respectively, compared with metformin non-users among diabetic cancer survivors, in a fully adjusted model. After stratifying metformin users into pre- and post-diagnosis of cancers, adjusted HRs (95% CIs) of pre- and post-diagnosis metformin users for all-cause mortality were 0.948 (0.839-1.071) and 0.530 (0.452-0.621) in men and 1.163 (0.921-1.469) and 0.439 (0.323-0.596) in women, respectively.Metformin use in cancer survivors with diabetes reduced overall mortality rates. In particular, metformin use after cancer diagnosis, not before cancer diagnosis, was inversely associated with overall mortality.Active treatment with metformin for diabetic cancer survivors after cancer diagnosis can improve their survival rates.

Koo, H. Y., et al. (2021). "Population-wide impacts of aspirin, statins, and metformin use on prostate cancer incidence and mortality." Sci Rep **11**(1): 16171.

We evaluated the association between aspirin, statins, and metformin use and prostate cancer (PC) incidence and mortality using a large population-based dataset. 388,760 men who participated in national health screening program in Korea during 2002-2003 were observed from 2004 to 2013. Hazard ratios of aspirin, statins, and metformin use for PC incidence and PC mortality were calculated with adjustment for simultaneous drug use. Cumulative use of each drug was inserted as time-dependent variable with 2-year time windows. Aspirin use >/= 1.5 year (per 2-year) was associated with borderline decrease in PC mortality when compared to non-users (adjusted hazard ratio [aHR] 0.71, 95% confidence interval [CI] 0.50-1.02). Statins use was not associated with either PC incidence or PC mortality. Metformin ever-use was associated with decreased PC incidence compared with non-diabetics (aHR 0.86, 95% CI 0.77-0.96). Diabetics who were not using metformin or using low cumulative doses had higher PC mortality than non-diabetics (aHR 2.01, 95% CI 1.44-2.81, and aHR 1.70, 95% CI 1.07-2.69, respectively). However, subjects with higher cumulative doses of metformin did not show increased PC mortality. In conclusion, metformin use was associated with lower PC incidence. Use of aspirin and that of metformin among diabetic patients were associated with lower PC mortality.

Korkes, F., et al. (2021). "Dramatic Impact of Centralization and a Multidisciplinary Bladder Cancer Program in Reducing Mortality: The CABEM Project." JCO Glob Oncol **7**: 1547-1555.

PURPOSE: Muscle-invasive bladder cancer (MIBC) is an aggressive disease with a complex treatment. In Brazil, as in most developing countries, data are scarce, but mortality seems exceedingly high. We have created a centralization program involving a multidisciplinary clinic in a region comprising seven municipalities. The aim of this study is to evaluate the impact of a multidisciplinary clinic and a centralization-of-care program (CABEM program) on MIBC treatment in Brazil. PATIENTS AND METHODS: A total of 116 consecutive patients were evaluated. In group 1, 58 patients treated for MIBC before establishing a bladder cancer program from 2011 to 2017 were retrospectively evaluated. Group 2 represented 58 patients treated for MIBC after the implementation of the CABEM centralization program. Age, sex, staging, comorbidity indexes, mortality rates, type of treatment, and perioperative outcomes were compared. RESULTS: Patients from group 2 versus 1 were older (68 v 64.2 years, P = .02) with a higher body mass index (25.5 v 22.6 kg/m(2), P = .017) and had more comorbidities according to both age-adjusted Charlson Comorbidity Index (4.2 v 2.8, P = .0007) and Isbarn index (60.6 v 43.9, P = .0027). Radical cystectomy (RC) was the only treatment modality for patients in group 1, whereas in group 2, there were 31 (53%) RC; three (5%) partial cystectomies; seven (12%) trimodal therapies; 13 (22%) palliative chemotherapies; and three (5%) exclusive transurethral resections of the bladder tumor. No patient in group 1 received neoadjuvant chemotherapy, whereas it was offered to 69% of patients treated with RC. Ninety-day mortality rates were 34.5% versus 5% for groups 1 versus 2 (P < .002). One-year mortality was also lower in group 2. CONCLUSION: Our data support that a centralization program, a structured bladder clinic associated with protocols, a multidisciplinary team, and inclusion of chemotherapy and radiotherapy treatments can pleasingly improve outcomes for patients with MIBC.

Kosaraju, N., et al. (2022). "Impact of frailty on mortality and quality of life in patients with a history of cancer undergoing transcatheter aortic valve replacement." Clin Cardiol **45**(10): 977-985.

BACKGROUND: Transcatheter aortic valve replacement (TAVR) is increasingly offered for aortic stenosis (AS) treatment in patients with a history of cancer. The impact of frailty on outcomes in this specific patient population is not well described. HYPOTHESIS: Frailty is associated with mortality and poorer quality of life (QOL) outcomes in patients undergoing TAVR with a history of cancer. METHODS: This retrospective single center cohort study included AS patients who underwent TAVR from August 1, 2012 to May 15, 2020. Frailty was measured using serum albumin, hemoglobin, gait speed, functional dependence, and cognitive impairment. The primary outcome was a composite of all-cause mortality and QOL at 1 year. A poor primary outcome was defined as either all-cause mortality, Kansas City Cardiomyopathy Questionnaire overall summary (KCCQ-OS) score <45 or a KCCQ-OS score decline of >/=10 points from baseline. Regression analysis was used to determine the impact of frailty on the primary outcome. RESULTS: The study population was stratified into active/recent cancer (n = 107), remote cancer (n = 85), and non-cancer (n = 448). Univariate analysis of each cohort showed that frailty was associated with the primary outcome only in the non-cancer cohort (p = .004). Multivariate analysis showed that cancer history was not associated with a poor primary outcome, whereas frailty was (1.7 odds ratio, 95% confidence interval [CI]: 1.1-2.8; p = .028). CONCLUSIONS: Frailty is associated with mortality and poor QOL in the overall and non-cancer cohorts. Further investigation is warranted to understand frailty's effect on the cancer population. Frailty should be heavily considered during TAVR evaluation.

Kothari, A. N., et al. (2020). "Weekend readmissions associated with mortality following pancreatic resection for cancer." Surg Oncol **34**: 218-222.

BACKGROUND: The weekend effect is associated with an increased risk of adverse events, with complex patient populations especially susceptible to its impact. The objective of this study was to determine if outcomes for patients readmitted following pancreas resection differed on the weekend compared to weekdays. METHODS: The Healthcare Cost and Utilization State Inpatient Database for Florida was used to identify patients undergoing pancreas resection for cancer who were readmitted within 30 days of discharge following surgery. Measured outcomes (for readmission encounters) included inpatient morbidity and mortality. RESULTS: Patients with weekend readmissions had an increased odds of inpatient mortality (aOR 2.7, 95% C.I.: 1.1-6.6) compared to those with weekday readmissions despite having similar index lengths of stay (15.9 vs. 15.5 days, P = .73), incidence of postoperative inpatient complications (22.4% vs. 22.3%, P = .98), reasons for readmission, and baseline comorbidity. DISCUSSION: Weekend readmissions following pancreatic resection are associated with increased risk of mortality. This is not explained by measured patient factors or clinical characteristics of the index hospital stay. Developing

strategies to overcome the weekend effect can result in improved care for patients readmitted on the weekend.

Kouka, M., et al. (2022). "Early Mortality among Patients with Head and Neck Cancer Diagnosed in Thuringia, Germany, between 1996 and 2016-A Population-Based Study." Cancers (Basel) **14**(13).

Population-based studies on early mortality in head and neck cancer (HNC) are sparse. This retrospective population-based study investigated early mortality of HNC and the influence of patients' tumor and treatment characteristics. All 8288 patients with primary HNC of the German federal state Thuringia from 1996 to 2016 were included. Univariate and multivariate analysis were performed to identify independent factors for 30-day, 90-day, and 180-day mortality. The 30-, 90-, and 180-day mortality risks were 1.8%, 5.1%, and 9.6%, respectively. In multivariable analysis, male sex (odds ratio (OR) 1.41; 95% confidence interval (CI) 1.08-1.84), increasing age (OR 1.81; CI 1.49-2.19), higher T (T4: OR 3.09; CI 1.96-4.88) and M1 classification (OR 1.97; CI 1.43-2.73), advanced stage (IV: OR 3.97; CI 1.97-8.00), tumors of the cavity of mouth (OR 3.47; CI 1.23-9.75), oropharynx (OR 3.01; CI 1.06-8.51), and hypopharynx (OR 3.27; CI 1.14-9.40) had a significantly greater 180-day mortality. Surgery (OR 0.51; CI 0.36-0.73), radiotherapy (OR 0.37; CI 0.25-0.53), and multimodal therapy (OR 0.10; CI 0.07-0.13) were associated with decreased 180-day mortality. Typical factors associated with worse overall survival had the most important impact on early mortality in a population-based setting.

Koyratty, N., et al. (2021). "Sugar-Sweetened Soda Consumption and Total and Breast Cancer Mortality: The Western New York Exposures and Breast Cancer (WEB) Study." Cancer Epidemiol Biomarkers Prev **30**(5): 945-952.

BACKGROUND: There is growing evidence of an association between sugar-sweetened beverages (SSB) and increased risk of mortality in various populations. However, SSB influence on mortality among patients with breast cancer is unknown. METHODS: We assessed the relationship between sugar-sweetened soda and both all-cause and breast cancer mortality among women with incident, invasive breast cancer from the Western New York Exposures and Breast Cancer Study. Breast cancer cases were followed for a median of 18.7 years, with ascertainment of vital status via the National Death Index. Frequency of sugar-sweetened soda consumption was determined via dietary recall using a food frequency questionnaire. Cox proportional hazards, adjusting for relevant variables, were used to estimate HRs and 95% confidence intervals (CI). RESULTS: Of the 927 breast cancer cases, 386 (54.7%) had died by the end of follow-up. Compared with never/rarely sugar-sweetened soda drinkers, consumption at >/=5 times per week was associated with increased risk of both total (HR = 1.62; 95% CI, 1.16-2.26; P (trend) < 0.01) and breast cancer mortality (HR = 1.85; 95% CI, 1.16-2.94; P (trend) < 0.01). Risk of mortality was similarly increased among ER-positive, but not ER-negative patients; among women with body mass index above the median, but not below the median; and among premenopausal, but not postmenopausal women for total mortality only. CONCLUSIONS: Reported higher frequency of sugar-sweetened soda intake was associated with increased risks of both total and breast cancer mortality among patients with breast cancer. IMPACT: These results support existing guidelines on reducing consumption of SSB, including for women with a diagnosis of breast cancer.

Kraav, S. L., et al. (2021). "The effects of loneliness and social isolation on all-cause, injury, cancer, and CVD mortality in a cohort of middle-aged Finnish men. A prospective study." Aging Ment Health **25**(12): 2219-2228.

OBJECTIVES: Loneliness and social isolation both increase mortality and are likely to affect health via several pathways. However, information on the potential pathways remains scarce. We investigated the associations between loneliness, social isolation, and mortality, and possible mechanisms underlying these connections. METHODS: The analyzed data comprised a prospective population-based cohort of Finnish men (42-61 years at baseline, n = 2588) who were followed up for an average of 23.2 years. Mortality data were obtained from the national population register in 2012. Cox proportional hazards analysis with adjustments for possible confounding factors was used to examine the associations between loneliness and social isolation at baseline and all-cause, injury, cancer, and cardiovascular disease (CVD) mortality. Mediation analysis was conducted to investigate the mechanisms underlying the associations of loneliness and social isolation with mortality. RESULTS: Loneliness predicted all-cause mortality, even after adjustments for all covariates. Loneliness predicted cancer mortality, except after adjustments for lifestyle variables or Human Population Laboratory (HPL) depression scores, and also predicted CVD mortality, except after adjustments for HPL depression scores. Social isolation predicted all-cause mortality and injury mortality. The effect of social isolation on all-cause mortality was mediated by loneliness and HPL depression scores. CONCLUSIONS: Our findings suggest that both loneliness and social isolation increase the risk of all-cause mortality, while they have differing effects on different causes of death.

Loneliness and depressive symptoms may mediate the effect of social isolation on increased mortality.

Krashin, E., et al. (2021). "Pre-diagnosis thyroid hormone dysfunction is associated with cancer mortality." Endocr Relat Cancer **28**(11): 705-713.

Research on the association between thyroid hormone levels and cancer mortality remains limited and inconclusive. We determined the relation of thyroid stimulating hormone (TSH), free T4 (FT4), and free T3 (FT3) levels with mortality in overall cancer and specific tumor types. Thyroid hormone levels 1-5 years prior to cancer diagnosis, as well as multiple clinical and demographic parameters, were retrospectively collected for 10,325 Israeli cancer patients, diagnosed between 2000 and 2016. Patients treated with thyroid altering medications were excluded. Cancer diagnosis was determined via the Israel National Cancer Registry. Multivariate-adjusted Cox proportional hazards model was used to assess the hazard ratios (HRs) based on thyroid hormone function for cancer mortality. A total of 5265 patients died during the follow-up period (median of 4.4 years). TSH, FT4, and FT3 levels in the hypothyroid range were associated with increase in overall mortality (adjusted HR 1.20, 1.74, 1.87, respectively). We further analyzed the association between TSH and mortality in 14 cancer subgroups. Specifically, TSH in both the hyperthyroid and hypothyroid range was associated with melanoma mortality (adjusted HR 2.20, 4.47, respectively). In conclusion, pre-diagnosis of thyroid dysfunction is associated with increased cancer mortality, a relation likely driven by specific cancer types. These findings suggest that thyroid hormones may potentially serve as prognostic markers in cancer.

Krasnoff, C. C., et al. (2021). "Predictors of Anastomotic Leak After Esophagectomy for Cancer: Not All Leaks Increase Mortality." Am Surg **87**(6): 864-871.

BACKGROUND: The impact of preoperative chemotherapy/radiation on esophageal anastomotic leaks (ALs) and the correlation between AL severity and mortality risk have not been fully elucidated. We hypothesized that lower severity ALs have a similar risk of mortality compared to those without ALs, and preoperative chemotherapy/radiation increases AL risk. METHODS: The 2016-2017 American College of Surgeons National Surgical Quality Improvement Program's procedure-targeted esophagectomy database was queried for patients undergoing any esophagectomy for cancer. A multivariable logistic regression analysis was performed for risk of ALs. RESULTS: From 2042 patients, 280 (13.7%) had ALs. AL patients requiring intervention had increased mortality risk including those requiring reoperation, interventional procedure, and medical therapy ($P < .05$). AL patients requiring no intervention had similar mortality risk compared to patients without ALs ($P > .05$). Preoperative chemotherapy/radiation was not predictive of ALs ($P > .05$). CONCLUSION: Preoperative chemotherapy/radiation does not contribute to risk for ALs after esophagectomy. There is a stepwise increased risk of 30-day mortality for ALs requiring increased invasiveness of treatment.

Kurian, A. W., et al. (2022). "Association of Genetic Testing Results With Mortality Among Women With Breast Cancer or Ovarian Cancer." J Natl Cancer Inst **114**(2): 245-253.

BACKGROUND: Breast cancer and ovarian cancer patients increasingly undergo germline genetic testing. However, little is known about cancer-specific mortality among carriers of a pathogenic variant (PV) in BRCA1/2 or other genes in a population-based setting. METHODS: Georgia and California Surveillance Epidemiology and End Results (SEER) registry records were linked to clinical genetic testing results. Women were included who had stages I-IV breast cancer or ovarian cancer diagnosed in 2013-2017, received chemotherapy, and were linked to genetic testing results. Multivariable Cox proportional hazard models were used to examine the association of genetic results with cancer-specific mortality. RESULTS: 22 495 breast cancer and 4320 ovarian cancer patients were analyzed, with a median follow-up of 41 months. PVs were present in 12.7% of breast cancer patients with estrogen and/or progesterone receptor-positive, HER2-negative cancer, 9.8% with HER2-positive cancer, 16.8% with triple-negative breast cancer, and 17.2% with ovarian cancer. Among triple-negative breast cancer patients, cancer-specific mortality was lower with BRCA1 (hazard ratio [HR] = 0.49, 95% confidence interval [CI] = 0.35 to 0.69) and BRCA2 PVs (HR = 0.60, 95% CI = 0.41 to 0.89), and equivalent with PVs in other genes (HR = 0.65, 95% CI = 0.37 to 1.13), vs noncarriers. Among ovarian cancer patients, cancer-specific mortality was lower with PVs in BRCA2 (HR = 0.35, 95% CI = 0.25 to 0.49) and genes other than BRCA1/2 (HR = 0.47, 95% CI = 0.32 to 0.69). No PV was associated with higher cancer-specific mortality. CONCLUSIONS: Among breast cancer and ovarian cancer patients treated with chemotherapy in the community, BRCA1/2 and other gene PV carriers had equivalent or lower short-term cancer-specific mortality than noncarriers. These results may reassure newly diagnosed patients, and longer follow-up is ongoing.

Kuronya, Z., et al. (2021). "Low socioeconomic position is a risk factor for delay to treatment and

mortality of testicular cancer patients in Hungary, a prospective study." BMC Public Health **21**(1): 1707.

BACKGROUND: In Hungary, the mortality rate for testicular germ cell cancer (TGCC) is 0,9/100000 which is significantly higher than the EU average. We prospectively evaluated the effect of socioeconomic position on patient delay and therapy outcomes. METHODS: Questionnaires on subjective social status (MacArthur Subjective Status Scale), objective socioeconomic position (wealth, education, and housing data), and on patient's delay were completed by newly diagnosed TGCC patients. RESULTS: Patients belonged to a relatively high socioeconomic class, a university degree was double the Hungarian average, Cancer-specific mortality in the highest social quartile was 1.56% while in the lowest social quartile 13.09% ($p = 0.02$). In terms of patient delay, 57.2% of deceased patients waited more than a year before seeking help, while this number for the surviving patients was 8.0% ($p = 0.0000$). Longer patient delay was associated with a more advanced stage in non-seminoma but not in seminoma, the correlation coefficient for non-seminoma was 0.321 ($p < 0.001$). For patient delay, the most important variables were the mother's and patient's education levels ($r = - 0.21$, $p = 0.0003$, and $r = - 0.20$, $p = 0.0005$), respectively. Since the patient delay was correlated with the social quartile and resulted in a more advanced stage in non-seminoma, the lower social quartile resulted in higher mortality in non-seminoma patients ($p = 0.005$) but not in seminoma patients ($p = 0.36$) where the patient delay was not associated with a more advanced stage. CONCLUSIONS: Based on our result, we conclude that to improve survival, we should promote testicular cancer awareness, especially among the most deprived populations, and their health care providers.

Kusne, Y. N., et al. (2020). "Mortality and glycemic control among patients with diabetes mellitus and uterine or ovarian cancer." Future Sci OA **7**(3): FSO670.

AIM: To evaluate associations between survival and glycemic control in age-matched patients with endometrial or ovarian cancer, with/without diabetes mellitus (DM). PATIENTS & METHODS: Patients with newly diagnosed ovarian or endometrial cancer with and without DM were compared. RESULTS: The study included 84 patients with ovarian cancer (28, DM); 96 with endometrial cancer (48 with, 48 without DM). DM patients did not have worse overall or progression-free survival than non-DM patients. Glycemic control was not associated with either cancer. CONCLUSION: There was no association between DM and survival for patients with uterine or ovarian cancer. In addition, there was no association between uterine and ovarian cancer and glycemic control. Additional studies to confirm these observations in larger populations are required.

Kuzmickiene, I. and R. Everatt (2021). "Trends and age-period-cohort analysis of upper aerodigestive tract and stomach cancer mortality in Lithuania, 1987-2016." Public Health **196**: 62-68.

OBJECTIVES: Lithuania has among the highest mortality rates for upper aerodigestive tract (UADT) and stomach cancer in Europe. The aim of this study was to analyze trends during the period 1987-2016 in Lithuania, evaluating the effect of birth-cohort, period, and age. STUDY DESIGN: Observational time trends study. METHODS: Data on numbers of deaths and population size by each calendar year in 5-year age groups in 1987-2016 were obtained from the WHO mortality database. Joinpoint regression analysis was used to evaluate changes in time trends. Age-period-cohort analysis was performed to assess age, calendar period of death, and birth-cohort effects. RESULTS: UADT cancer mortality in men increased between 1987 and 1993, annual percentage change (APC) = 6.6% (95% confidence interval [CI]: 3.8, 9.4), and was stable thereafter, APC = 0.3% (95% CI: 0.0, 0.6). The age-standardized mortality rate (ASMR) was 23.6/100,000 in 2016. In women, rates increased steadily by 1.6% (95% CI: 0.9%, 2.3%) per year from 1987 to 2016, ASMR = 2.3/100,000 in 2016. Age-period-cohort analysis showed statistically significant cohort effects in both sexes. In men, rates peaked in birth-cohorts born around 1952, declined in 1957-1962 birth-cohorts, and fluctuated in later birth-cohorts. In women, rates started rising in 1947 birth cohort and peaked in the 1967 birth cohort. Stomach cancer mortality declined throughout the study period in men by -2.4%, (95% CI: -2.6%, -2.1%) annually, and women by -2.8% (95% CI: -3.1%, -2.4%), ASMR = 16.1/100,000 and 6.0/100,000 in 2016, respectively. Birth-cohort effects were significant in both sexes. Rates decreased in cohorts born around 1920 onwards, but declines in the youngest generations have slowed in men and reversed in women. CONCLUSIONS: The birth-cohort effects in UADT and stomach cancer mortality trends imply that the elevated burden in Lithuania could be reduced by effective strategies targeting known risk factors. Further research in causes of unfavorable trends in younger cohorts is warranted.

Kvale, R., et al. (2021). "Does a history of cardiovascular disease or cancer affect mortality after SARS-CoV-2 infection?" Tidsskr Nor Laegeforen **140**(2).

BACKGROUND: Cardiovascular disease and cancer have been described as possible risk factors for COVID-19 mortality. The purpose of this study was to

investigate whether a history of cardiovascular disease or cancer affects the risk of dying after a COVID-19 diagnosis in Norway. MATERIAL AND METHOD: Data were compiled from the Norwegian Surveillance System for Communicable Diseases, the Norwegian Cardiovascular Disease Registry and the Cancer Registry of Norway. Univariable and multivariable regression models were used to calculate both relative and absolute risk. RESULTS: In the first half of 2020, 8 809 people tested positive for SARS-CoV-2 and 260 COVID-19-associated deaths were registered. Increasing age, male sex (relative risk (RR): 1.5; confidence interval (CI): 1.2-2.0), prior stroke (RR: 1.5; CI: 1.0-2.1) and cancer with distant metastasis at the time of diagnosis (RR: 3.0; CI: 1.1-8.2) were independent risk factors for death after a diagnosis of COVID-19. After adjusting for age and sex, myocardial infarction, atrial fibrillation, heart failure, hypertension, and non-metastatic cancer were no longer statistically significant risk factors for death. INTERPRETATION: The leading risk factor for death among individuals who tested positive for SARS-CoV-2 was age. Male sex, and a previous diagnosis of stroke or cancer with distant metastasis were also associated with an increased risk of death after a COVID-19 diagnosis.

Kwak, J. H., et al. (2022). "The Associations of Dietary Intake of High Sodium and Low Zinc with Gastric Cancer Mortality: A Prospective Cohort Study in Korea." Nutr Cancer **74**(10): 3501-3508.

Sodium and zinc display opposite effects on immune cells, such as regulatory T cells (Tregs) and T helper 17 cells (Th17), resulting in an altered immune response. Immune cells have a pivotal role in regulating tumor progression, which may affect gastric cancer (GC) mortality. Thus, this cohort study investigated the associations between the combination of sodium and zinc intake and GC mortality and whether these associations differ by histological type by following up deaths of GC cases in Korea. A total of 490 patients with GC were enrolled between 2002 and 2006. Survival or death was prospectively followed up until December 31, 2016. Finally, 300 patients with the two main histological types of GC were included; 99 GC deaths occurred during a median follow-up period of 7.1 years. Patients with high sodium and low zinc intake had a significantly higher GC mortality than those with low sodium and high zinc intake (hazard ratio [HR], 2.07; 95% confidence interval [CI], 1.09-3.93). However, no significant association was found between the histological types of GC. In conclusion, we found that high sodium and low zinc intake may worsen the survival rate of patients with GC.

Kwak, J. H., et al. (2022). "Dietary zinc intake and mortality in patients with intestinal-type gastric cancer: A prospective cohort study in Korea." Front Oncol **12**: 947405.

PURPOSE: Current evidence regarding the association between zinc intake and gastric cancer (GC)-specific survival in patients with intestinal-type GC is lacking. Therefore, this cohort study investigated the association between zinc intake and GC mortality through follow-up on GC death among patients with intestinal-type GC and whether these effects differ according to the source of zinc intake. METHODS: A total of 185 patients with intestinal-type GC were enrolled from two hospitals between 2002 and 2006. Their survival or death was prospectively followed up until December 31, 2016, through a review of medical records and telephone surveys. RESULTS: A total of 178 patients were included and analyzed. The median follow-up period was 7.3 years. In the fully adjusted models, the highest tertile of total zinc intake showed a significantly lower GC mortality than the lowest tertile (hazard ratio, 0.22; 95% confidence interval: 0.08-0.64). In addition, the tertile of total zinc intake showed a dose-response association with GC mortality (p=0.015). Analysis of the source of zinc intake revealed that when zinc intake from staples (rice and noodles), animal, and plant food sources were combined, the results were similar to those of total zinc intake and GC mortality. CONCLUSION: Zinc intake through various foods may be effective in reducing GC mortality by achieving balance with other nutrients. Our results suggest that zinc improves the survival of patients with intestinal-type GC in Korea.

LaBarge, B., et al. (2021). "In-depth analysis of thyroid cancer mortality." Head Neck **43**(3): 977-983.

BACKGROUND: There are reports of an increasing thyroid cancer mortality rate. This study aimed to analyze the latest trends in this rate over time and compare findings from different cancer registries. METHODS: Thyroid cancer incidence-based mortality (IBM) rates were obtained from the Surveillance, Epidemiology, and End Results (SEER) program, including SEER-9, SEER-13, and SEER-18. The National Center for Health Statistics (NCHS) thyroid cancer mortality rate was acquired for comparison. Statistical analysis was performed using the JoinPoint software. RESULTS: NCHS data revealed an overall annual percent change (APC) over 1987 to 2017 of 0.61 ($P < .01$), and the value was nearly four times greater for males compared to females. The overall IBM APC values for SEER-9, SEER-13, and SEER-18 were also positive and statistically significant ($P < .01$). CONCLUSIONS: The increased thyroid cancer mortality rate observed in previous studies continues to

be statistically significant based on updated NCHS and SEER IBM data.

Lagace, F., et al. (2021). "Incidence and Mortality of Prostate Cancer in Canada during 1992-2010." Curr Oncol **28**(1): 978-990.

In Canada, prostate cancer is the most common reportable malignancy in men. We assessed the temporal trends of prostate cancer to gain insight into the geographic incidence and mortality trends of this disease. Three independent population-based cancer registries were used to retrospectively analyze demographic data on Canadian men diagnosed with prostate cancer and men who died of prostate cancer between the years of 1992 and 2010. The incidence and mortality rates were calculated at the provincial, city, and forward sortation area (FSA) postal code levels by using population counts that were obtained from the Canadian Census of Population. The Canadian average incidence rate was 113.57 cases per 100,000 males. There has been an overall increasing trend in crude prostate cancer incidence between 1992 and 2010 with three peaks, in 1993, 2001, and 2007. However, age-adjusted incidence rates showed no significant increase over time. The national mortality rate was calculated to be 24.13 deaths per 100,000 males per year. A decrease was noted in crude and age-adjusted mortality rates between 1992 and 2010. Several provinces, cities, and FSAs had higher incidence/mortality rates than the national average. Several of the FSA postal codes with the highest incidence/mortality rates were adjacent to one another. Several Canadian regions of high incidence for prostate cancer have been identified through this study and temporal trends are consistent with those reported in the literature. These results will serve as a foundation for future studies that will seek to identify new regional risk factors and etiologic agents.

Laguna, J. C., et al. (2021). "Simple sugar intake and cancer incidence, cancer mortality and all-cause mortality: A cohort study from the PREDIMED trial." Clin Nutr **40**(10): 5269-5277.

OBJECTIVE: To examine associations between intake of simple sugars and cancer incidence, cancer mortality, and total mortality in a prospective cohort study based on the PREDIMED trial conducted from 2003 to 2010. METHODS: Participants were older individuals at high cardiovascular risk. Exposures were total sugar, glucose and fructose from solid or liquid sources, and fructose from fruit and 100% fruit juice. Cancer incidence was the primary outcome; cancer mortality and all-cause mortality were secondary outcomes. Multivariable-adjusted, time-dependent Cox proportional hazard models were used. RESULTS: Of 7447 individuals enrolled, 7056 (94.7%) were included (57.6% women, aged 67.0 +/- 6.2 years). 534 incident cancers with 152 cancer deaths and 409 all-cause deaths were recorded after a median follow-up of 6 years. Intake of simple sugars in solid form was unrelated to outcomes. Higher cancer incidence was found per 5 g/day increase in intake of liquid sugars, with multivariable-adjusted HR of 1.08 (95% CI, 1.03-1.13) for total liquid sugar, 1.19 (95% CI, 1.07-1.31) for liquid glucose, 1.14 (95% CI, 1.05-1.23) for liquid fructose, and 1.39 (95% CI, 1.10-1.74) for fructose from fruit juice. Cancer and all-cause mortality increased to a similar extent with intake of all sugars in liquid form. In categorical models, cancer risk was dose-related for all liquid sugars. CONCLUSIONS: Simple sugar intake in drinks and fruit juice was associated with an increased risk of overall cancer incidence and mortality and all-cause mortality. This suggests that sugary beverages are a modifiable risk factor for cancer and all-cause mortality.

Lahtinen, S., et al. (2021). "Perioperative Risk Factors for One-Year Mortality in Patients With Free-Flap Reconstruction Due to Cancer of the Head and Neck." J Oral Maxillofac Surg **79**(6): 1384 e1381-1384 e1385.

PURPOSE: Head and neck cancer requiring free-flap reconstruction is associated with relatively high mortality. We aimed to evaluate perioperative risk factors for 1-year mortality in this patient group. METHODS: This is a single-center retrospective analysis of 204 patients operated during 2008 to 2018. RESULTS: A total of 47 (23.0%) patients died within 1 year. In univariate analysis, there were no differences in the intraoperative course between 1-year survivors and nonsurvivors. Among the 1-year nonsurvivors, preoperative albumin level was lower (39 [36 to 43] vs 42 [39 to 44], P = .032) and the Sequential Organ Failure Assessment admission score was higher (4 [3 to 5] vs 3 [2 to 4], P = .003) than those of the 1-year survivors. Among the nonsurvivors, the preoperative and postoperative levels of leukocytes were higher (7.6 [6.7 to 9.5] vs 6.9 [5.5 to 8.4], P = .002; 11.4 [9.0 to 14.2] vs 8.7 [7.2 to 11.3], P < .001). The highest odds ratios for 1-year mortality in multivariate analysis were American Society of Anesthesiologists A classification greater than 2 (3.9 CI 1.4 to 10.5), male gender (4.0 CI 1.5 to 11), and increase in leukocyte count (1.3 CI 1.1 to 1.5). CONCLUSIONS: One-year nonsurvivors had higher American Society of Anesthesiologists classification and were more often men. The postoperative inflammatory markers were higher in nonsurvivors, while the intraoperative course did not have a significant impact on the 1-year mortality.

Lai, A. G., et al. (2020). "Estimated impact of the COVID-19 pandemic on cancer services and excess 1-year mortality in people with cancer and

multimorbidity: near real-time data on cancer care, cancer deaths and a population-based cohort study." BMJ Open **10**(11): e043828.

OBJECTIVES: To estimate the impact of the COVID-19 pandemic on cancer care services and overall (direct and indirect) excess deaths in people with cancer. METHODS: We employed near real-time weekly data on cancer care to determine the adverse effect of the pandemic on cancer services. We also used these data, together with national death registrations until June 2020 to model deaths, in excess of background (pre-COVID-19) mortality, in people with cancer. Background mortality risks for 24 cancers with and without COVID-19-relevant comorbidities were obtained from population-based primary care cohort (Clinical Practice Research Datalink) on 3 862 012 adults in England. RESULTS: Declines in urgent referrals (median=-70.4%) and chemotherapy attendances (median=-41.5%) to a nadir (lowest point) in the pandemic were observed. By 31 May, these declines have only partially recovered; urgent referrals (median=-44.5%) and chemotherapy attendances (median=-31.2%). There were short-term excess death registrations for cancer (without COVID-19), with peak relative risk (RR) of 1.17 at week ending on 3 April. The peak RR for all-cause deaths was 2.1 from week ending on 17 April. Based on these findings and recent literature, we modelled 40% and 80% of cancer patients being affected by the pandemic in the long-term. At 40% affected, we estimated 1-year total (direct and indirect) excess deaths in people with cancer as between 7165 and 17 910, using RRs of 1.2 and 1.5, respectively, where 78% of excess deaths occured in patients with >/=1 comorbidity. CONCLUSIONS: Dramatic reductions were detected in the demand for, and supply of, cancer services which have not fully recovered with lockdown easing. These may contribute, over a 1-year time horizon, to substantial excess mortality among people with cancer and multimorbidity. It is urgent to understand how the recovery of general practitioner, oncology and other hospital services might best mitigate these long-term excess mortality risks.

Lai, R. W. (2021). "Full Analysis of Lung Cancer Mortality/Radon Relationship with Simple Nonlinear Concepts." Dose Response **19**(1): 1559325820960994.

We analyze the relationship between the lung cancer mortality and the indoor radon intensity from the viewpoint of nonlinear mathematics. We conclude that their relationship is governed by the proportionality law where the cumulative lung cancer mortality Y is negatively proportional to the cumulative radon intensity X; or specifically, the nonlinear change of nonlinear face value (qYu - qY) is negatively proportional to the nonlinear change of nonlinear face value (X - Xb). The author obtained a set of data from late Professor Cohen on the lung-cancer mortality rate versus indoor radon level collected from 1,597 counties and territory of the USA. We initially presented the data as various primitive elementary graphs; then extended them to the primary graphs, leading graphs, and the proportionality graphs. The article emphasizes the building of a straight-line proportionality relationship for the dose-response data in a log-linear and/or log-log graphs. It demonstrates a straightforward methodology for solving the key upper asymptotes (Yu) for the proportionality equation using the Microsoft Excel via determining the "coefficient of determination". (Note: q = log, Yu = upper asymptote of Y, Xb = bottom asymptote of X).

Lai, Y. C., et al. (2022). "The Association between Smoking and Mortality in Women with Breast Cancer: A Real-World Database Analysis." Cancers (Basel) **14**(19).

Smoking increases the cancer-specific and overall mortality risk in women with breast cancer (BC). However, the effect of smoking cessation remains controversial, and detailed research is lacking in Asia. We aimed to investigate the association between smoking status and mortality in women with BC using the population-based cancer registry. The Taiwan Cancer Registry was used to identify women with BC from 2011 to 2017. A total of 54,614 women with BC were enrolled, including 1687 smokers and 52,927 non-smokers. The outcome, mortality, was identified using Taiwan's cause-of-death database. The association between smoking status and mortality was estimated using Cox proportional regression. Women with BC who smoked had a 1.25-fold higher (95% C.I.: 1.08-1.45; p = 0.0022) risk of overall mortality and a 1.22-fold higher (95% C.I.: 1.04-1.44; p = 0.0168) risk of cancer-specific mortality compared with non-smokers. The stratified analysis also indicated that women with BC who smoked showed a significantly higher overall mortality risk (HR: 1.20; 95% CI: 1.01-1.43; p = 0.0408) than women with BC who did not smoke among women without comorbidities. Additionally, current smokers had a 1.57-fold higher risk (95% CI: 1.02-2.42; p = 0.0407) of overall mortality compared with ever smokers among women with BC who smoked. It was shown that a current smoking status is significantly associated with an increase in overall and cancer-specific mortality risk in women with BC. Quitting smoking could reduce one's mortality risk. Our results underscore the importance of smoking cessation for women with BC.

Lai, Z., et al. (2022). "Association of hormone receptor status with cardiovascular disease mortality in 399,209

patients with stage I to III breast cancer: A population-based study." Medicine (Baltimore) **101**(46): e31911.

Adjuvant endocrine therapy (AET) is known to reduce the risk of hormone receptor-positive (HR+) breast cancer (BC) recurrence and mortality rates, but its impact on cardiovascular disease (CVD) events is unclear. The primary objective of this study was to analyze the association of HR status with CVD mortality in patients with stage I to III BC. A retrospective study of patients with stage I to III BC was conducted using the 2004 to 2016 Surveillance, Epidemiology, and End Results (SEER) database, and patients were grouped according to their HR status. Propensity score matching (PSM) was used to adjust for heterogeneity between the groups. The cumulative incidence rate of CVD mortality was evaluated via a cumulative incidence curve. Univariate and multivariate Fine and Gray's competing risk regression models were used to identify risk factors associated with CVD mortality. In total, 399,209 patients with BC were included in this study, and 329,958 patients (82.65%) were HR-positive. The cumulative incidence of CVD death was 8.28% in stage I to III BC patients. In the constituent ratio analysis, primary BC was the leading cause of death (45.29%, N = 31,465), followed by heart disease (16.07%, N = 11,166). Compared to the second year following BC diagnosis, the risk of CVD-specific death gradually increased. After PSM, 65,952 pairs of patients were matched, which led to the equilibrium of all variables between the HR-negative cohort and HR+ cohort. Multivariate analysis indicated that HR status was not significantly associated with the risk of CVD mortality, with a hazard ratio of 1.01 (P = .895). This study highlights the importance of understanding the associations between risk factors and CVD for BC patients. HR status was not associated with the risk of CVD mortality in this study.

Lam, C. S., et al. (2022). "Associations of dietary supplement use with all-cause and cause-specific mortality in patients diagnosed with cancer: a large prospective cohort study in the UK Biobank." Eur J Nutr.

PURPOSE: Despite the increasing popularity of supplement use among the cancer community, the current evidence on its effect on mortality in large studies is inconclusive. This study examined the association of dietary supplement use with mortality risk in a large population-based cohort. METHODS: This prospective cohort study analyzed data from the UK Biobank on participants who were diagnosed with cancer before July 31, 2019 and self-reported whether they had regular intake of dietary supplements (vitamins, minerals, or non-vitamin non-mineral [NVNM] supplements) after cancer diagnosis. The associations between the use of supplements with mortality were analyzed using Cox proportional hazards models, adjusting for confounders (sociodemographic factors, lifestyle and comorbidities). RESULTS: This analysis included 30,239 participants (mean age: 60.0 years; 61.9% female). Over half (57.8%) were supplement users. At a median follow-up of 11.9 years, 5577 all-cause deaths were registered. A marginal protective effect of supplement use on the risk of all-cause (adjusted hazard ratio [aHR] = 0.95, 95% CI = 0.90-0.99) and cancer (aHR = 0.89, 95% CI = 0.83-0.95) mortality were found, but not the risk of mortality due to other causes. In subgroup analyses, only NVNM dietary supplements were significantly associated with a lower risk of all-cause mortality (aHR = 0.88, 95% CI = 0.83-0.93). Both vitamins (aHR = 0.93, 95% CI = 0.87-0.99) and NVNM dietary supplements (aHR = 0.88, 95% CI = 0.82-0.94) were associated with a modest decrease in cancer mortality which were marginally significant. CONCLUSIONS: This is one of the largest cohort studies that identified the associations of dietary supplements with survival in the cancer population. However, the associations are small and should be interpreted cautiously due to the variations among different supplements and the small effect size. Future studies should investigate the effect of individual supplements, particularly NVNM supplements, on improving other cancer-related outcomes.

Lee, P. F., et al. (2021). "Population-Based Study on the All-Cause and Cause-Specific Risks of Mortality among Long-Term Opioid Analgesics Users without Cancer in Taiwan." Healthcare (Basel) **9**(11).

(1) Background: The prevalence of opioid use in Taiwan increased by 41% between 2002 and 2014. However, little is known regarding the risk of mortality among long-term opioid analgesics users who do not have cancer. This study investigated this mortality risk with an emphasis on the calendar year and patients' age and sex. (2) Methods: This retrospective cohort study included 12,990 adult individuals without cancer who were long-term users of opioid analgesics and were randomly selected from the data set of Taiwan's National Health Insurance program from 2000 to 2012. They were then followed up through 2013. Information on the underlying causes of death was retrieved from the Taiwan Death Registry. Age, sex, and calendar year-standardized mortality ratios (SMRs) of all-cause and cause-specific mortality were calculated with reference to those of the general population. (3) Results: With up to 14 years of follow-up, 558 individuals had all-cause mortality in 48,020 person-years (cumulative mortality: 4.3%, mortality rate: 11.62 per 1000 person-years). Compared with the general population, the all-cause SMR of 4.30 (95% confidence interval (95% CI): 3.95-4.66) was

significantly higher: it was higher in men than in women, declined with calendar year and age, and was significantly higher for both natural (4.15, 95% CI: 3.78-4.53) and unnatural (5.04, 95% CI: 3.88-6.45) causes. (4) Conclusions: Long-term opioid analgesics use among individuals without cancer in Taiwan was associated with a significantly increased risk of mortality. The notably increased mortality in younger adults warrants attention. Strategies to reduce long-term opioid analgesics use, especially their overuse or misuse, are in an urgent need.

Lee, S., et al. (2021). "Impact of comorbidity assessment methods to predict non-cancer mortality risk in cancer patients: a retrospective observational study using the National Health Insurance Service claims-based data in Korea." BMC Med Res Methodol **21**(1): 66.

BACKGROUND: Cancer patients' prognoses are complicated by comorbidities. Prognostic prediction models with inappropriate comorbidity adjustments yield biased survival estimates. However, an appropriate claims-based comorbidity risk assessment method remains unclear. This study aimed to compare methods used to capture comorbidities from claims data and predict non-cancer mortality risks among cancer patients. METHODS: Data were obtained from the National Health Insurance Service-National Sample Cohort database in Korea; 2979 cancer patients diagnosed in 2006 were considered. Claims-based Charlson Comorbidity Index was evaluated according to the various assessment methods: different periods in washout window, lookback, and claim types. The prevalence of comorbidities and associated non-cancer mortality risks were compared. The Cox proportional hazards models considering left-truncation were used to estimate the non-cancer mortality risks. RESULTS: The prevalence of peptic ulcer, the most common comorbidity, ranged from 1.5 to 31.0%, and the proportion of patients with >/=1 comorbidity ranged from 4.5 to 58.4%, depending on the assessment methods. Outpatient claims captured 96.9% of patients with chronic obstructive pulmonary disease; however, they captured only 65.2% of patients with myocardial infarction. The different assessment methods affected non-cancer mortality risks; for example, the hazard ratios for patients with moderate comorbidity (CCI 3-4) varied from 1.0 (95% CI: 0.6-1.6) to 5.0 (95% CI: 2.7-9.3). Inpatient claims resulted in relatively higher estimates reflective of disease severity. CONCLUSIONS: The prevalence of comorbidities and associated non-cancer mortality risks varied considerably by the assessment methods. Researchers should understand the complexity of comorbidity assessments in claims-based risk assessment and select an optimal approach.

Lee, S., et al. (2022). "Association between body mass index and oesophageal cancer mortality: a pooled analysis of prospective cohort studies with >800 000 individuals in the Asia Cohort Consortium." Int J Epidemiol **51**(4): 1190-1203.

BACKGROUND: The association between body mass index (BMI) and oesophageal cancer (OC) has been consistently negative among Asians, whereas different associations based on histological OC subtypes have been observed in Europeans and North Americans. We examined the association between BMI and OC mortality in the Asia Cohort Consortium. METHODS: We performed a pooled analysis to evaluate the association between BMI and OC mortality among 842 630 Asians from 18 cohort studies. Cox regression models were used to estimate hazard ratios (HRs) and 95% CIs. RESULTS: A wide J-shaped association between BMI and overall OC mortality was observed. The OC mortality risk was increased for underweight (BMI <18.5 kg/m2: HR = 2.20, 95% CI 1.80-2.70) and extreme obesity (BMI >/=35 kg/m2: HR = 4.38, 95% CI 2.25-8.52) relative to the reference BMI (23-25 kg/m2). This association pattern was confirmed by several alternative analyses based on OC incidence and meta-analysis. A similar wide J-shaped association was observed in oesophageal squamous cell carcinoma (OSCC). Smoking and alcohol synergistically increased the OC mortality risk in underweight participants (HR = 6.96, 95% CI 4.54-10.67) relative to that in reference BMI participants not exposed to smoking and alcohol. CONCLUSION: Extreme obesity and being underweight were associated with an OC mortality risk among Asians. OC mortality and BMI formed a wide J-shaped association mirrored by OSCC mortality. Although the effect of BMI on OSCC and oesophageal adenocarcinoma mortality can be different in Asians, further research based on a large case-control study is recommended.

Lee, S. A., et al. (2022). "The Association of Serum High-Sensitivity C-Reactive Protein Level With the Risk of Site-Specific Cancer Mortality: The Health Examinees (HEXA) Study Cohort." Am J Epidemiol **191**(12): 2002-2013.

Few studies have investigated the association between high-sensitivity C-reactive protein (hsCRP) level and site-specific cancer mortality. In this study, we aimed to examine the associations of hsCRP with overall and site-specific cancer mortality among South Koreans using data on the Health Examinees (HEXA) Study cohort (41,070 men and 81,011 women aged >/=40 years). We obtained mortality information from the National Statistical Office of Korea, which provided the dates and causes of all deaths occurring

through December 31, 2015, by linking mortality data with each participant's unique national identifier. Cox proportional hazards and restricted cubic spline models were used to assess the association between hsCRP and cancer mortality with adjustment for covariates. An analysis of site-specific cancer mortality was focused on 5 major cancers (lung, liver, gastric, colorectal, and breast/prostate). Median hsCRP levels were 0.77 mg/L and 0.59 mg/L for men and women, respectively. A dose-response association between hsCRP and overall cancer mortality was observed in men but disappeared in women after exclusion of deaths occurring in the first 1 or 2 years of follow-up. Elevated hsCRP levels increased the risks of lung, liver, and gastric cancer mortality in men, but the risks of colorectal and breast cancer mortality were not increased. The dose-response association between hsCRP and cancer mortality was observed differently depending on site-specific cancer mortality by sex.

Lee, W. R., et al. (2022). "Disparities in All-Cause Mortality in Older Patients with Colorectal Cancer According to Disability Status: A Nationwide Analysis." Curr Oncol **29**(10): 7430-7438.

BACKGROUND: Although investigating patterns of cancer mortality is important in understanding the effect of cancer on population health, knowledge regarding mortality in cancer patients with disability is scarce. This study examined the association between disability status and all-cause mortality in older patients with colorectal cancer. METHODS: Data were obtained from the 2008-2019 National Health Insurance Service claims data. The study population included patients with colorectal cancer aged 60 years or above. The outcome measure was all-cause 5-year and overall mortality. A survival analysis was performed using the Cox proportional hazards model to analyze the association between all-cause mortality and disability status. Subgroup analysis was conducted based on disability severity. RESULTS: The study population consisted of 6340 patients, and disability was reported in 15.8% of the included individuals. Participants with disability had a higher risk of both all-cause 5-year (hazard ratio (HR) 1.21, 95% confidence interval (95% CI) 1.07-1.37) and overall mortality (HR 1.15, 95% CI 1.03-1.28). These findings were particularly significant in individuals with severe rather than mild disability. CONCLUSION: Older colorectal cancer patients with disabilities showed a higher risk of overall and 5-year all-cause mortality, which was evident in individuals with severe disabilities. The findings indicated disparities in mortality according to disability status. Further, we suggest that policies that can mediate such disparities must be strengthened.

Lee, Y. B., et al. (2021). "Association of Metabolic Risk Factors With Risks of Cancer and All-Cause Mortality in Patients With Chronic Hepatitis B." Hepatology **73**(6): 2266-2277.

BACKGROUND AND AIMS: Long-term antiviral therapy can effectively suppress viral replication and improve clinical outcomes in patients with chronic hepatitis B (CHB), but it cannot eliminate risk of HCC. We investigated the association of metabolic risk factors with the risks of cancer and all-cause mortality in patients with CHB. APPROACH AND RESULTS: This nationwide population-based study from the Korean National Health Insurance Service database consisted of adults with CHB who underwent health examinations from 2007 through 2012. We collected baseline data on metabolic risk factors, including obesity, high blood pressure, hypercholesterolemia, and diabetes. The risks of developing HCC, non-HCC cancer, and overall death were analyzed according to the metabolic risk profile. The study population composed of 317,856 patients (median age, 46 years [interquartile range, 37-54 years]; 219,418 men [69.0%]) had 2,609,523.8 person-years of follow-up. A total of 18,850 HCCs, 22,164 non-HCC cancers, and 15,768 deaths were observed during a median follow-up period of 8.5 years. The metabolic risk factor burden was positively associated with the risks of HCC, non-HCC cancer, and all-cause mortality (all $P < 0.0001$ for trend). Patients with >/=3 metabolic risk factors, compared with those without metabolic risk factors, showed adjusted hazard ratios of 1.23 (95% CI, 1.16-1.31) for HCC, 1.34 (95% CI, 1.27-1.41) for non-HCC cancer, and 1.31 (95% CI, 1.23-1.39) for all-cause mortality. Among patients receiving antiviral therapy for over 5 years, the risk-increasing association of the sum of metabolic risk factors with the risks of HCC and overall death was consistent. CONCLUSION: The metabolic risk factor burden was associated with increased risks of HCC, non-HCC cancer, and all-cause mortality in patients with CHB.

Lee, Y. H. A., et al. (2023). "Metformin use and mortality in Asian, diabetic patients with prostate cancer on androgen deprivation therapy: A population-based study." Prostate **83**(1): 119-127.

BACKGROUND: This study aims to examine the associations between metformin use concurrent with androgen deprivation therapy (ADT) and mortality risks in Asian, diabetic patients with prostate cancer (PCa). METHODS: This study identified diabetic adults with PCa receiving any ADT attending public hospitals in Hong Kong between December 1999 and March 2021 retrospectively, with follow-up until September 2021. Patients with <6 months of medical castration without subsequent bilateral orchidectomy, <6 months of concurrent metformin use

and ADT, or missing baseline HbA1c were excluded. Metformin users had >/=180 days of concurrent metformin use and ADT, while non-users had no concurrent metformin use and ADT or never used metformin. The primary outcome was PCa-related mortality. The secondary outcome was all-cause mortality. The study used inverse probability treatment weighting to balance covariates. RESULTS: The analyzed cohort consisted of 1971 patients (1284 metformin users and 687 non-users; mean age 76.2 +/- 7.8 years). Over a mean follow-up of 4.1 +/- 3.2 years, metformin users had significantly lower risks of PCa-related mortality (weighted hazard ratio [wHR]: 0.49 [95% confidence interval, CI: 0.39-0.61], p < 0.001) and all-cause mortality (wHR 0.53 [0.46-0.61], p < 0.001), independent of diabetic control or status of chronic kidney disease. Such effects appeared stronger in patients with less advanced PCa, which is reflected by the absence of androgen receptor antagonist or chemotherapy use (p value for interaction: 0.017 for PCa-related mortality; 0.048 for all-cause mortality). CONCLUSIONS: Metformin use concurrent with ADT was associated with lower risks of mortality in Asian, diabetic patients with PCa.

Lee, Y. R., et al. (2020). "Statin adherence and risk of all-cause, cancer, and cardiovascular mortality among dyslipidemia patients: A time-dependent analysis." Nutr Metab Cardiovasc Dis **30**(12): 2207-2214.

BACKGROUND AND AIM: Results have been mixed and uncertainty still remains regarding the impact of statin adherence on premature deaths. Thus, we investigated the association between statin adherence and risks of all-cause, cancer, and cardiovascular mortality among dyslipidemia patients in South Korea. METHODS AND RESULTS: We used data from the National Health Insurance Service (NHIS) National Sample Cohort for the years 2003-2013, which included data on 107,954 middle-aged and elderly dyslipidemia patients. Among these patients, a time-dependent Cox proportional hazards model was used to estimate the hazard ratios (HRs) of all-cause, cancer, and cardiovascular mortality depending on proportion of days covered (PDC) by statin medication. A total of 3073 (2.85%) individuals died within the study period. Of these individuals, 1143 (1.06%) died from cancer, and 687 (0.64%) died from cardiovascular diseases. Relative to good medication adherence (>80%), moderate (50-80%) (hazard ratio [HR]: 1.28, 95% confidence interval [CI]: 1.14-1.43) and poor (<50%) (HR: 1.58, 95% CI: 1.41-1.78) adherence were associated with increased risk of all-cause mortality. Poor adherence was also associated with increased risk of cancer (HR: 1.33, 95% CI: 1.16-1.52) and cardiovascular (HR: 1.27, 95% CI: 1.06-1.51) mortality. CONCLUSION: Such findings reveal that relative to good statin adherence, moderate and/poor adherence is associated with increased risks of all-cause, cancer, and cardiovascular mortality. Clinicians should assess for dyslipidemia, link statin adherence problems to potential mortality risk, and monitor outcomes in both medication adherence and disease complications.

Lee, Y. T., et al. (2021). "The Mortality and Overall Survival Trends of Primary Liver Cancer in the United States." J Natl Cancer Inst **113**(11): 1531-1541.

BACKGROUND: Recent trends of hepatocellular carcinoma (HCC) mortality and outcome remain unknown in the United States. We investigated the recent trends of primary liver cancer (excluding intrahepatic cholangiocarcinoma) mortality and HCC stage, treatment, and overall survival (OS) in the United States. METHODS: The National Center for Health Statistics Database was analyzed to investigate the trend of primary liver cancer mortality. We analyzed the Surveillance, Epidemiology, and End Results 18 Database to assess the temporal trend of tumor size, stage, treatment, and OS of HCC. We investigated the association between HCC diagnosis year and OS using Cox regression analysis. All statistical tests were 2-sided. RESULTS: During 2000-2018, liver cancer mortality rates increased until 2013, plateaued during 2013-2016 (annual percent change = 0.1%/y, 95% confidence interval [CI] = -2.1%/y to 2.4%/y, P = .92), and started to decline during 2016-2018 (annual percent change = -1.5%/y, 95% CI = -3.2%/y to 0.2%/y, P = .08). However, mortality continues to increase in American Indian and Alaska Native, individuals aged 65 years or older, and in 33 states. There was a 0.61% (95% CI = 0.53% to 0.69%, P < .001) increase in localized stage HCC and a 0.86-mm (95% CI = -1.10 to -0.62 mm, P < .001) decrease in median tumor size per year. The 1-year OS rate increased from 36.3% (95% CI = 34.3% to 38.3%) to 58.1% (95% CI = 56.9% to 59.4%) during 2000-2015, and the 5-year OS rate almost doubled from 11.7% (95% CI = 10.4% to 13.1%) to 21.3% (95% CI = 20.2% to 22.4%) during 2000-2011. Diagnosis year (per year) (adjusted hazard ratio = 0.96, 95% CI = 0.96 to 0.97) was independently associated with OS in multivariable analysis. CONCLUSIONS: Primary liver cancer mortality rates have started to decline in the United States with demographic and state-level variation. With an increasing detection of localized HCC, the OS of HCC has improved over the past decades.

Lei, H., et al. (2021). "Higher mortality in lung cancer patients with COVID-19? A systematic review and meta-analysis." Lung Cancer **157**: 60-65.

OBJECTIVE: Given that the coronavirus disease 2019 (COVID-19) mainly spreads through the respiratory system and is associated with severe pulmonary complications, lung cancer patients may have worse outcomes than those with other tumors. There is no confirmed evidence about the mortality comparison between COVID-19 patients with lung cancer and other tumors. We performed a systematic review and pooled analysis to provide precise estimates of the mortality rate of COVID-19 patients with lung cancer and other tumors. MATERIALS AND METHODS: Our study systemically included and reviewed 13 studies on the characteristics of COVID-19 patients with lung cancer published up to November 1, 2020. The primary endpoint was all-cause mortality. We also compared the all-cause mortality rates in China and other regions as a secondary endpoint. The mortality rate was assessed with a fixed-effects model, which was used to derive the pooled mortality and 95 % con fi dence interval (CI). RESULTS: Thirteen studies from different countries, involving 1,229 patients with both COVID-19 and cancer, were selected for the pooled analysis. A total of 343 deaths were recorded in this population: 86 for lung cancers and 257 for other tumors. The mortality rate varies from 18 % to 60 % for patients with lung cancer and COVID-19 and 10%-41% for other tumor patients with COVID-19. The overall meta-analysis did not show a significant mortality difference for the lung cancer and other tumor subgroups (OR = 1.47, 95 %CI = 0.98-2.20, p = 0.06, I(2) = 23 %). Nevertheless, in regions other than China, the pooled mortality of lung cancer patients with COVID-19 was 42 %, which was significantly higher than that of other tumors (24 %) (OR = 2.73, 95 % CI = 1.54-4.86, p = 0.0006, I(2) = 16 %). CONCLUSION: Appropriate and aggressive preventive measures should be implemented to reduce the risk of COVID-19 in patients with cancer and optimally manage those who contract the infection.

Lei, S., et al. (2021). "Breast cancer incidence and mortality in women in China: temporal trends and projections to 2030." Cancer Biol Med **18**(3): 900-909.

OBJECTIVE: Breast cancer was the most common cancer and the fifth cause of cancer deaths among women in China in 2015. The evaluation of the long-term incidence and mortality trends and the prediction of the future burden of breast cancer could provide valuable information for developing prevention and control strategies. METHODS: The burden of breast cancer in China in 2015 was estimated by using qualified data from 368 cancer registries from the National Central Cancer Registry. Incident cases and deaths in 22 cancer registries were used to assess the time trends from 2000 to 2015. A Bayesian age-period-cohort model was used to project the burden of breast cancer to 2030. RESULTS: Approximately 303,600 new cases of breast cancer (205,100 from urban areas and 98,500 from rural areas) and 70,400 breast cancer deaths (45,100 from urban areas and 24,500 from rural areas) occurred in China in 2015. Urban regions of China had the highest incidence and mortality rates. The most common histological subtype of breast cancer was invasive ductal carcinoma, followed by invasive lobular carcinoma. The age-standardized incidence and mortality rates increased by 3.3% and 1.0% per year during 2000-2015, and were projected to increase by more than 11% until 2030. Changes in risk and demographic factors between 2015 and 2030 in cases are predicted to increase by approximately 13.3% and 22.9%, whereas deaths are predicted to increase by 13.1% and 40.9%, respectively. CONCLUSIONS: The incidence and mortality of breast cancer continue to increase in China. There are no signs that this trend will stop by 2030, particularly in rural areas. Effective breast cancer prevention strategies are therefore urgently needed in China.

Lei, S., et al. (2021). "Global patterns of breast cancer incidence and mortality: A population-based cancer registry data analysis from 2000 to 2020." Cancer Commun (Lond) **41**(11): 1183-1194.

BACKGROUND: Breast cancer is the most commonly diagnosed cancer and leading cause of cancer death among women worldwide but has patterns and trends which vary in different countries. This study aimed to evaluate the global patterns of breast cancer incidence and mortality and analyze its temporal trends for breast cancer prevention and control. METHODS: Breast cancer incidence and mortality data in 2020 were obtained from the GLOBOCAN online database. Continued data from the Cancer Incidence in Five Continents Time Trends, the International Agency for Research on cancer mortality and China National Central Cancer Registry were used to analyze the time trends from 2000 to 2015 through Joinpoint regression, and annual average percent changes of breast cancer incidence and mortality were calculated. Association between Human Development Index and breast cancer incidence and mortality were estimated by linear regression. RESULTS: There were approximately 2.3 million new breast cancer cases and 685,000 breast cancer deaths worldwide in 2020. Its incidence and mortality varied among countries, with the age-standardized incidence ranging from the highest of 112.3 per 100,000 population in Belgium to the lowest of 35.8 per 100,000 population in Iran, and the age-standardized mortality from the highest of 41.0 per 100,000 population in Fiji to the lowest of 6.4 per 100,000 population in South Korea. The peak age of breast cancer in some Asian and African countries were over 10 years earlier than in European or American

countries. As for the trends of breast cancer, the age-standardized incidence rates significantly increased in China and South Korea but decreased in the United States of America (USA) during 2000-2012. Meanwhile, the age-standardized mortality rates significantly increased in China and South Korea but decreased in the United Kingdom, the USA, and Australia during 2000 and 2015. CONCLUSIONS: The global burden of breast cancer is rising fast and varies greatly among countries. The incidence and mortality rates of breast cancer increased rapidly in China and South Korea but decreased in the USA. Increased health awareness, effective prevention strategies, and improved access to medical treatment are extremely important to curb the snowballing breast cancer burden, especially in the most affected countries.

Leimanis Laurens, M., et al. (2020). "Racial/Ethnic Minority Children With Cancer Experience Higher Mortality on Admission to the ICU in the United States." Pediatr Crit Care Med **21**(10): 859-868.

OBJECTIVE: We investigated whether differences in survival exist between children of various racial/ethnic groups with cancer admitted to the PICU. DESIGN: A retrospective multicenter analysis was conducted using Virtual Pediatric Systems data from reporting centers. Demographic information, Pediatric Risk for Mortality III score, and outcome variables were analyzed using mixed-effects logistic regression modeling to assess for differences in mortality. SETTING: One hundred thirty-five PICUs in the United States. PATIENTS: Pediatric patients with cancer admitted to PICUs in the United States. INTERVENTIONS: None. MEASUREMENTS AND MAIN RESULTS: This study details the analysis of 23,128 PICU admissions of 12,232 unique oncology patients representing 3% of all PICU admissions with 1,610 deaths (7.0% case fatality). African American (8.5%) and Hispanic children (8.1%) had significantly higher mortality ($p < 0.05$) compared with Caucasian children (6.3%). Regional analysis showed Hispanic patients to have higher mortality in the West in the United States, whereas African American patients in the South in the United States had higher mortality. A pulmonary disease diagnosis in Hispanics increased odds of mortality (odds ratio, 1.39; 95% CI, 1.13-1.70), whereas a diagnosis of shock/sepsis increased risk for mortality in African Americans (odds ratio, 1.56; 95% CI, 1.11-2.20) compared with Caucasians. There were no differences between races/ethnic groups in the rates of limitations of care. After controlling for Pediatric Risk of Mortality III, PICU length of stay, stem cell transplant status, readmissions, cancer type (solid, brain, hematologic), mechanical ventilation days, and sex, Hispanic (odds ratio, 1.24; 95% CI, 1.05-1.47) and African Americans (odds ratio, 1.37; 95% CI, 1.14-1.66) had significantly higher odds of mortality compared with Caucasians. CONCLUSIONS: The results show that after controlling for severity and cancer type, a child's race, ethnicity, and region of presentation influence mortality in the PICU. This suggests that additional investigation is warranted along with a need to rethink our approach to the evaluation and treatment of critically ill African American and Hispanic children with cancer.

Leitao, F. N. C., et al. (2021). "Breast and cervical cancer mortality in the western Amazon: A time series study between 1980 and 2014." Medicine (Baltimore) **100**(21): e26157.

Among the main types of neoplasms in the female population, breast and cervical cancers are the most important due to their high morbidity and mortality rates. The mortality has been proportionally higher in developing countries. Analysis of the trend of cancer mortality in Brazil revealed a considerable difference in the pattern of deaths between the regions.To analyze the trend of mortality due to breast and cervical cancers in women.Retrospective study of a series of death cases, using secondary data from the mortality information system (SIM) of the Ministry of Health. The deaths were identified as the underlying cause of breast and cervical cancers, including malignant neoplasms of the uterus without other specifications, occurring from 1980 to 2014. Thus, the annual standardized age-specific mortality rates by the world population were applied. For trend analysis, regression models were utilized in which the mortality rates were considered dependent variables and years the independent variable. Polynomial regression models and a Prais-Winsten regression model were adopted.Cervical cancer presented a mortality rate ranging from 2.15 to 10.69 per 100,000 women from 1980 to 2014, with a tendency for stability.Breast cancer mortality rate varied from 3.81 to 11.47 per 100,000 women from 1981 to 2014, indicating a growing trend.There is a significant increase in the mortality rate for breast cancer and stability of cervical cancers in the State of Acre from 1980 to 2014, evidencing a concern in their care and monitoring. Above all, guaranteed access, especially to the population of women at social risk, and the search for effective screening should be emphasized in the formation of the care line and the Health Care Network in the State of Acre.

Leminski, A., et al. (2022). "Increased One-Year Mortality Among Elderly Patients After Radical Cystectomy for Muscle-Invasive Bladder Cancer: A Retrospective, Observational Comparative Study." Clin Interv Aging **17**: 255-263.

INTRODUCTION: Muscle invasive bladder cancer (MIBC) is a common malignancy amongst elderly. Increasing life expectancy, prevalence of smoking, lifelong exposure to environmental pollutants and immunosenescence contribute to growing number of cases. Traditionally, radical cystectomy (RC) with pelvic lymph node dissection (PLND) constituted the mainstay of treatment for MIBC, but despite proven feasibility in elderly population, it has been associated with significant burden of morbidity, mortality, and complications. STUDY OBJECTIVE: We aimed to re-evaluate the safety and efficacy of RC amongst the elderly patients with MIBC. MATERIAL AND METHODS: This single-center, retrospective, observational comparative study was conducted among 568 patients who underwent RC due to MIBC between 2003 and 2021. We evaluated the influence of chronological age (<70 vs >/=70 years) on clinical, demographic, and pathological variables related to MIBC and RC. RESULTS: Elderly patients had similar clinical and pathological features of disease compared to their younger counterparts; nonetheless, they more often received simplified urinary diversion, ie ureterostomy (60.25% vs 39.33%, p<0.001) and had no PLND (15.76% vs 8.5%, p=0.01) during RC. Furthermore, more elderly patients were treated for secondary MIBCs and fewer had history of smoking. Severe complication and 90-day mortality rates were comparable between groups; however, the elderly had significantly higher all-cause mortality at one year post RC (46.67% vs 33.25%, p=0.003). On multivariate analysis, one-year mortality risk was independently associated with elderly age (HR=2.119, 95% CI: 1.227-3.660, p=0.007), rural residency (HR=1.760, 95% CI: 1.043-2.968, p=0.034), extravesical extension of tumor (HR=2.109, 95% CI: 1.155-3.850, p=0.015), lymph node metastasis (HR=2.268, 95% CI: 1.290-3.987, p=0.004) and omission of PLND (HR=6.064, 95% CI: 2.926-12.568, p<0.001). CONCLUSION: Radical cystectomy in elderly patients is associated with significant one-year mortality. Our study emphasizes the unmet need for considerate planning of treatment for MIBC in potentially vulnerable groups of elderly patients. Efforts are needed to reliably identify those unlikely to benefit from surgery and facilitate patient-centered choice of alternative therapies.

Lent, A. B., et al. (2021). "The association between breast cancer capacity and resources with incidence and mortality in Arizona's low populous counties." Rural Remote Health **21**(3): 6357.

INTRODUCTION: While cancer deaths have decreased nationally, declines have been much slower in rural areas than in urban areas. Previous studies on rural cancer service capacity are limited to specific points along the cancer care continuum (eg screening, diagnosis or treatment) and require updating to capture the current rural health landscape since implementation of the 2010 Affordable Care Act in the USA. The association between current rural cancer service capacity across the cancer care continuum and cancer incidence and death is unclear. This cross-sectional study explored the association between breast cancer service capacity and incidence and mortality in Arizona's low populous counties. METHODS: To measure county-level cancer capacity, clinical organizations operating within low populous areas of Arizona were surveyed to assess on-site breast cancer services provided (screening, diagnosis and treatment) and number of healthcare providers were pulled from Centers for Medicare and Medicaid Services National Provider Identifier database. The number of clinical sites and healthcare providers were converted to county-level per capita rates. Rural-Urban Continuum codes were used to designate rural or urban county status. Age-adjusted county-level breast cancer incidence and death rates from 2010 to 2016 were obtained from the Arizona Department of Health Services, Arizona Cancer Registry. Descriptive statistics were used to summarize the results. Multivariate regression was used to evaluate the association between cancer service capacity and incidence and mortality in 13 out of Arizona's 15 counties. RESULTS: Rural counties had more per capita clinical sites (20.4) than urban counties (8.9) (p=0.02). Urban counties had more per capita pathologists (1.0) than rural counties (0) (p≤0.01). In addition to zero pathologists, rural counties had zero medical oncologists. Rural county status was associated with a decrease in breast cancer incidence (β=-20.1, 95% confidence interval: -37.2-3.1). CONCLUSION: While Arizona's sparsely populated rural counties may have more physical infrastructure per capita, these services are dispersed over vast geographic areas. They lack specialists providing cancer services. Non-physician clinical providers may be more prevalent in rural areas and represent opportunities for improving access to cancer preventive services and care. Compared to urban counties, rural county status was associated with lower detected breast cancer incidence rates although there were no statistically significant differences in breast cancer mortality. Other factors may contribute to rural-urban differences in breast cancer incidence. Future research should explore these factors and the association between cancer capacity and local resources because the use of county-level data represents a challenge in Arizona, where counties average over 19 425 km2 (7500 square miles).

Leoce, N. M., et al. (2021). "Modeling risks of cardiovascular and cancer mortality following a

diagnosis of loco-regional breast cancer." Breast Cancer Res **23**(1): 91.

BACKGROUND: Many women with breast cancer also have a high likelihood of cardiovascular mortality, and while there are several cardiovascular risk prediction models, none have been validated in a cohort of breast cancer patients. We first compared the performance of commonly-used cardiovascular models, and then derived a new model where breast cancer and cardiovascular mortality were modeled simultaneously, to account for the competing risk endpoints and commonality of risk factors between the two events. METHODS: We included 20,462 women diagnosed with stage I-III breast cancer between 2000 and 2010 in Kaiser Permanente Northern California (KPNC) with follow-up through April 30, 2015, and examined the performance of the Framingham, CORE and SCOREOP cardiovascular risk models by area under the receiver operating characteristic curve (AUC), and observed-to -expected (O/E) ratio. We developed a multi-state model based on cause-specific hazards (CSH) to jointly model the causes of mortality. RESULTS: The extended models including breast cancer characteristics (grade, tumor size, nodal involvement) with CVD risk factors had better discrimination at 5-years with AUCs of 0.85 (95% CI 0.83, 0.86) for cardiovascular death and 0.80 (95% CI 0.78, 0.87) for breast cancer death compared with the existing cardiovascular models evaluated at 5 years AUCs ranging 0.71-0.78. Five-year calibration for breast and cardiovascular mortality from our multi-state model was also excellent (O/E = 1.01, 95% CI 0.91-1.11). CONCLUSION: A model incorporating cardiovascular risk factors, breast cancer characteristics, and competing events, outperformed traditional models of cardiovascular disease by simultaneously estimating cancer and cardiovascular mortality risks.

Leone, J. P., et al. (2022). "Estimating long-term mortality in women with hormone receptor-positive breast cancer: The 'ESTIMATE' tool." Eur J Cancer **173**: 20-29.

PURPOSE: The risk of breast cancer-specific mortality (BCSM) persists for at least 20 years from diagnosis. Estimating the risk of BCSM over this extended period along with competing risks of death would aid clinical decision-making. We aimed to develop an interactive tool called 'ESTIMATE', to explore the Surveillance, Epidemiology, and End Results (SEER) registry to quantify residual risks of BCSM, non-BCSM and all-cause mortality in non-metastatic, hormone receptor (HR)-positive breast cancer patient subgroups at any given time after diagnosis, up to 20 years. METHODS: Using SEER data, we included 264,237 women with invasive, non-metastatic, HR-positive breast cancer diagnosed from 1990 to 2006. We developed a tool that provides a nonparametric estimate of the residual cumulative risk of BCSM and non-BCSM by year 20 after any specified time from initial diagnosis, among patients defined by baseline clinical and pathologic variables, using Gray's subdistribution method. RESULTS: ESTIMATE allows the user to input patient and tumour characteristics and the preferred timeframe. For example, patients in the age group of 40-49 diagnosed with T1cN1, grade II breast cancer who survived 7 years, have a 14% (95% confidence interval [CI]: 11.9%-16.1%) residual cumulative risk of BCSM in the next 13 years, and a 6.4% (95% CI: 4.7%-8.1%) residual cumulative risk of non-BCSM over the same period. CONCLUSIONS: ESTIMATE provides population-based risks of BCSM, non-BCSM and all-cause mortality through 20 years after diagnosis of HR-positive breast cancer, based on patient and tumour characteristics. ESTIMATE can inform discussions about prognosis, a balance between competing risks and aid clinical decision-making.

Leone, J. P., et al. (2021). "Twenty-year risks of breast cancer-specific mortality for stage III breast cancer in the surveillance, epidemiology, and end results registry." Breast Cancer Res Treat **187**(3): 843-852.

PURPOSE: We aimed to report the 20-year risk of breast cancer-specific mortality (BCSM), report the risk of BCSM conditional on having survived 5 years, and identify factors associated with late deaths in stage III breast cancer. METHODS: Using Surveillance, Epidemiology, and End Results data, we included women with stage III breast cancer diagnosed from 1990 to 2005. We excluded women with unknown hormone receptor (HR) status, women who did not undergo resection of the primary tumor or axillary nodes, or unknown cause of death. We estimated risks of BCSM using cumulative incidence function and used Fine and Gray regression to identify factors associated with late deaths. RESULTS: Final sample was 36,500 patients with 14 years of median follow-up. For each stage subgroup, the risk of BCSM at 20 years was significantly higher for HR-negative vs HR-positive tumors (IIIA: 49.8% vs 43.2%, $P < 0.0001$; IIIB: 60.9% vs 47.6%, $P < 0.0001$; IIIC: 68.7% vs 63.1%, $P < 0.0001$). Compared with the risks of non-BCSM, the risks of BCSM at 20 years were four times higher in stage IIIC HR-positive disease and seven times higher in stage IIIC HR-negative disease. Risks of BCSM conditional on having survived 5 years depended on tumor size, nodal status, race, and tumor grade for HR-positive disease and depended on tumor size, nodal status, and age for HR-negative disease. CONCLUSIONS: In stage III breast cancer, the risk of BCSM at 20 years is very high and remains important

even beyond the first 5 years in both HR-positive and HR-negative disease. Late BCSM depends on traditional clinicopathologic factors.

Li, Q., et al. (2022). "The associations of healthy lifestyle index with breast cancer incidence and mortality in a population-based study." Breast Cancer **29**(6): 957-966.

PURPOSE: To investigate how a healthy lifestyle index (HLI) is associated with breast cancer risk and survival in a population-based breast cancer study. METHODS: The study included 1319 breast cancer cases and 1310 controls from the population-based Long Island Breast Cancer Study Project and its follow-up study where vital status was ascertained using the National Death Index (521 deaths, 210 from breast cancer; median follow-up 214.5 months). HLI scores were generated from body mass index, physical activity, intake of plant and animal foods, alcohol consumption, breastfeeding, and smoking, with higher values corresponding to healthier behaviors obtained from baseline questionnaire. Multivariable logistic and Cox regression models were used to estimate breast cancer odds ratios (ORs) and mortality hazards ratios (HRs), respectively. RESULTS: Compared to women in the low HLI tertile, a significant reduction in risk of breast cancer was observed for women in the intermediate (OR = 0.78, 95% CI 0.64-0.93) and high (OR = 0.73, 95% CI 0.60-0.88) tertiles; a one-point increase in HLI score was associated with a 14% reduction in breast cancer risk (OR = 0.86, 95% CI 0.80-0.93). For survival, a significant reduction in all-cause mortality was also observed in women in the intermediate (HR = 0.68, 95% CI 0.56-0.84) and high (HR = 0.72, 95% CI 0.58-0.88) HLI tertiles with a 17% reduction in all-cause mortality (HR = 0.83, 95% CI 0.76-0.91) for one-point increase in HLI score. These inverse associations were more prominent among postmenopausal women. CONCLUSION: A healthy lifestyle is beneficial not only in reducing breast cancer risk but also in improving overall survival after breast cancer diagnosis, especially among postmenopausal women.

Li, Q., et al. (2022). "Association of Physical Activity Intensity with All-Cause Mortality in Cancer Survivors: A National Prospective Cohort Study." Cancers (Basel) **14**(23).

We designed this study to investigate the associations between physical activity (PA) and the risk of all-cause mortality in cancer survivors using a nationally representative cohort of US adults. This cohort study included 13 cycles of the National Health Interview Surveys, and by matching participants with the National Death Index (2015), survival status was determined. The main outcome was all-cause mortality during follow-up. A total of 20,088 participants aged 62.2 (15.9) years (62.4% women) were analyzed. After an average follow-up of 117.5 months, 7214 (35.9%) participants died. Compared with inactive cancer survivors, we observed a 25% lower all-cause mortality risk among participants performing PA 10 min to 1 h/week (hazard ratio [HR] = 0.75, 95% confidence interval [CI] = 0.67-0.85), a 28% lower risk among those performing PA 1-2.5 h/week (HR = 0.72, 95% CI = 0.67-0.78), a 34% lower risk among those performing PA 2.5-5 h/week (HR = 0.66, 95% CI = 0.60-0.72), a 37% lower risk among those performing PA 5-7.5 h/week (HR = 0.63, 95% CI = 0.56-0.70), a 47% lower risk among those performing PA 7.5-13.3 h/week (HR = 0.53, 95% CI = 0.47-0.61), and a 43% lower risk among those performing PA 13.3-24 h/week (adjusted HR = 0.53, 95% CI = 0.49-0.66). In cancer survivors, leisure-time PA was associated with a lower all-cause mortality. Inactive cancer survivors should be encouraged to perform more PA to reduce the risk of all-cause mortality.

Li, Q., et al. (2021). "Limited Lymph Node Resection Does Not Decrease Postoperative Mortality After Esophagectomy in Octogenarians With Thoracic Esophageal Cancer." J Surg Res **259**: 538-545.

BACKGROUND: Octogenarians with esophageal cancer typically have a poor physical condition, reduced physiological reserves, and high postoperative mortality (POM). Extensive lymph node dissection increases surgical trauma and postoperative complications. The purpose of this study was to examine the associations between the number of dissected lymph nodes and short-term and long-term postoperative outcomes in octogenarians with thoracic esophageal cancer. METHODS: We examined the data of patients from the Surveillance, Epidemiology, and End Results database. We divided the patients into two groups in accordance with the number of lymph nodes dissected: patients with <15 examined lymph nodes (eLNs) and patients with >/=15 eLNs. Mortality was quantified at 30, 60, and 90 d after surgery. Univariable and multivariable logistic regression analyses were performed to identify predictors of 90-day mortality. Kaplan-Meier analysis and the log-rank test were used to analyze the overall survival and cause-specific survival of the patients. RESULTS: A total of 208 octogenarians with thoracic esophageal cancer were included in the analysis. The 30-day POM rates were 10.3% and 6.9%, the 60-day POM rates were 16.9% and 13.9%, and the 90-day POM rates were 21.3% and 19.4% for patients with <15 eLNs and >/=15 eLNs, respectively. However, the differences in POM between the two groups were statistically nonsignificant (all P > 0.05). In accordance with the multivariable logistic regression analysis, age and

marital status were significantly associated with 90-day POM. Furthermore, no significant difference was found between the groups in terms of long-term survival. The 5-year overall survival rates were 29% and 26.8% (P = 0.719) and the 5-year cause-specific survival rates were 43.2% and 34.1% (P = 0.446) in patients with <15 eLNs and >/=15 eLNs, respectively. CONCLUSIONS: We have demonstrated that octogenarians undergoing esophagectomy are associated with an unacceptably high POM, and less extensive lymph node resection does not decrease POM. Octogenarians may not benefit from esophagectomy with lymphadenectomy. Additional studies need to be conducted to further guide clinicians performing highly selective esophagectomy.

Li, R., et al. (2022). "Comparison of Secular Trends in Esophageal Cancer Mortality in China and Japan during 1990-2019: An Age-Period-Cohort Analysis." Int J Environ Res Public Health **19**(16).

Esophageal cancer is a prevalent and often fatal malignancy all over the world, with China and Japan bearing a disproportionately high burden. Consequently, we explored and compared the long-term changes in esophageal cancer mortality in China and Japan from 1990 to 2019 to see if there were any etiological clues. From 1990 to 2019, data on mortality in China and Japan were gathered from the Global Burden of Disease Study 2019 (GBD 2019). The age-period-cohort (APC) model was utilized to evaluate the effects of age, period, and cohort. Between 1990 and 2019, the age-standardized mortality rates (ASMRs) for esophageal cancer fell in both nations, with China showing a tremendous reduction after 2005. The overall net drifts per year were more impressive in China (-5.22% [95% CI, -5.77 to -4.68] for females, -1.98% [-2.22 to -1.74] for males) than in Japan (-0.50% [-0.91 to -0.08] for females, -1.86% [-2.12 to -1.59] for males), and the local drift values in both countries were less than zero in all age groups for both sexes. The longitudinal age curves of esophageal cancer mortality increased as age advances and the sex disparity gradually exacerbates with age. The period and cohort effects were uncovered to have similar declining patterns for both sexes in both nations; however, the improvement of cohort effects for China's younger generation has stagnated. The ASMRs, period effects, and cohort effects have decreased for both countries and sexes over the 1990-2019 period. The decline in cohort effects for China's younger generation has plateaued, possibly due to the rising rates of smoking and obesity among Chinese youngsters. Comprehensive population-level treatments aimed at smoking cessation, obesity prevention, and gastrointestinal endoscopy screening should be carried out immediately, particularly for men and older birth cohorts at a higher risk of esophageal cancer.

Li, W., et al. (2021). "A Novel Nomogram and Risk Classification System Predicting the Cancer-Specific Mortality of Patients with Initially Diagnosed Metastatic Cutaneous Melanoma." Ann Surg Oncol **28**(7): 3490-3500.

BACKGROUND: Cutaneous melanoma and distant organ metastasis has varying outcomes. Considering all prognostic indicators in a prediction model might assist in selecting cases who could benefit from a personalized therapy strategy. OBJECTIVE: This study aimed to develop and validate a prognostic model for patients with metastatic melanoma. METHODS: A total of 1535 cases diagnosed with metastatic cutaneous melanoma (stage IV) were identified from the Surveillance, Epidemiology, and End Results database. Patients were randomly divided into the training (n = 1023) and validation (n = 512) cohorts. A prognostic nomogram was established based predominantly on results from the competing-risk regression model for predicting cancer-specific death (CSD). The area under the time-dependent receiver operating characteristic curve (AUC), calibration curves, and decision curve analyses (DCAs) were used to evaluate the nomogram. RESULTS: No significant differences were observed in the clinical characteristics between the training and validation cohorts. In the training cohort, patient-, tumor-, and treatment-related predictors of CSD for metastatic melanoma included age, sex, race, marital status, insurance, American Joint Committee on Cancer T and N stage, number of metastatic organs, surgical treatment, and chemotherapy. All these factors were used for nomogram construction. The time-dependent AUC values of the training and validation cohorts suggested a favorable performance and discrimination of the nomogram. The 6-, 12-, and 18-month AUC values were 0.706, 0.700, and 0.706 in the training cohort, and 0.702, 0.670, and 0.656 in the validation cohort, respectively. The calibration curves for the probability of death at 6, 12, and 18 months showed acceptable agreement between the values predicted by the nomogram and the observed outcomes in both cohorts. DCA curves showed good positive net benefits in the prognostic model among most of the threshold probabilities at different time points (death at 6, 12, and 18 months). Based on the total nomogram scores of each case, all patients were divided into the low-risk (n = 511), intermediate-risk (n = 512), and high-risk (n = 512) groups, and the risk classification could identify cases with a high risk of death in both cohorts. CONCLUSIONS: A predictive nomogram and a corresponding risk classification system for CSD in patients with metastatic melanoma were developed in

this study, which may assist in patient counseling and in guiding clinical decision making for cases with metastatic melanoma.

Li, W., et al. (2022). "Attributable fraction of tobacco smoking on selected cancer deaths in the past decade using mortality case-control study in Tianjin, China." Tob Induc Dis **20**: 75.

INTRODUCTION: This study aims to estimate the impact of smoking-attributable mortality of selected cancers, in the period 2010-2019 in Tianjin, China. METHODS: A case-control study was conducted to assess the smoking-attributed major causes of cancer deaths. Unmatched multiple logistic regression was used to calculate mortality risk ratios. RESULTS: Smoking-attributable cancer deaths were 23709 (28.87%) among adult males and 8648 (13.37%) among adult females in the period 2010-2019 in Tianjin, China. Lung cancer remains the largest cause of smoking-attributable deaths; among men, the death rates were 49.06% of lung cancers, 27.55% of mouth, pharynx, larynx, or esophagus cancers, 13.56% of kidney and other urinary cancers, and 10.11% of liver cancers; among women the corresponding death rates were 31.56% of lung cancers and 10.59% of the mouth, pharynx, larynx, or esophagus cancer, 10.56% of bladder cancers. Smoking-attributed cancer deaths in men increased from 1817 in 2010 to 2695 in 2019; for women, the number remained stable at just over 800 per year during the past decade. CONCLUSIONS: At least one in three cancer deaths in men and one in six in women would be potentially preventable through appropriate control of tobacco smoking in Tianjin, China. Effective control programs against tobacco smoking should be further implemented.

Li, Y., et al. (2021). "Television Viewing Time and the Risk of Colorectal Cancer Mortality among Japanese Population: The JACC Study." Cancer Res Treat **53**(2): 497-505.

PURPOSE: Sedentary behavior attributes to the increased risk of some cancers and all-cause mortality. The evidence is limited for the association between television (TV) viewing time, a major sedentary behavior, and risk of colorectal cancer death. We aimed to examine this association in Japanese population. MATERIALS AND METHODS: A prospective cohort study encompassed of 90,834 men and women aged 40-79 years with no prior history of colorectal cancer who completed a self-administered food frequency questionnaire, and provided their TV viewing information. The participants were followed-up from 1988-1990 to the end of 2009. The hazard ratios (HRs) and 95% confidence intervals (CIs) were calculated by the Cox proportional hazard regression for risk of colorectal cancer mortality according to TV viewing time. RESULTS: During the median 19.1-year follow-up period, we documented 749 (385 men and 364 women) colorectal cancer deaths. The multivariable-adjusted HRs for mortality from colorectal cancer were 1.11 (0.88-1.41) for 1.5 to < 3 hr/day, 1.14 (0.91-1.42) for 3 to < 4.5 hr/day and 1.33 (1.02-1.73) for >/= 4.5 hr/day in comparison to < 1.5 hr/day TV watching; p-trend=0.038, and that for 1-hour increment in TV viewing time was 1.06 (1.01-1.11). Moreover, the multivariable-adjusted HR (95%CI) of colon cancer for 1-hour increment in TV viewing time was 1.07 (1.02-1.13). Age, body mass index, and level of leisure-physical activity did not show significant effect modifications on the observed associations. CONCLUSION: TV viewing time is associated with the increased risk of colorectal cancer mortality among Japanese population, more specifically colon rather than rectal cancer.

Li, Y., et al. (2022). "Low Serum Bicarbonate Levels Increase the Risk of All-Cause, Cardiovascular Disease, and Cancer Mortality in Type 2 Diabetes." J Clin Endocrinol Metab **107**(11): 3055-3065.

CONTEXT: The evidence regarding bicarbonate status and mortality among diabetes is scarce. OBJECTIVE: The purpose of this study was to investigate the associations of bicarbonate concentrations with risk of all-cause, cardiovascular disease (CVD), and cancer mortality among patients with type 2 diabetes (T2D). METHODS: This study included 8163 adult diabetic patients from the National Health and Nutrition Examination Survey (NHANES), 1999 to 2018. Death outcomes were ascertained by linkage to National Death Index records through 31 December 2019. The Cox proportional-risk model was used to estimate hazard ratios (HR) and 95% CIs for mortality from all causes, CVD, and cancer. The mediating effects of 11 metabolic, cardiovascular, and renal biomarkers were evaluated using a logistic regression model within a counterfactual framework. RESULTS: During 8163 person-years of follow-up, 2310 deaths were documented, including 659 CVD deaths and 399 cancer deaths. After multivariate adjustment, lower serum bicarbonate levels were significantly linearly correlated with higher all-cause, CVD, and cancer mortality: The risk of all-cause death increased by 40%, the risk of CVD death increased by 48%, and the risk of cancer death increased by 84% compared with the normal group (all P < .05). Altered levels of estimated glomerular filtration rate explained 12.10% and 16.94% of the relation between serum bicarbonate with all-cause and CVD mortality, respectively. Total cholesterol mediated 4.70% and 10.51% of the associations of all-cause and CVD mortality, respectively. CONCLUSION: Lower serum bicarbonate concentrations were significantly

associated with higher all-cause, CVD, and cancer mortality. These findings suggest that maintaining adequate bicarbonate status may lower mortality risk in individuals with T2D.

Li, Y., et al. (2021). "Association of Mitochondrial DNA Copy Number and Telomere Length with Prevalent and Incident Cancer and Cancer Mortality in Women: A Prospective Swedish Population-Based Study." Cancers (Basel) **13**(15).

Changes in mitochondrial DNA copy number (mtDNA-CN) and telomere length have, separately, been proposed as risk factors for various cancer types. However, those results are conflicting. Here, mtDNA-CN and relative telomere length were measured in 3225 middle-aged women included in a large population-based prospective cohort. The baseline mtDNA-CN in patients with prevalent breast cancer was significantly higher (12.39 copies/microL) than cancer-free individuals. During an average of 15.2 years of follow-up, 520 patients were diagnosed with cancer. Lower mtDNA-CN was associated with decreased risk of genital organ cancer (hazard ratio (HR), 0.84), and shorter telomere length was associated with increased risk of urinary system cancer (HR, 1.79). Furthermore, mtDNA-CN was inversely associated with all-cause (HR, 1.20) and cancer-specific mortality (HR, 1.21) when considering all cancer types. Surprisingly, shorter telomere length was associated with decreased risk of cancer-specific mortality when considering all cancer types (HR, 0.85). Finally, lower mtDNA-CN and shorter telomere length were associated with increased risk of both all-cause and cancer-specific mortality in genital organ cancer patients. In this study population, we found that mtDNA-CN and telomere length were significantly associated with prevalent and incident cancer and cancer mortality. However, these associations were cancer type specific and need further investigation.

Li, Y., et al. (2021). "Influence of Statin Therapy on the Incidence of Cardiovascular Events, Cancer, and All-Cause Mortality in People Living With HIV: A Meta-Analysis." Front Med (Lausanne) **8**: 769740.

Background: Possible influences of statin therapy on the risk of cardiovascular events, cancer, and all-cause mortality in people living with HIV (PLWH) remain unclear. We performed a meta-analysis to systematically evaluate the efficacy of statin in PLWH. Methods: Relevant cohort studies were retrieved via a search of the Medline, the Embase, and the Web of Science databases until June 14, 2021. The data were combined with a random-effects model by incorporating the between-study heterogeneity. Results: A total of 12 multivariate cohort studies with 162,252 participants were eligible for the meta-analysis and 36,253 (22.3%) of them were statin users. Pooled results showed that statin use was independently related to a reduced mortality risk in PLWH [adjusted risk ratio (RR): 0.56, 95% CI: 0.44 to 0.72, $p < 0.001$, $I(2) = 41\%$]. In addition, results of the meta-analysis showed that statin use was not significantly associated with a reduced risk of cardiovascular events in PLWH compared to the statin non-users (RR: 1.14, 95% CI: 0.80 to 1.63, $p = 0.48$, $I(2) = 42\%$). However, statin use was significantly related to a reduced risk of cancer in PLWH (RR: 0.73, 95% CI: 0.58 to 0.93, $p = 0.009$, $I(2) = 49\%$). Sensitivity analyses by excluding one study at a time showed consistent results. No significant publication biases were observed. Conclusion: Statin use is associated with reduced all-cause mortality in PLWH. In addition, statin use is related to a reduced risk of cancer, although the risk of cardiovascular events seems not significantly affected.

Li, Z., et al. (2021). "Novel Dietary and Lifestyle Inflammation Scores Directly Associated with All-Cause, All-Cancer, and All-Cardiovascular Disease Mortality Risks Among Women." J Nutr **151**(4): 930-939.

BACKGROUND: Exogenous exposures collectively may contribute to chronic, low-grade inflammation and increase risks for major chronic diseases and mortality. We previously developed, validated, and reported a novel, FFQ-based and lifestyle questionnaire-based, inflammation biomarker panel-weighted, predominantly whole foods-based 19-component dietary inflammation score (DIS) and 4-component lifestyle inflammation score (LIS; comprising physical activity, alcohol intake, BMI, and current smoking status). Both scores were more strongly associated with circulating biomarkers of inflammation in 3 populations than were previously reported dietary inflammation indices. Associations of the DIS and LIS with mortality risk have not been reported. OBJECTIVES: To investigate separate and joint associations of the DIS and LIS with all-cause, all-cancer, and cardiovascular disease (CVD) mortality risks in the prospective Iowa Women's Health Study (1986-2012; n = 33,155 women, ages 55-69 years, of whom 17,431 died during follow-up, including 4379 from cancer and 6574 from CVD). METHODS: We summed each study participant's scores' components, weighted by their published weights, to yield the participant's inflammation score; a higher score was considered more pro-inflammatory. We assessed DIS and LIS mortality associations using multivariable Cox proportional hazards regression. RESULTS: Among participants in the highest relative to the lowest DIS and LIS quintiles, the adjusted HRs for all-cause mortality were 1.11 (95% CI: 1.05-1.16) and 1.60 (95% CI: 1.53-1.68), respectively; for all-cancer mortality

were 1.07 (95% CI: 0.97-1.17) and 1.51 (95% CI: 1.38-1.66), respectively; and for CVD mortality were 1.12 (95% CI: 1.03-1.21) and 1.79 (95% CI: 1.66-1.94), respectively (all Ptrend values < 0.01). Among those in the highest relative to the lowest joint LIS/DIS quintiles, the HRs for all-cause, all-cancer, and all-CVD mortality were 1.88 (95% CI: 1.71-2.08), 1.82 (95% CI: 1.50-2.20), and 1.92 (95% CI: 1.64-2.24), respectively. CONCLUSIONS: More pro-inflammatory diets and lifestyles, separately but especially jointly, may be associated with higher all-cause, all-cancer, and all-CVD mortality risks among women.

Lian, T. and X. Zhang (2022). "Tyrosine Kinase Inhibitors In Reduction Of Mortality Of Non-Small Cell Lung Cancer: A Meta-Analysis." Comb Chem High Throughput Screen.

BACKGROUND: Tyrosine kinase inhibitors are widely used in the treatment of non-small cell lung cancer. However, exact role of these inhibitors particularly in the reduction of mortality of non-small cell lung cancer is unclear so far. As a result, we used RevMan 5 to conduct a meta-analysis of accessible data from randomised clinical trials. METHODS: The studies were categorised based on the inclusion and exclusion criteria after being collected from PubMed using appropriate MeSH terms. The fixed or random effect model was used based on heterogeneity among studies. The overall estimate was estimated as an odd ratio with a confidence interval of 95 %. The heterogeneity among studies was calculated by I2 and Cochrane Q test. The qualitative analysis of publication bias was done using funnel plot. RESULTS: The overall estimate measures [OR 1.02 (0.83, 1.25)] have shown non-significant role of tyrosine kinase inhibitors in reduction of deaths of non-small cell lung cancer patients as compared to non-tyrosine kinase inhibitors group. The subgroup analysis of individual tyrosine kinase inhibitors (erlotinib, gefitinib, afatinib, osimertinib and vandetanib) has also shown similar kind of findings. CONCLUSION: Based on available data, there is no significant role of tyrosine kinase inhibitors in the reduction of deaths of non-small cell lung cancer patients.

Liang, J., et al. (2021). "Clinical characteristics and risk factors for mortality in cancer patients with COVID-19." Front Med **15**(2): 264-274.

Patients with cancer are at increased risk of severe infections. From a cohort including 3060 patients with confirmed COVID-19, 109 (3.4%) cancer patients were included in this study. Among them, 23 (21.1%) patients died in the hospital. Cancer patients, especially those with hematological malignancies (41.6%), urinary carcinoma (35.7%), malignancies of the digestive system (33.3%), gynecological malignancies (20%), and lung cancer (14.3%), had a much higher mortality than patients without cancer. A total of 19 (17.4%) cancer patients were infected in the hospital. The clinical characteristics of deceased cancer patients were compared with those of recovered cancer patients. Multivariate Cox regression analysis indicated that a Nutritional Risk Screening (NRS2002) score $\geqslant 3$ (adjusted hazard ratio (HR) 11.00; 95% confidence interval (CI) 4.60-26.32; $P < 0.001$), high-risk type (adjusted HR 18.81; 95% CI 4.21-83.93; $P < 0.001$), tumor stage IV (adjusted HR 4.26; 95% CI 2.34-7.75; $P < 0.001$), and recent adjuvant therapy (< 1 month) (adjusted HR 3.16; 95% CI 1.75-5.70; $P < 0.01$) were independent risk factors for in-hospital death after adjusting for age, comorbidities, D-dimer, and lymphocyte count. In conclusion, cancer patients showed a higher risk of COVID-19 infection with a poorer prognosis than patients without cancer. Cancer patients with high-risk tumor, NRS2002 score $\geqslant 3$, advanced tumor stage, and recent adjuvant therapy (< 1 month) may have high risk of mortality.

Liang, X., et al. (2020). "Association between prediagnosis depression and mortality among postmenopausal women with colorectal cancer." PLoS One **15**(12): e0244728.

BACKGROUND: There are no epidemiologic data on the relation of depression before colorectal cancer diagnosis to colorectal cancer mortality among women with colorectal cancer, especially those who are postmenopausal. Our aim was to fill this research gap. METHODS: We analyzed data from a large prospective cohort in the US, the Women's Health Initiative (WHI). The study included 2,396 women with incident colorectal cancer, assessed for depressive symptoms and antidepressant use before cancer diagnosis at baseline (screening visit in the WHI study) during 1993-1998. Participants were followed up from cancer diagnosis till 2018. We used Cox proportional hazards regression to estimate adjusted hazard ratios (HRs) between depression (depressive symptoms or antidepressant use) at baseline, and all-cause mortality and colorectal cancer-specific mortality. RESULTS: Among women with colorectal cancer, there was no association between baseline depression and all-cause mortality or colorectal cancer-specific mortality after adjusting for age or multiple covariates. CONCLUSION: Among women with colorectal cancer, there was no statistically significant association between depression before colorectal cancer diagnosis and all-cause mortality or colorectal cancer-specific mortality. Further studies are warranted to assess depressive symptoms and antidepressant use, measured at multiple points from baseline to diagnosis, and their

interactions with specific types of colorectal cancer treatment on the risk of death from colorectal cancer.

Liang, Z., et al. (2022). "Dietary Inflammatory Index and Mortality from All Causes, Cardiovascular Disease, and Cancer: A Prospective Study." Cancers (Basel) **14**(19).

The Energy-adjusted Dietary Inflammatory Index (E-DII(TM)) is a comprehensive, literature-derived index for assessing the effect of dietary constituents on inflammatory biomarkers and inflammation-related chronic diseases. Several studies have examined the association between E-DII scores and mortality, with results that vary across populations. Therefore, in the present study, we aimed to investigate the potential association between E-DII scores and all-cause, cardiovascular disease (CVD), and cancer mortality using data from the Prostate, Lung, Colorectal and Ovarian (PLCO) Screening Trial. E-DII scores, calculated based on a food-frequency questionnaire, were analyzed both as a continuous variable and after categorization into quintiles. A multivariate Cox proportional hazards model was used to estimate hazard ratios (HRs) and 95% confidence intervals (CIs). A total of 101,832 individuals were included, with 24,141 deaths recorded after a median of 17.0 years of follow-up. In multivariable-adjusted analyses, the E-DII score was significantly associated with all-cause mortality. The HR (95% CI) in the highest E-DII quintile compared to the lowest quintile was 1.23 (1.18-1.29). The E-DII was also statistically related to CVD mortality (Q5 vs. Q1; HR, 1.30 [95% CI, 1.20-1.41]) and cancer mortality (Q5 vs. Q1; HR, 1.14 [95% CI, 1.06-1.24]). Similar results were obtained from sensitivity analyses and subgroup analyses. In conclusion, the inflammatory potential of the diet, as calculated by the E-DII, was significantly associated with overall and CVD- and cancer-specific mortality risk in the PLCO study.

Liao, K. C., et al. (2021). "Quality of Life as a Mediator between Cancer Stage and Long-Term Mortality in Nasopharyngeal Cancer Patients Treated with Intensity-Modulated Radiotherapy." Cancers (Basel) **13**(20).

BACKGROUND: Quality of life (QoL) attained before, during, or after treatments is recognized as a vital factor associated with therapeutic benefits in cancer patients. This nasopharyngeal cancer (NPC) patient longitudinal study assessed the relationship among QoL, cancer stage, and long-term mortality in patients with nasopharyngeal carcinoma (NPC) treated with intensity-modulated radiotherapy (IMRT). PATIENTS AND METHODS: The European Organization for Research and Treatment of Cancer (EORTC) core QoL questionnaire (QLQ-C30) and the head and neck cancer-specific QoL questionnaire module (QLQ-HN35) were employed to evaluate four-dimensional QoL outcomes at five time points: pre- (n = 682), during (around 40 Gy) (n = 675), 3 months (n = 640), 1 year (n = 578) and 2 years post-IMRT (n = 505), respectively, for 682 newly diagnosed NPC patients treated between 2003 and 2017 at a single institute. The median followed-up time was 7.5 years, ranging from 0.3 to 16.1 years. Generalized estimating equations, multivariable proportional hazards models, and Baron and Kenny's method were used to assess the investigated effects. RESULTS: Advanced AJCC stage (III-IV) patients revealed a 2.26-fold (95% CI-1.56 to 3.27) higher covariate-adjusted mortality risk than early-stage (I-II) patients. Compared with during IMRT, advanced-stage patients had a significantly low global health QoL and a significantly high QoL-HN35 symptom by a large magnitude at pre-, 3 months, and 2 years post-IMRT. QoL scales at pre-IMRT, 1 year, and 2 years post-IMRT were significantly associated with mortality. The effect changes of mortality risk explained by global health QoL, QoL-C30, and QoL-HN35 symptom were 5.8-9.8% at pre-IMRT but at 2 years post-IMRT were 39.4-49.4% by global health QoL and QoL-HN35 symptoms. CONCLUSIONS: We concluded advanced cancer stage correlates with a long-term high mortality in NPC patients treated with IMRT and the association is partially intermediated by QoL at pre-IMRT and 2 years post-IMRT. Therefore, QoL-HN35 symptom and global health QoL-dependent medical support and care should be focused and tailored at 2 years post-IMRT.

Lin, Y. S., et al. (2021). "Mortality associated with the use of non-vitamin K antagonist oral anticoagulants in cancer patients: Dabigatran versus rivaroxaban." Cancer Med **10**(20): 7079-7088.

OBJECTIVE: This study assesses the mortality outcomes of non-vitamin K antagonist oral anticoagulants (NOACs) in cancer patients with venous thromboembolism (VTE) and atrial fibrillation (AF). METHODS: Medical records of cancer patients receiving NOACs for VTE or AF between January 1, 2011, and December 31, 2016, were retrieved from Taiwan's National Health Institute Research Database. NOACs were compared using the inverse probability of treatment weighting (IPTW) method. The primary outcome was cancer-related death. Secondary outcomes were all-cause mortality, major bleeding, and gastrointestinal (GI) bleeding. RESULTS: Among 202,754 patients who received anticoagulants, 3591 patients (dabigatran: 907; rivaroxaban: 2684) with active cancers were studied. Patients who received dabigatran were associated with lower risks of cancer-related death at one year (HR = 0.71, 95% CI = 0.54-0.93) and at the end of follow-ups (HR = 0.79, 95% CI

= 0.64-0.98) compared with rivaroxaban. Patients who received dabigatran were also associated with lower risks of all-cause mortality (HR = 0.81, 95% CI = 0.67-0.97), major bleeding (HR = 0.64, 95% CI = 0.47-0.88), and GI bleeding (HR = 0.57, 95% CI = 0.39-0.84) at the end of follow-ups compared with rivaroxaban. CONCLUSION: Compared with rivaroxaban, the use of dabigatran may be associated with a lower risk of cancer-related death and all-cause mortality.

Lin, Z., et al. (2021). "Impact of anti-cancer therapy on disease severity and mortality in cancer patients with COVID-19: a systematic review and meta-analysis." Expert Rev Anticancer Ther **21**(9): 1055-1066.

Background: Cancer patients are more vulnerable to Coronavirus disease-2019 (COVID-19) and have a higher risk of adverse outcomes than the general population. Therefore, it is necessary to evaluate whether anti-cancer therapies such as surgery, chemotherapy, immunotherapy, and targeted therapy will increase the severity and mortality of cancer patients with COVID-19.Methods: Relevant articles were retrieved from PubMed, Embase, Web of Science, Cochrane Library and China National Knowledge Infrastructure (CNKI). The search time was from December 1, 2019 to January 23, 2021. Meta-analysis was conducted using Revman 5.3 statistical software.Results: A total of 26 studies were included in this meta-analysis, involving 5571 cancer patients infected with SARS-CoV-2. Meta-analysis showed that surgery, chemotherapy, immunotherapy and targeted therapy were not associated with disease severity or mortality (107/688, OR =1.30, 95% CI[0.79, 2.13], P =0.30; 1956/2674, OR =1.27, 95% CI [0.95, 1.69], P =0.10; 342/1455, OR =1.20, 95% CI [0.90, 1.61], P =0.21; 503/1378, OR =0.92, 95% CI [0.72, 1.19], P =0.54, respectively).Conclusion: In cancer patients with COVID-19, anti-cancer therapy had no adverse effect on disease severity or mortality. Further research is necessary to determine the complex interrelationship between anti-cancer therapy, particularly chemotherapy, and COVID-19.

Lindstrom, M., et al. (2022). "Health locus of control and all-cause, cardiovascular, cancer and other cause mortality: A population-based prospective cohort study in southern Sweden." Prev Med **161**: 107114.

The aim was to investigate associations between health locus of control (HLC) and all-cause, cardiovascular (CVD), cancer and other cause mortality. A public health postal questionnaire was distributed in the autumn of 2008 to a stratified random sample of the 18-80 year old adult population in Scania in southernmost Sweden. The participation rate was 54.1%, and 25,517 participants were included in the present study. Baseline 2008 survey data was linked to cause of death register data to create a prospective cohort with 8.3-year follow-up. Associations between health locus of control and mortality were investigated in survival (Cox) regression models. Prevalence of internal HLC was 69.0% and external HLC 31.0% among women. Internal HLC was 67.6% and external HLC 32.4% among men. In the models with women and men combined, external HLC had significantly higher all-cause, CVD, cancer and other cause mortality even after adjustments for sociodemographic factors and chronic disease at baseline, but after the introduction of health-related behaviors, external HLC only displayed higher cancer mortality compared to internal HLC. External HLC displayed higher all-cause, cancer and other cause mortality for men in the final model adjusted for health-related behaviors, but not for women. Other pathways than health-related behaviors may exist for the association between external HLC and cancer mortality, particularly among men.

Linehan, A., et al. (2022). "COVID-19-related mortality in cancer patients in an Irish setting." Ir J Med Sci **191**(5): 2013-2018.

BACKGROUND: The COVID-19 pandemic has impacted significantly on healthcare across the globe. It has been reported to have higher incidence and be associated with worse outcomes in patients with cancer. AIM: To examine the characteristics of patients with cancer who were diagnosed with COVID-19 and to identify factors which may predict a poorer outcome. METHODS: Patients attending oncology services in Beaumont Hospital who were diagnosed with COVID-19 between March and May 2020 were included. Demographics and outcomes were determined by chart review. RESULTS: Twenty-seven patients were included in the study. The median age was 62; 59% were male. Ten patients (37%) died all of whom had metastatic or incurable locally advanced disease. Patients with lung cancer had a higher rate of COVID-19 and poorer outcomes. Those with a performance status (PS) >/= 3 were more likely to die than those with PS </= 2. Compared to those who recovered, patients who died had a higher number of organs affected by cancer and a higher mean Palliative Prognostic Score. CONCLUSION: Patients attending oncology services during the initial phase of the COVID-19 pandemic had an increased rate of SARS-CoV-2 infection and a higher mortality rate than the general population. Those who died had more advanced cancer as demonstrated by poorer performance status, a greater burden of metastatic disease and a higher Palliative Prognostic Score.

Ling, S., et al. (2021). "Risk of cancer incidence and mortality associated with diabetes: A systematic review with trend analysis of 203 cohorts." Nutr Metab Cardiovasc Dis **31**(1): 14-22.

AIM: Whether the relative risk of cancer incidence and mortality associated with diabetes has changed over time is unknown. DATA SYNTHESIS: On August 12th, 2020, we electronically searched for observational studies reporting on the association between diabetes and cancer. We estimated temporal trends in the relative risk of cancer incidence or mortality associated with diabetes and calculated the ratio of relative risk (RRR) comparing different periods. As many as 193 eligible articles, reporting data on 203 cohorts (56,852,381 participants; 3,735,564 incident cancer cases; 185,404 cancer deaths) and covering the period 1951-2013, were included. The relative risk of all-site cancer incidence increased between 1980 and 2000 [RRR 1990 vs.1980: (1.24; 95% CI: 1.16, 1.34); 2000 vs.1990: (1.23; 1.15, 1.31)] and stabilised thereafter at a relative risk of 1.2; the relative risk of all-site cancer mortality was constant at about 1.2 from 1980 to 2010. Both magnitudes and trends in relative risk varied across cancer sites: the relative risk of colorectal, female breast, and endometrial cancer incidence and pancreatic cancer mortality was constant during the observed years; it increased for bladder, stomach, kidney, and pancreatic cancer incidence until 2000; and decreased for liver while increased for prostate, colon and gallbladder cancer incidence after 2000. CONCLUSIONS: Alongside the increasing prevalence of diabetes, the temporal patterns of the relative risk of cancer associated with diabetes may have contributed to the current burden of cancer in people with diabetes.

Little, M. P., et al. (2020). "Lifetime Mortality Risk from Cancer and Circulatory Disease Predicted from the Japanese Atomic Bomb Survivor Life Span Study Data Taking Account of Dose Measurement Error." Radiat Res **194**(3): 259-276.

Dosimetric measurement error is known to potentially bias the magnitude of the dose response, and can also affect the shape of dose response. In this report, generalized relative and absolute rate models are fitted to the latest Japanese atomic bomb survivor solid cancer, leukemia and circulatory disease mortality data (followed from 1950 through 2003), with the latest (DS02R1) dosimetry, using Bayesian techniques to adjust for errors in dose estimates and assessing other model uncertainties. Linear-quadratic models are fitted and used to assess lifetime mortality risks for contemporary UK, USA, French, Russian, Japanese and Chinese populations. For a test dose of 0.1 Gy absorbed dose weighted by neutron relative biological effectiveness, solid cancer, leukemia and circulatory disease mortality risks for a UK population using a generalized linear-quadratic relative rate model were estimated to be 3.88% Gy-1 [95% Bayesian credible interval (BCI): 1.17, 6.97], 0.35% Gy-1 (95% BCI: -0.03, 0.78) and 2.24% Gy-1 (95% BCI: -0.17, 13.76), respectively. Using a generalized absolute rate linear-quadratic model at 0.1 Gy, the lifetime risks for these three end points were estimated to be 3.56% Gy-1 (95% BCI: 0.54, 6.78), 0.41% Gy-1 (95% BCI: 0.01, 0.86) and 1.56% Gy-1 (95% BCI: -1.10, 7.21), respectively. There was substantial evidence of curvature for solid cancer (in particular, the group of solid cancers excluding lung, breast and stomach cancers) and leukemia, so that for solid cancer and leukemia, estimates of excess risk per unit dose were nearly doubled by increasing the dose from 0.01 to 1.0 Gy, with most of the increase occurring in the interval from 0.1 to 1.0 Gy. For circulatory disease, the dose-response curvature was inverse, so that risk per unit dose was nearly halved by going from 0.01 t o 1.0 Gy weighted absorbed dose, although there were substantial uncertainties. In general, there were higher radiation risks for females compared to males. This was true for solid cancer and circulatory disease overall, as well as for lung, breast, stomach and the group of other solid cancers, and was the case whether relative or absolute rate projection models were employed; however, for leukemia this pattern was reversed. Risk estimates varied somewhat between populations, with lower cancer risks in aggregate for China and Russia, but higher circulatory disease risks for Russia, particularly using the relative rate model. There was more pronounced variation for certain cancer sites and certain types of projection models, so that breast cancer risk was markedly lower in China and Japan using a relative rate model, but the opposite was the case for stomach cancer. There was less variation between countries using the absolute rate models for stomach cancer and breast cancer, but this was not the case for lung cancer and the group of other solid cancers, or for circulatory disease.

Liu, F. H., et al. (2022). "Pre-diagnosis fiber : carbohydrate intake ratio and mortality of ovarian cancer: results from a prospective cohort study." Food Funct **13**(19): 10046-10054.

Background: The association between the ratio of fiber to carbohydrate (F : C-R) and cancer mortality is not currently well-known. We prospectively evaluated for the first time the aforementioned topic among ovarian cancer (OC) patients. Methods: A total of 703 newly diagnosed OC patients aged 18-79 years were included. Pre-diagnosis diet intake details were collected with a validated food frequency questionnaire. Deaths were ascertained until March 31, 2021, based on medical records and the

cancer registry. Cox proportional hazard models were used to evaluate hazard ratios (HRs) and 95% confidence intervals (CIs) between pre-diagnostic fiber, carbohydrate, and F : C-R intake and OC mortality. Restricted cubic splines were used to analyze the potential nonlinear relationship between F : C-R and OC mortality. Results: During the follow-up period (median: 37.2 months; interquartile: 24.7-50.2 months), we observed 130 (18.49%) OC patients died. The pre-diagnosis higher fiber intake (comparing the highest with the lowest tertile of intake: HR = 0.56, 95% CI = 0.35-0.92; HR per 1 SD increment: 0.78, 95% CI = 0.64-0.96; P trend < 0.05) and higher F : C-R intake (comparing the highest with the lowest tertile of intake: HR = 0.51, 95% CI = 0.31-0.85; HR per 1-SD increment: 0.73; 95% CI = 0.59-0.91; P trend < 0.05) were significantly associated with lower mortality for OC patients, but no evidence of the association between pre-diagnosis carbohydrate intake and OC mortality was observed. We found no evidence of a nonlinear relationship between F : C-R and OC mortality. Significant inverse associations were also observed for subgroup analyses stratified by age at diagnosis, menopausal status, residual lesions, histological type, FIGO stage, and body mass index, although not all associations showed statistical significance. Conclusion: Pre-diagnosis high fiber intake and high F : C-R diet intake were associated with a decreased risk of OC mortality.

Liu, H., et al. (2021). "Global, regional, and national mortality trends of female breast cancer by risk factor, 1990-2017." BMC Cancer **21**(1): 459.

BACKGROUND: Female breast cancer (FBC) is a malignancy involving multiple risk factors and has imposed heavy disease burden on women. We aim to analyze the secular trends of mortality rate of FBC according to its major risk factors. METHODS: Death data of FBC at the global, regional, and national levels were retrieved from the online database of Global Burden of Disease study 2017. Deaths of FBC attributable to alcohol use, high body-mass index (BMI), high fasting plasma glucose (FPG), low physical activity, and tobacco were collected. Estimated average percentage change (EAPC) was used to quantify the temporal trends of age-standardized mortality rate (ASMR) of FBC in 1990-2017. RESULTS: Worldwide, the number of deaths from FBC increased from 344.9 thousand in 1990 to 600.7 thousand in 2017. The ASMR of FBC decreased by 0.59% (95% CI, 0.52, 0.66%) per year during the study period. This decrease was largely driven by the reduction in alcohol use- and tobacco-related FBC, of which the ASMR was decreased by 1.73 and 1.77% per year, respectively. In contrast, the ASMR of FBC attributable to high BMI and high FPG was increased by 1.26% (95% CI, 1.22, 1.30%) and 0.26% (95% CI, 0.23, 0.30%) per year between 1990 and 2017, respectively. CONCLUSIONS: The mortality rate of FBC experienced a reduction over the last three decades, which was partly owing to the effective control for alcohol and tobacco use. However, more potent and tailored prevention strategies for obesity and diabetes are urgently warranted.

Liu, H., et al. (2022). "Morbidity, Mortality, and Pathologic Outcomes of Transanal Versus Laparoscopic Total Mesorectal Excision for Rectal Cancer Short-term Outcomes From a Multicenter Randomized Controlled Trial." Ann Surg.

OBJECTIVE: To determine the morbidity, mortality, and pathologic outcomes of transanal total mesorectal resection (taTME) versus laparoscopic total mesorectal excision (laTME) among patients with rectal cancer with clinical stage I to III rectal cancer below the peritoneal reflection. BACKGROUND: Studies with sufficient numbers of patients allowing clinical acceptance of taTME for rectal cancer are lacking. Thus, we launched a randomized clinical trial to compare the safety and efficacy of taTME versus laTME. METHODS: A randomized, open-label, phase 3, noninferiority trial was performed at 16 different hospitals in 10 Chinese provinces. The primary endpoints were 3-year disease-free survival and 5-year overall survival. The morbidity and mortality within 30 days after surgery, and pathologic outcomes were compared based on a modified intention-to-treat principle; this analysis was preplanned. RESULTS: Between April 13, 2016, and June 1, 2021, 1115 patients were randomized 1:1 to receive taTME or laTME. After exclusion of 26 cases, modified intention-to-treat set of taTME versus laTME groups included 544 versus 545 patients. There were no significant differences between taTME and laTME groups in intraoperative complications [26 (4.8%) vs 33 (6.1%); difference, -1.3%; 95% confidence interval (CI), -4.2% to 1.7%; P=0.42], postoperative morbidity [73 (13.4%) vs 66 (12.1%); difference, 1.2%; 95% CI, -2.8% to 5.2%; P=0.53), or mortality [1 (0.2%) vs 1 (0.2%)]. Successful resection occurred in 538 (98.9%) versus 538 (98.7%) patients in taTME versus laTME groups (difference, 0.2%; 95% CI, -1.9% to 2.2%; P>0.99). CONCLUSIONS: Experienced surgeons can safely perform taTME in selected patients with rectal cancer.

Liu, J. M., et al. (2021). "Association between Helicobacter pylori infection and mortality risk in prostate cancer patients receiving androgen deprivation therapy: A real-world evidence study." Cancer Med **10**(22): 8162-8171.

PURPOSE: Helicobacter pylori (H. pylori) is a major risk factor for gastric cancer and may affect androgen activity in men. The association between H. pylori and androgen deprivation therapy (ADT) in patients with prostate cancer (PCa) remains unclear. METHODS: This retrospective cohort study linked National Health Insurance (NHI) data to Taiwan Cancer Registry (TCR) and Taiwan Death Registry (TDR) between 1995 and 2016. PCa patients who received ADT were classified into H. pylori infection and non-H. pylori infection groups. The outcomes were overall mortality, prostate cancer-specific mortality, and castration-resistant prostate cancer (CRPC). Propensity score matching was adopted for the primary analysis and inverse probability of treatment weighting (IPTW) was used for the sensitivity analysis. RESULTS: Of the 62,014 selected PCa patients, 23,701 received ADT, of whom 3516 had H. pylori infections and 20,185 did not. After matching, there were 3022 patients in the H. pylori infection group and 6044 patients in the non-H. pylori infection group. The mean follow-up period for the matched cohort was 4.8 years. Compared to the non-H. pylori group, the H. pylori group was significantly associated with decreased risks of all-cause mortality (hazard ratio [HR] 0.90; 95% confidence interval [CI] 0.84-0.96) and prostate cancer-specific mortality (HR 0.88; 95% CI 0.81-0.95) in the matched analysis. CONCLUSIONS: H. pylori infection was associated with a reduced risk of mortality in PCa patients receiving ADT.

Luzzago, S., et al. (2020). "Effect of Age on Cancer-specific Mortality in Patients With Urothelial Carcinoma of the Urinary Bladder: A Population-based Competing-risks Analysis Across Disease Stages." Am J Clin Oncol **43**(12): 880-888.

OBJECTIVE: The objective of the study is to test the effect of age on cancer-specific mortality (CSM) in patients with urothelial carcinoma of the urinary bladder (UCUB), across all disease stages. MATERIALS AND METHODS: Within the Surveillance, Epidemiology, and End Results (SEER) registry (2004-2016), we identified 207,714 patients. Age was categorized as: below 60 versus 60 to 69 versus 70 to 79 versus 80 years and above. Multivariable competing-risks regression (CRR) models were used according to disease stage (low-risk nonmuscle invasive: TaN0M0 low grade, high-risk nonmuscle invasive: Ta high grade or Tis-1N0M0, muscle invasive: T2-3N0M0, regional: T4N0M0/TanyN1-3M0, and metastatic: TanyNanyM1). RESULTS: Overall, 33,970 (16.4%) versus 52,173 (25.1%) versus 64,537 (31.1%) versus 57,034 (27.4%) patients were below 60 versus 60 to 69 versus 70 to 79 versus 80 years and above, respectively. In multivariable CRR models that focused on low-risk nonmuscle invasive UCUB, advanced age was associated with higher CSM rates (hazard ratio [HR]: 7.04 in patients aged 80 y and above, relative to below 60 y; P<0.001). Moreover, advanced age was also associated with higher CSM rates in high-risk nonmuscle invasive UCUB (HR: 2.77 in patients aged 80 y and above, relative to below 60 y; P<0.001) and in muscle invasive UCUB patients (HR: 1.38 in patients aged 80 y and above, relative to below 60 y; P<0.001). Conversely, lower CSM rates with advanced age were observed in multivariable CRR that focused on regional (HR: 0.91 for patients aged 80 y and above, relative to below 60 y; P=0.02) or metastatic UCUB (HR: 0.75 for patients aged 80 y and above, relative to below 60 y; P<0.001). CONCLUSIONS: The direction and the magnitude of the association between advanced age and CSM in UCUB patients changes according to tumor stage. In low-risk nonmuscle invasive, high-risk nonmuscle invasive, and muscle invasive UCUB, more advanced age is associated with higher CSM rates. Conversely, in regional and metastatic UCUB patients, more advanced age is associated with lower CSM rates.

Ma, C., et al. (2022). "Factors Associated With Geographic Disparities in Gastrointestinal Cancer Mortality in the United States." Gastroenterology **163**(2): 437-448 e431.

BACKGROUND & AIMS: Significant geographic variability in gastrointestinal (GI) cancer-related death has been reported in the United States. We aimed to evaluate both modifiable and nonmodifiable factors associated with intercounty differences in mortality due to GI cancer. METHODS: Data from the Centers for Disease Control and Prevention's Wide-ranging Online Data for Epidemiologic Research platform were used to calculate county-level mortality from esophageal, gastric, pancreatic, and colorectal cancers. Multivariable linear regression models were fit to adjust for county-level covariables, considering both patient (eg, sex, race, obesity, diabetes, alcohol, and smoking) and structural factors (eg, specialist density, poverty, insurance prevalence, and colon cancer screening prevalence). Intercounty variability in GI cancer-related mortality explained by these covariables was expressed as the multivariable model R(2). RESULTS: There were significant geographic disparities in GI cancer-related county-level mortality across the US from 2010-2019 with the ratio of mortality between 90th and 10th percentile counties ranging from 1.5 (pancreatic) to 2.1 (gastric cancer). Counties with the highest 5% mortality rates for gastric, pancreatic, and colorectal cancer were primarily in the Southeastern United States. Multivariable models explained 43%, 61%, 14%, and

39% of the intercounty variability in mortality rates for esophageal, gastric, pancreatic, and colorectal cancer, respectively. Cigarette smoking and rural residence (independent of specialist density) were most strongly associated with GI cancer-related mortality. CONCLUSIONS: Both patient and structural factors contribute to significant geographic differences in mortality from GI cancers. Our findings support continued public health efforts to reduce smoking use and improve care for rural patients, which may contribute to a reduction in disparities in GI cancer-related death.

Ma, G. F., et al. (2022). "Patterns and Trends of the Mortality From Bone Cancer in Pudong, Shanghai: A Population-Based Study." Front Oncol **12**: 873918.

INTRODUCTION: The burden of cancer-related mortality of common malignancies has been reported worldwide. However, whether bone cancer (BC), as a highly aggressive and heterogeneous group of rare cancers, followed a similar or distinct epidemiological pattern during such process remains largely unknown. We aimed to analyze the mortality and the temporal trends of BC in relation to gender, age, and premature death in Shanghai, China. METHODS: We conducted a population-based analysis of the mortality data of BC in Shanghai Pudong New Area (PNA) from 2005 to 2020. The epidemiological characteristics and long-term trends in crude mortality rates (CMRs), age-standardized mortality rates worldwide (ASMRWs), and rate of years of life lost (YLL) was analyzed using the Joinpoint regression program. The demographic and non-demographic factors affecting the mortality rate were evaluated by the decomposition method. RESULTS: There are 519 BC-specific deaths accounting for 0.15% of all 336,823 deaths and 0.49% of cancer-specific death in PNA. The CMR and ASMRW of BC were 1.15/10(5) person-year and 0.61/10(5) person-year, respectively. The YLL due to premature death from BC was 6,539.39 years, with the age group of 60-69 years having the highest YLL of 1,440.79 years. The long-term trend of CMR, ASMRW, and YLL rate significantly decreased by -5.14%, -7.64%, and -7.27%, respectively, per year (all $p < 0.05$) in the past 16 years. However, the proportion of BC-specific death within the total cancer-specific death dropped to a plateau without further improvement since 2016, and a remarkable gender and age disparity was noticed in the observed reduction in mortality. Specifically, the elderly benefited less but accounted for a larger percentage of BC population in the last decades. Although the overall mortality of BC decreased, there was still a significant upward trend toward an increased mortality rate caused by the aging of the BC patients. CONCLUSION: Our study provides novel insights on the epidemiological characteristics and longitudinal dynamics of BC in a fast urbanization and transitioning city. As a rare disease affecting all ages, the burden of BC among the elderly emerged to form an understudied and unmet medical need in an aging society.

Ma, J. Y., et al. (2021). "[Incidence and mortality of corpus uteri cancer in China, 2015]." Zhonghua Zhong Liu Za Zhi **43**(1): 108-112.

Objective: To estimate the incidence and mortality of corpus uteri cancer in China, 2015. Methods: Quality audit and evaluation of the data from 2015 cancer registration reported by 501 cancer registries were conducted, and 368 cancer registries were included in the analysis. The incidence rate and mortality rate of corpus uteri cancer were calculated according to the factors of the region (urban, rural, east, central, western), sex and age groups. The incidence and mortality of corpus uteri cancer with the 2015 population were estimated. Chinese standard population in 2000 and world Segi's population were used for the calculation of age-standardized rates (ASR) of incidence and mortality. Results: In 2015, 368 cancer registries included in the analysis covered a total of 309 553 499 populations in China, accounting for 22.52% of the national population. It is estimated that there were about 68 900 new cases of corpus uteri cancer in 2015, the incidence rate was 10.28/10(5), age-standardized incidence rates by Chinese standard population (ASR China) and world standard population (ASR world) were 6.86/10(5) and 6.66/10(5), respectively. The incidence rate of urban area (11.35/10(5)) was higher than that of rural area (8.90/10(5)), and the incidence of eastern region (12.12/10(5)) was higher than the central region (9.94/10(5)) and the western region (8.25/10(5)). It is estimated that in 2015, there were about 16 000 deaths of corpus uteri cancer, the mortality rate was 2.39/10(5), ASR China was 1.49/10(5), ASR world was 1.47/10(5). The mortality in urban areas (2.40/10(5)) is close to rural areas (2.39/10(5)); the mortality in central areas (2.55/10(5)) was higher than the eastern areas (2.32/10(5)) and the western areas (2.31/10(5)). Conclusions: In China, the incidence of corpus uteri cancer is on the rise and has a trend of youth, the burden of disease is gradually increasing, which threatens the health of women. Targeted prevention and control measures should be carried out in the different regions.

Ma, L., et al. (2022). "The Incidence, Mortality, and DALYs Trends Associated with Esophageal Cancer - China, 1990-2019." China CDC Wkly **4**(43): 956-961.

WHAT IS ALREADY KNOWN ABOUT THIS TOPIC? Esophageal cancer (EC) is one of the

most common malignant tumors in China. The new cases and deaths in China account for more than half of the world, and the disease burden of esophageal cancer is serious. WHAT IS ADDED BY THIS REPORT? From 1990 to 2019, the disease burden of EC in China showed a decrease overall; it first increased between 1990 and 2004, but then decreased between 2004 and 2019. The burden of EC in men was much higher than that in women. Age was an important factor affecting the burden of EC, with disease burden rising rapidly after 40 years old. WHAT ARE THE IMPLICATIONS FOR PUBLIC HEALTH PRACTICES? The screening, early diagnosis, and treatment for EC should continue to be strengthened in China. Middle-aged and elderly men are high-risk groups of EC and should be a key population for EC prevention and control.

Ma, S., et al. (2021). "Does aspirin reduce the incidence, recurrence, and mortality of colorectal cancer? A meta-analysis of randomized clinical trials." Int J Colorectal Dis **36**(8): 1653-1666.

BACKGROUND: Colorectal cancer (CRC) is the third most common diagnosed cancer and the third leading cause of all cancer deaths in the USA. Some evidences are shown that aspirin can reduce the morbidity and mortality of different cancers, including CRC. Aspirin has become a new focus of cancer prevention and treatment research so far; clinical studies, however, found conflicting conclusions of its anti-cancer characteristics. This study is to summarize the latest evidence of correlation between aspirin use and CRC and/or colorectal adenomas. METHODS: Databases were searched to identify randomized controlled trials (RCTs) in the salvage setting. The pooled relative risk (RR) with 95% confidence interval (CI) was used to estimate the effect of aspirin on colorectal cancer and/or colorectal adenomas. Subgroup analysis and sensitivity analysis were also conducted. RESULTS: The result showed that aspirin use was not associated with incidence of CRC (RR 0.97; 95% CI 0.84-1.12; P = 0.66; I(2) = 34%), aspirin use was found to be associated with reduced recurrence of colorectal adenomas (RR 0.83; 95% CI 0.72-0.95; P = 0.006; I(2) = 63%) and reduced mortality of CRC (RR 0.79; 95% CI 0.64-0.97; P = 0.02; I(2) = 14%). Subgroup analysis found a statistically significant association in low dose with a pooled RR of 0.85 (95% CI 0.74-0.99; P = 0.03; I(2) = 31%). CONCLUSIONS: This meta-analysis of randomized controlled trial data indicates that aspirin reduces the overall risk of recurrence and mortality of CRC and/or colorectal adenomas. Incidence of CRC was also reduced with low-dose aspirin. The emerging evidence on aspirin's cancer protection role highlights an exciting time for cancer prevention through low-cost interventions. TRIAL REGISTRATION: Clinicaltrials.gov no: CRD42020208852; August 18, 2020; https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42020208852).

Ma, W., et al. (2021). "Association of Screening Lower Endoscopy With Colorectal Cancer Incidence and Mortality in Adults Older Than 75 Years." JAMA Oncol **7**(7): 985-992.

IMPORTANCE: Evidence indicates that screening for colorectal cancer (CRC) beginning at 50 years of age can detect early-stage CRC and premalignant neoplasms (eg, adenomas) and thus prevent CRC-related mortality. At present, the US Preventive Services Task Force recommends continuing CRC screening until 75 years of age and individualized decision-making for adults older than 75 years, while accounting for a patient's overall health and screening history. However, scant data exist to support these recommendations. OBJECTIVE: To examine the association of lower gastrointestinal tract screening endoscopy with the risk of CRC incidence and CRC-related mortality in older US adults. DESIGN, SETTING, AND PARTICIPANTS: This prospective cohort study of health care professionals in the US included data from the Nurses' Health Study (NHS) and Health Professionals Follow-up Study (HPFS) from January 1, 1988, through January 31, 2016, for the HPFS and June 30, 2016, for the NHS. Data were analyzed from May 8, 2019, to July 9, 2020. EXPOSURES: History of screening sigmoidoscopy or colonoscopy (routine/average risk or positive family history) to 75 years of age and after 75 years of age, assessed every 2 years. MAIN OUTCOMES AND MEASURES: Incidence of CRC and CRC-related mortality confirmed by National Death Index, medical records, and pathology reports. RESULTS: Among 56 374 participants who reached 75 years of age during follow-up (36.8% men and 63.2% women), 661 incident CRC cases and 323 CRC-related deaths were documented. Screening endoscopy after 75 years of age was associated with reduced risk of CRC incidence (multivariable hazard ratio [HR], 0.61; 95% CI, 0.51-0.74) and CRC-related mortality (HR, 0.60; 95% CI, 0.46-0.78), regardless of screening history. The HR comparing screening with nonscreening after 75 years of age was 0.67 (95% CI, 0.50-0.89) for CRC incidence and 0.58 (95% CI, 0.38-0.87) for CRC-related mortality among participants who underwent screening endoscopy before 75 years of age, and 0.51 (95% CI, 0.37-0.70) for CRC incidence and 0.63 (95% CI, 0.43-0.93) for CRC-related mortality among participants without a screening history. However, screening endoscopy after 75 years of age was not associated with risk reduction in CRC death among participants with cardiovascular disease (HR, 1.18; 95% CI, 0.59-2.35) or significant comorbidities (HR,

1.17; 95% CI, 0.57-2.43). CONCLUSIONS AND RELEVANCE: In this cohort study, endoscopy among individuals older than 75 years was associated with lower risk of CRC incidence and CRC-related mortality. These data support continuation of screening after 75 years of age among individuals without significant comorbidities.

Macek, P., et al. (2020). "Competing Risks of Cancer and Non-Cancer Mortality When Accompanied by Lifestyle-Related Factors-A Prospective Cohort Study in Middle-Aged and Older Adults." Front Oncol **10**: 545078.

BACKGROUND: The study aimed to identify the association between the lifestyle-related factors and the cancer-specific, or non-cancer-specific mortality, when accompanied by a competing risk. Two statistical methods were applied, i.e., cause-specific hazard (CSH), and sub-distribution hazard ratio (SHR). Their respective key advantages, relative to the actual study design, were addressed, as was overall application potential. METHODS: Source data from 4,584 residents (34.2% men), aged 45-64 years, were processed using two different families of regression models, i.e., CSH and SHR; principal focus upon the impact of lifestyle-related factors on the competing risk of cancer and non-cancer mortality. The results were presented as hazard ratios (HR) with 95% confidence intervals (95% CI). RESULTS: Age, smoking status, and family history of cancer were found the leading risk factors for cancer death; the risk of non-cancer death higher in the elderly, and smoking individuals. Non-cancer mortality was strongly associated with obesity and hypertension. Moderate to vigorous physical activity decreased the risk of death caused by cancer and non-cancer causes. CONCLUSIONS: Specific, lifestyle-related factors, instrumental in increasing overall, and cancer-specific mortality, are modifiable through health-promoting, individually pursued physical activities. Regular monitoring of such health-awareness boosting pursuits seems viable in terms of public health policy making.

MacEwan, J. P., et al. (2020). "Changes in mortality associated with cancer drug approvals in the United States from 2000 to 2016." J Med Econ **23**(12): 1558-1569.

AIMS: To estimate the extent to which the approvals of new pharmacological therapies were associated with cancer mortality in the USA between 2000 and 2016. MATERIALS AND METHODS: The analysis quantified cancer drug approvals across the 15 tumor types with the highest incidence. Number of approvals in a given time period for each tumor was translated into a treatment stock measure, defined as a weighted sum of new indication approvals since 1976. The primary outcome was the annual tumor-specific cancer mortality, defined as the number of deaths per 100,000 U.S. population. The analysis used a multivariable ordinary least squares and a fixed effects model, controlling for incidence (new cases per 100,000 U.S. population) and the primary exposure, the treatment stock measure by year. RESULTS: Between 2000 and 2016, deaths per 100,000 population across the 15 most common tumor types declined by 24%. Additionally, 10.2 new indications were approved per year across the 15 most common tumor types. Cancer drug approvals were associated with statistically significant deaths averted in 2016 for colorectal cancer (4,991, $p = 0.004$), lung cancer (33,825, $p < 0.001$), breast cancer (11,502, $p < 0.001$), non-Hodgkin's lymphoma (6,636, $p < 0.001$), leukemia (4,011, $p < 0.001$), melanoma (1,714, $p < 0.001$), gastric cancer (758, $p = 0.019$), and renal cancer (739, $p < 0.001$). Between 2000 and 2016, new cancer treatments were correlated with 1,291,769 ($p < 0.001$) total deaths prevented across the 15 most common tumor types. LIMITATIONS AND CONCLUSIONS: Cancer drug approvals between 2000 and 2016 were associated with significant reduction in deaths from the most common cancers in the USA. Mortality changes were largest in prevalent tumor types with relatively more approvals, i.e. lung cancer, breast cancer, melanoma, lymphoma and leukemia. Future research evaluating the relationship between drug approvals and cancer mortality post 2016 is needed.

Mady, L. J., et al. (2022). "The impact of frailty on mortality in non-surgical head and neck cancer treatment: Shifting the clinical paradigm." Oral Oncol **126**: 105766.

OBJECTIVE: Compare survival of head and neck cancer (HNC) patients treated with surgical or non-surgical management according to frailty, quantify frailty with the Risk Analysis Index (RAI), a validated 14-item instrument. MATERIALS AND METHODS: Prospective cohort study of newly diagnosed HNC patients (>/=18 years) who had frailty assessment from April 13, 2016 to September 30, 2016. Primary outcome was overall survival at 1- and 3-years. Cox proportional hazard models were utilized to examine mortality with predictor variables. Adjusted and unadjusted (Kaplan-Meier) survival curves stratified by either RAI scores or treatment modality were plotted. Kruskal-Wallis and likelihood ratio chi-square tests were used for comparing clinicodemographic variables. RESULTS: Of 165 patients, 54 (32.7%) were managed non-surgically, 49 (29.7%) were treated with definitive surgery only, and 62 (37.6%) were treated with multimodality (surgery + adjuvant) therapy. Among the full cohort and subgroup analysis of the frail/very frail (RAI >/= 37), non-surgical patients had worse or

similar 3-year survival than those treated with surgery +/- adjuvant therapy. Multivariable Cox proportional hazard models demonstrate that frail patients treated non-surgically experienced worse survival than their counterparts treated with surgery (HR = 2.50, p = 0.015, 95% CI: 1.19, 5.23) or multimodality therapy (HR = 3.91, p < 0.001, 95% CI: 1.94-7.89). CONCLUSION: Across all levels of frailty, long term survival of HNC patients treated without surgery is either worse than or like those treated with surgery. These findings (1) challenge current practices of steering patients "too frail for surgery" towards non-surgical, "non-invasive" therapy, and (2) suggest equipoise warranting randomized trials to clarify treatment of frail patients.

Maeda, H., et al. (2021). "Association of day of the week with mortality after elective right hemicolectomy for colon cancer: Case analysis from the National Clinical Database." Ann Gastroenterol Surg **5**(3): 331-337.

AIM: We aimed to investigate whether later weekdays are related to worse short-term outcomes after elective right hemicolectomy for colon cancer. METHODS: We retrospectively analyzed adult patients who underwent elective right hemicolectomy for colon cancer between 2012 and 2017. Records lacking details about surgical mortality were excluded, and multiple imputation was performed for other missing data (variables). The primary endpoint was surgical mortality, defined as the sum of 30-day mortality and in-hospital deaths within 90 days postoperatively. Using 22 clinical variables, hierarchal logistic regression modeling with clustering of patients from the same institutes was performed. RESULTS: Of the 112 658 patients undergoing elective right hemicolectomy for colon cancer, the 30-day mortality and surgical mortality were 0.6% and 1.1%, respectively. Surgery on Friday was less frequent, accounting for 17.1% of all cases. The occurrence of severe postoperative complications, anastomotic leakage, or unadjusted odds ratio for surgical mortality did not show significant differences between weekdays. A hierarchal logistic regression model identified 19 independent factors for surgical mortality. Adjusted odds ratios for surgical mortality were 1.01 (95% confidence interval: 0.83-1.22, P = .915), 0.86 (95% confidence interval: 0.71-1.05, P = .144), 0.86 (95% confidence interval: 0.71-1.05, P = .408), and 0.83 (95% confidence interval: 0.68-1.03, P = .176) for Tuesday, Wednesday, Thursday, and Friday, respectively, showing no significant differences. CONCLUSION: This study did not identify an evident difference in surgical mortality between weekdays; a safe elective right hemicolectomy for colon cancer is being offered throughout the week in Japan.

Mafra da Costa, A., et al. (2022). "Cancer Statistics over Time in Northwestern Sao Paulo State, Brazil: Incidence and Mortality." Cancer Epidemiol Biomarkers Prev **31**(4): 707-714.

BACKGROUND: Population studies can serve as an essential source of information on cancer's etiology, and assessments of cancer trends over time can detect changes. This study aimed to provide statistics over time on cancer incidence and mortality in the Barretos Region, Brazil. METHODS: Cancer incidence data were obtained from the population-based cancer registry of the Barretos Region, and mortality data were obtained from the Official Federal Database from 2002 to 2016. Age-standardized rates for incidence and mortality were calculated. Joinpoint Regression software was used to estimate the average annual percentage changes (AAPC). RESULTS: Age-standardized rates of incidence increased significantly for colon cancer (AAPC: 2.2), rectum and rectosigmoid (AAPC: 2.4), liver (AAPC: 4.7), female breast (AAPC: 2.2), and thyroid cancer (AAPC: 3.8) but decreased for esophageal (AAPC: -3.2), stomach (AAPC: -4.2), lung (AAPC: -2.0), and ovarian cancer (AAPC: -5.6). The mortality increased for liver cancer (AAPC: 2.3) and decreased for pharyngeal cancer (AAPC: -5.8), stomach cancer (AAPC: -6.6), cervical uterine cancer (AAPC: -5.9), prostate cancer (AAPC: -2.4), and ovarian cancer (AAPC: -3.3). CONCLUSIONS: We observed decreases in some cancers related to tobacco smoking and cervical and stomach cancers related to infectious agents, showing strong regional and national prevention programs' successes. But, we also observed rises in many cancer sites linked to lifestyle factors, such as breast or colorectal cancer, without a sign of declining mortality. IMPACT: These results can impact and support cancer control program implementation and improvement at the community level and extrapolate to the state level and/or the whole country.

Magliocco, A. M., et al. (2022). "Analysis of MRE11 and Mortality Among Adults With Muscle-Invasive Bladder Cancer Managed With Trimodality Therapy." JAMA Netw Open **5**(11): e2242378.

IMPORTANCE: Bladder-preserving trimodality therapy can be an effective alternative to radical cystectomy for treatment of muscle-invasive bladder cancer (MIBC), but biomarkers are needed to guide optimal patient selection. The DNA repair protein MRE11 is a candidate response biomarker that has not been validated in prospective cohorts using standardized measurement approaches. OBJECTIVE: To evaluate MRE11 expression as a prognostic biomarker in MIBC patients receiving trimodality therapy using automated quantitative image analysis. DESIGN, SETTING, AND PARTICIPANTS: This

prognostic study analyzed patients with MIBC pooled from 6 prospective phase I/II, II, or III trials of trimodality therapy (Radiation Therapy Oncology Group [RTOG] 8802, 8903, 9506, 9706, 9906, and 0233) across 37 participating institutions in North America from 1988 to 2007. Eligible patients had nonmetastatic MIBC and were enrolled in 1 of the 6 trimodality therapy clinical trials. Analyses were completed August 2020. EXPOSURES: Trimodality therapy with transurethral bladder tumor resection and cisplatin-based chemoradiation therapy. MAIN OUTCOMES AND MEASURES: MRE11 expression and association with disease-specific (bladder cancer) mortality (DSM), defined as death from bladder cancer. Pretreatment tumor tissues were processed for immunofluorescence with anti-MRE11 antibody and analyzed using automated quantitative image analysis to calculate a normalized score for MRE11 based on nuclear-to-cytoplasmic (NC) signal ratio. RESULTS: Of 465 patients from 6 trials, 168 patients had available tissue, of which 135 were analyzable for MRE11 expression (median age of 65 years [minimum-maximum, 34-90 years]; 111 [82.2%] men). Median (minimum-maximum) follow-up for alive patients was 5.0 (0.6-11.7) years. Median (Q1-Q3) MRE11 NC signal ratio was 2.41 (1.49-3.34). Patients with an MRE11 NC ratio above 1.49 (ie, above first quartile) had a significantly lower DSM (HR, 0.50; 95% CI, 0.26-0.93; P = .03). The 4-year DSM was 41.0% (95% CI, 23.2%-58.0%) for patients with an MRE11 NC signal ratio of 1.49 or lower vs 21.0% (95% CI, 13.4%-29.8%) for a ratio above 1.49. MRE11 NC signal ratio was not significantly associated with overall survival (HR, 0.84; 95% CI, 0.49-1.44). CONCLUSIONS AND RELEVANCE: Higher MRE11 NC signal ratios were associated with better DSM after trimodality therapy. Lower MRE11 NC signal ratios identified a poor prognosis subgroup that may benefit from intensification of therapy.

Magouliotis, D. E., et al. (2021). "Validation of the Surgical Outcome Risk Tool (SORT) for Predicting Postoperative Mortality in Colorectal Cancer Patients Undergoing Surgery and Subgroup Analysis." World J Surg **45**(6): 1940-1948.

BACKGROUND: The accurate evaluation of perioperative risk is crucial to facilitate the shared decision-making process. Surgical outcome risk tool (SORT) has been developed to provide enhanced and more feasible identification of high-risk surgical patients. Nonetheless, SORT has not been validated for patients with colorectal cancer undergoing surgery. Our aim was to determine whether SORT can accurately predict mortality after surgery for colorectal cancer and to compare it with traditional risk models. METHOD: 526 patients undergoing surgery performed by a colorectal surgical team in a single Greek tertiary hospital (2011-2019) were included. Five risk models were evaluated: (1) SORT, (2) Physiology and Operative Severity Score for the enumeration of Mortality and Morbidity (POSSUM), (3) Portsmouth POSSUM (P-POSSUM), (4) Colorectal POSSUM (CR-POSSUM), and (5) the Association of Great Britain and Ireland (ACPGBI) score. Model accuracy was assessed by observed to expected (O:E) ratios, and area under Receiver Operating Characteristic curve (AUC). RESULTS: Ten patients (1.9%) died within 30 days of surgery. SORT was associated with an excellent level of discrimination [AUC:0.81 (95% CI:0.68-0.94); p = 0.001] and provided the best performing calibration of all models in the entire dataset analysis (H-L:2.82; p = 0.83). Nonetheless, SORT underestimated mortality. SORT model demonstrated excellent discrimination and calibration predicting perioperative mortality in patients undergoing (1) open surgery, (2) emergency/acute surgery, and (3) in cases with colon-located cancer. CONCLUSION: SORT is an easily adopted risk-assessment tool, associated with enhanced accuracy, that could be implemented in the perioperative pathway of patients undergoing surgery for colorectal cancer.

Majdinasab, E. J. and Y. Puckett (2020). "Dyspnoea at rest predictor of increased in-hospital mortality in metastatic cancer patients undergoing emergent surgery in United States." Ecancermedicalscience **14**: 1112.

BACKGROUND: Dyspnoea is an extremely common finding in patients presenting with metastatic cancer and can be caused by cancer progression, treatment toxicity or pathology secondary to deteriorating overall health. In this study, we decided to analyse post-operative outcomes to understand if dyspnoea is a significant prognostic predictor of in-hospital mortality in patients with stage IV cancer who underwent emergent surgery in the United States. METHODS: We performed a search of the 2014 National Surgical Quality Improvement Program database (NSQIP) for patients with a diagnosis of malignancy (ICD-9 Codes 145.00-200.00). Cases were divided into two groups: metastatic cancer and non-metastatic cancer. Demographical data including preoperative, intraoperative and postoperative factors, as well as data regarding complications and comorbidities were compared between these two groups. Independent t-testing was used to compare continuous variables. Chi-square testing was used to compare categorical variables. Multiple logistic regression was used to assess for predictors of mortality in metastatic cancer. Mortality was adjusted for demographics, comorbid conditions and perioperative factors. RESULTS: Referring to the NSQIP database, a total of 80,275 cancer patients were

analysed, 11.8% (9,423) of whom had metastatic cancer. Dyspnoea at rest/moderate exertion (OR 5.7/2.4; 95% CI 2.7/1.6-11.9/3.7; p < 0.0001) were found to be the biggest predictors of in-hospital mortality in stage IV cancer patients who underwent emergent surgery. CONCLUSION: Dyspnoea at rest and with moderate exertion may be used as predictors of in-hospital mortality for metastatic cancer patients undergoing emergent surgery.

Majdinasab, E. J., et al. (2021). "Increased in-hospital mortality and emergent cases in patients with stage IV cancer." Support Care Cancer **29**(6): 3201-3207.

BACKGROUND: Cancer patients in the USA are still being treated with aggressive, life-prolonging interventions. Palliative care services remain vastly underutilized despite surges in both quality and quantity of programs. We evaluated surgical outcomes of metastatic cancer patients to question whether palliative care may be a better option. STUDY DESIGN: We queried the 2014 National Surgical Quality Improvement Program database (NSQIP) for patients with a diagnosis of malignancy (ICD 9 Codes 145.00 to 200.00). Cases were divided into metastatic and non-metastatic cancer. Demographic data including preoperative, intraoperative, and postoperative factors, as well as complications and comorbidities were compared between these two groups. Independent t testing was used to compare continuous variables. Chi-square testing was used to compare categorical variables. Multiple logistic regression was used to assess for predictors of mortality in metastatic cancer. RESULTS: A total of 80,275 cancer patients were analyzed, 11.8% (9423) of whom had metastatic disease. In-hospital mortality rate was found to be 4 times higher among patients with metastatic cancer (2.1% vs. 0.5%; P = < 0.0001). Of those metastatic cancer patients that died while in hospital, 18.5% had an emergency surgery performed. After adjusting for confounders, dyspnea at rest/moderate exertion (OR 5.7/2.4; 95% CI 2.7/1.6 to 11.9/3.7; P < 0.0001) was found to be the most significant predictor of in hospital mortality in stage IV cancer patients. CONCLUSION: Aggressive treatment in advanced cancer patients contributes to alarmingly high in-hospital mortality. Improved, deliberate communication of palliative care options with patients is exceedingly conducive to enhancing end-of-life cancer care.

Malagon, T., et al. (2022). "Predicted long-term impact of COVID-19 pandemic-related care delays on cancer mortality in Canada." Int J Cancer **150**(8): 1244-1254.

The COVID-19 pandemic has affected cancer care worldwide. This study aimed to estimate the long-term impacts of cancer care disruptions on cancer mortality in Canada using a microsimulation model. The model simulates cancer incidence and survival using cancer incidence, stage at diagnosis and survival data from the Canadian Cancer Registry. We modeled reported declines in cancer diagnoses and treatments recorded in provincial administrative datasets in March 2020 to June 2021. Based on the literature, we assumed that diagnostic and treatment delays lead to a 6% higher rate of cancer death per 4-week delay. After June 2021, we assessed scenarios where cancer treatment capacity returned to prepandemic levels, or to 10% higher or lower than prepandemic levels. Results are the median predictions of 10 stochastic simulations. The model predicts that cancer care disruptions during the COVID-19 pandemic could lead to 21 247 (2.0%) more cancer deaths in Canada in 2020 to 2030, assuming treatment capacity is recovered to 2019 prepandemic levels in 2021. This represents 355 172 life years lost expected due to pandemic-related diagnostic and treatment delays. The largest number of expected excess cancer deaths was predicted for breast, lung and colorectal cancers, and in the provinces of Ontario, Quebec and British Columbia. Diagnostic and treatment capacity in 2021 onward highly influenced the number of cancer deaths over the next decade. Cancer care disruptions during the COVID-19 pandemic could lead to significant life loss; however, most of these could be mitigated by increasing diagnostic and treatment capacity in the short-term to address the service backlog.

Malinowski, C., et al. (2022). "Association of Medicaid Expansion With Mortality Disparity by Race and Ethnicity Among Patients With De Novo Stage IV Breast Cancer." JAMA Oncol **8**(6): 863-870.

IMPORTANCE: Patients who are uninsured and belong to racial and ethnic minority groups or have low socioeconomic status have suboptimal access to health care, likely affecting outcomes. The association of the Affordable Care Act's Medicaid expansion with survival among patients with metastatic breast cancer is unknown. OBJECTIVE: To examine the association between Medicaid expansion and mortality disparity among patients with de novo stage IV breast cancer. DESIGN, SETTING, AND PARTICIPANTS: Cross-sectional, population-based study of survival using Cox proportional hazards regression and difference-in-difference (DID) analysis of data from the National Cancer Database and patients diagnosed as having de novo stage IV breast cancer between January 1, 2010, and December 31, 2016, residing in states that underwent Medicaid expansion on January 1, 2014. The preexpansion period was January 1, 2010, to December 31, 2013; the postexpansion period was January 1, 2014, to December 31, 2016. Data were analyzed between September 4, 2020, and November 16, 2021. EXPOSURES: Comparison of survival

improvement between patients of racial and ethnic minority groups and White patients in the preexpansion and postexpansion periods. Because of small numbers in the specific racial and ethnic minority groups, these patients were combined into 1 category for comparisons. MAIN OUTCOMES AND MEASURES: Overall survival (OS) and 2-year mortality rate. RESULTS: Among 9322 patients included (mean [SD] age, 55 [7] years), 5077 were diagnosed in the preexpansion and 4245 in the postexpansion period. The racial and ethnic minority group comprised 2545 (27.3%), which included 500 (5.4%) Hispanic (any race), 1515 (16.3%) non-Hispanic Black, and 530 (5.7%) non-Hispanic other including 25 (0.3%) American Indian or Alaska Native, 357 (3.8%) Asian or Pacific Islander, and 148 (1.6%) unknown, and 6777 (72.7%) were in the White patient group. In the preexpansion period, White patients had increased OS compared with patients of racial and ethnic minority groups (adjusted hazard ratio [aHR], 1.22; 95% CI, 1.10-1.35); this difference was not observed in the postexpansion period (aHR, 0.96; 95% CI, 0.86-1.08). A reduction in 2-year mortality was observed between the preexpansion and postexpansion periods (32.2% vs 26.0%). The adjusted 2-year mortality decreased from 40.6% to 36.3% among White patients and from 45.6% to 35.8% among patients of racial and ethnic minority groups (adjusted DID, -5.5%; 95% CI, -9.5 to -1.6; P = .006). Among patients in the lowest income quartile (n = 1510), patients of racial and ethnic minority groups had an increased risk of death in the preexpansion period (aHR, 1.28; 95% CI, 1.01-1.61) but lower risk in the postexpansion period (aHR, 0.75; 95% CI, 0.59-0.95). In this subset of patients, those of racial and ethnic minority groups had a greater reduction in 2-year mortality compared with White patients (adjusted DID, -12.8%; 95% CI, -22.2 to -3.5; P = .007). CONCLUSIONS AND RELEVANCE: In this cross-sectional study, survival differences observed between patients of racial and ethnic minority groups and White patients in the preexpansion period were no longer present in the postexpansion period. A greater reduction in 2-year mortality was observed among patients of racial and ethnic minority groups compared with White patients. These results suggest that policies aimed at improving equity and increasing access to health care may reduce racial and ethnic disparities in breast cancer outcomes.

Malvezzi, M., et al. (2021). "Childhood cancer mortality trends in the Americas and Australasia: An update to 2017." Cancer **127**(18): 3445-3456.

BACKGROUND: Marked reductions in childhood cancer mortality occurred over the last decades in high-income countries and, to a lesser degree, in middle-income countries. This study aimed to monitor mortality trends in the Americas and Australasia, focusing on areas showing unsatisfactory trends. METHODS: Age-standardized mortality rates per 100,000 children (aged 0-14 years) from 1990 to 2017 (or the last available calendar year) were computed for all neoplasms and 8 leading childhood cancers in countries from the Americas and Australasia, using data from the World Health Organization database. A joinpoint regression was used to identify changes in slope of mortality trends for all neoplasms, leukemia, and neoplasms of the central nervous system (CNS) for major countries. RESULTS: Over the last decades, childhood cancer mortality continued to decrease by approximately 2% to 3% per year in Australasian countries (ie, Japan, Korea, and Australia), by approximately 1.5% to 2% in North America and Chile, and 1% in Argentina. Other Latin American countries did not show any substantial decrease. Leukemia mortality declined in most countries, whereas less favorable trends were registered for CNS neoplasms, particularly in Latin America. Around 2016, death rates from all neoplasms were 4 to 6 per 100,000 boys and 3 to 4 per 100,000 girls in Latin America, and 2 to 3 per 100,000 boys and approximately 2 per 100,000 girls in North America and Australasia. CONCLUSIONS: Childhood cancer mortality trends declined steadily in North America and Australasia, whereas they were less favorable in most Latin American countries. Priority must be given to closing the gap by providing high-quality care for all children with cancer worldwide. LAY SUMMARY: Advances in childhood cancer management have substantially improved the burden of these neoplasms over the past 40 years, particularly in high-income countries. This study aimed to monitor recent trends in America and Australasia using mortality data from the World Health Organization. Trends in childhood cancer mortality continued to decline in high-income countries by approximately 2% to 3% per year in Japan, Korea, and Australia, and 1% to 2% in North America. Only a few Latin American countries showed favorable trends, including Argentina, Chile, and Mexico, whereas other countries with limited resources still lagged behind.

Man, J., et al. (2021). "Spatiotemporal Trends of Colorectal Cancer Mortality Due to Low Physical Activity and High Body Mass Index From 1990 to 2019: A Global, Regional and National Analysis." Front Med (Lausanne) **8**: 800426.

Background: Understanding the spatiotemporal trends of colorectal cancer (CRC) deaths caused by low physical activity (LPA) and high body mass index (BMI) is essential for the prevention and control of CRC. We assessed patterns of LPA and high BMI-induced CRC deaths from 1990 to 2019 at

global, regional, and national levels. Methods: Data on CRC deaths due to LPA and high BMI was downloaded from the Global Burden of Disease 2019 Study. We calculated estimated annual percentage change (EAPC) to quantify spatiotemporal trends in the CRC age-standardized mortality rate (ASMR) due to LPA and high BMI. Results: In 2019, CRC deaths due to LPA and high BMI were estimated as 58.66 thousand and 85.88 thousand, and the corresponding ASMRs were 0.77/100,000 and 1.07/100,000, with EAPCs of-0.39 [95% confidence interval (CI):-0.49,-0.29] and 0.64[95% CI: 0.57, 0.71] from 1990 to 2019 respectively. Since 1990, the ASMR of CRC attributable to LPA and high BMI has been on the rise in many geographic regions, especially in low middle and middle sociodemographic index (SDI) regions. Thirteen countries had a significant downward trend in CRC ASMR attributed to LPA, with EAPCs < -1. And, only 4 countries had a significant downward trend in CRC ASMR attributable to high BMI, with EAPCs < -1. Countries with a higher baseline burden in 1990 and a higher SDI in 2019 had a faster decline in ASMR due to high BMI and LPA. Conclusions: The burden of CRC caused by LPA and high BMI is on the rise in many countries. Countries should adopt a series of measures to control the local prevalence of obesity and LPA in order to reduce disease burden, including CRC.

Man, X., et al. (2020). "Aspirin Use and Mortality in Women With Ovarian Cancer: A Meta-Analysis." Front Oncol **10**: 575831.

BACKGROUND: Aspirin use has been suggested to reduce the incidence of ovarian cancer (OC) in women. However, previous studies regarding the association between aspirin use and mortality in women with OC showed inconsistent results. We aimed to evaluate the association between aspirin use and mortality in women with OC in a meta-analysis. METHODS: Relevant cohort studies were obtained via search of PubMed, Cochrane's Library, and Embase databases from inception to May 3, 2020. A random-effect model, which incorporates the potential heterogeneity among the included studies, was used to pool the results. Predefined stratified analyses were applied to evaluate the potential study characteristics on the outcome, including the timing of aspirin use, dose of aspirin, age of the women, and the clinical stages of the cancer. Sensitivity analysis by omitting one study at a time was used to assess the stability of the results. RESULTS: Six cohort studies including 17,981 women with OC were included. Pooled results showed that aspirin use had no statistically significant association with mortality in these patients (adjusted risk ratio [RR]: 0.85, 95% confidence interval [CI]: 0.70 to 1.02, p = 0.08; I(2) = 69%). The results were similar for OC-specific mortality (RR: 0.85, 95% CI: 0.57 to 1.26, p = 0.41) and all-cause mortality (RR: 0.78, 95% CI: 0.55 to 1.11, p = 0.17). Stratified analyses suggested that aspirin use had no statistically significant association with mortality risk in OC regardless the timing of aspirin use, dose of aspirin, age of the women, or the clinical stages of the cancer. Funnel plots suggested potential risk of publication bias (p all > 0.05). However, further "trim-and-fill" analysis incorporating hypothesized unpolished studies to achieve symmetrical funnel plots showed similar results of the meta-analysis (RR: 0.91, 95% CI: 0.74 to 1.13, p = 0.39). CONCLUSIONS: Current evidence from observational studies indicated that aspirin use had no statistically significant association with mortality in women with OC.

Mangone, L., et al. (2021). "Cumulative COVID-19 incidence, mortality and prognosis in cancer survivors: A population-based study in Reggio Emilia, Northern Italy." Int J Cancer **149**(4): 820-826.

The aim of this population-based study was to evaluate the impact of being a cancer survivor (CS) on COVID-19 risk and prognosis during the first wave of the pandemic (27 February 2020 to 13 May 2020) in Reggio Emilia Province. Prevalent cancer cases diagnosed between 1996 and 2019 were linked with the provincial COVID-19 surveillance system. We compared CS' cumulative incidence of being tested, testing positive for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), being hospitalized and dying of COVID-19 with that of the general population; we compared COVID-19 prognosis in CS and in patients without cancer. During the study period, 15 391 people (1527 CS) underwent real-time polymerase chain reaction for SARS-CoV-2, of whom 4541 (447 CS) tested positive; 541 (113 CS) died of COVID-19. CS had higher age- and sex-adjusted incidence rate ratios (IRR) of testing (1.28 [95% confidence interval, CI = 1.21-1.35]), of positive test (IRR 1.06 [95% CI = 0.96-1.18]) and of hospitalization and death (IRR 1.27 [95% CI = 1.09-1.48] and 1.39 [95%CI = 1.12-1.71], respectively). CS had worse prognosis when diagnosed with COVID-19, particularly those below age 70 (adjusted odds ratio [OR] of death 5.03; [95% CI = 2.59-9.75]), while the OR decreased after age 70. The OR of death was higher for CS with a recent diagnosis, that is, <2 years (OR = 2.92; 95% CI = 1.64-5.21), or metastases (OR = 2.09; 95% CI = 0.88-4.93). CS showed the same probability of being infected, despite a slightly higher probability of being tested than the general population. Nevertheless, CS were at higher risk of death once infected.

Mangone, L., et al. (2021). "A Population-Based Study of Cardiovascular Disease Mortality in Italian Cancer Patients." Cancers (Basel) **13**(23).

The present research describes 25 years of cardiovascular mortality in a cohort of patients in Northern Italy. The study included patients with malignant cancer enrolled in the period of 1996-2019, and describes cardiovascular and cancer mortality in relation to sex, age, year of diagnosis, months of survivorship, tumor site, and standardized mortality ratio (SMR). Out of 67,173 patients, 38,272 deaths (57.7%) were recorded: 4466 from cardiovascular disease (CVD) (6.6%), and 28,579 (42.6%) from cancer. The proportion of CVD death increased from 4.5% in the first two years after diagnosis, to 7.3% after more than 10 years, while the proportion of deaths from cancer decreased from 70.5% to 9.4%. The CVD SMR comparing cancer patients with the general population was 0.87 (95% CI: 0.82-0.92) in 1996-1999, rising to 0.95 (95% CI: 0.84-1.08) in 2015-2019, without differences in terms of sex or age. The risk of dying from CVD was higher compared with the general population (SMR 1.31; 95% CI: 1.24-1.39) only in the first two years after diagnosis. The trend over time underscored that CVD deaths increased in patients with breast, bladder, prostate, and colorectal cancers, and, in the more recent period, for kidney cancer and melanoma patients. Our data confirmed that cardiovascular mortality is an important issue in the modern management of cancer patients, suggesting the need for an extensive interdisciplinary approach.

Mangone, L., et al. (2022). "Trends in Incidence and Mortality of Kidney Cancer in a Northern Italian Province: An Update to 2020." Biology (Basel) **11**(7).

The aim of this study was to examine the incidence and mortality trends for tumors and cardiovascular disease (CVD) in a province of northern Italy. The study included kidney cancers recorded in the period 1996-2020, divided by sex, age, year of incidence and years from diagnosis. The standardized incidence rate was calculated using the European population, and the Annual Percent Change (APC) was reported. In total, 2331 patients with kidney cancers were identified, mainly males (1504 cases) aged 60-79 years (1240 cases). There were 1257 deaths; there were no differences according sex but there were differences according to age (12.1% among younger adults and 80.4% among 80+). The incidence rate increased in males between 1996 and 2011 (APC = 2.3), while the mortality rate decreased in both males (APC = -3.3%) and females (APC = -4.5%). Comparing the same periods, kidney cancer-specific mortality decreased from 81.8% to 43.7%, while in the same period there was an increasing trend for CVD mortality. Moreover, the risk of CVD mortality increased as we moved away from the diagnosis (from 6.2% to 27.5%, p < 0.01). The same trend was observed for other causes of death (from 12.6% to 32.1%, p < 0.01). Thus, a multidisciplinary approach seems necessary during the follow-up and treatments of patients with kidney cancer.

Manz, C. R., et al. (2020). "Validation of a Machine Learning Algorithm to Predict 180-Day Mortality for Outpatients With Cancer." JAMA Oncol **6**(11): 1723-1730.

IMPORTANCE: Machine learning (ML) algorithms can identify patients with cancer at risk of short-term mortality to inform treatment and advance care planning. However, no ML mortality risk prediction algorithm has been prospectively validated in oncology or compared with routinely used prognostic indices. OBJECTIVE: To validate an electronic health record-embedded ML algorithm that generated real-time predictions of 180-day mortality risk in a general oncology cohort. DESIGN, SETTING, AND PARTICIPANTS: This prognostic study comprised a prospective cohort of patients with outpatient oncology encounters between March 1, 2019, and April 30, 2019. An ML algorithm, trained on retrospective data from a subset of practices, predicted 180-day mortality risk between 4 and 8 days before a patient's encounter. Patient encounters took place in 18 medical or gynecologic oncology practices, including 1 tertiary practice and 17 general oncology practices, within a large US academic health care system. Patients aged 18 years or older with outpatient oncology or hematology and oncology encounters were included in the analysis. Patients were excluded if their appointment was scheduled after weekly predictions were generated and if they were only evaluated in benign hematology, palliative care, or rehabilitation practices. EXPOSURES: Gradient-boosting ML binary classifier. MAIN OUTCOMES AND MEASURES: The primary outcome was the patients' 180-day mortality from the index encounter. The primary performance metric was the area under the receiver operating characteristic curve (AUC). RESULTS: Among 24 582 patients, 1022 (4.2%) died within 180 days of their index encounter. Their median (interquartile range) age was 64.6 (53.6-73.2) years, 15 319 (62.3%) were women, 18 015 (76.0%) were White, and 10 658 (43.4%) were seen in the tertiary practice. The AUC was 0.89 (95% CI, 0.88-0.90) for the full cohort. The AUC varied across disease-specific groups within the tertiary practice (AUC ranging from 0.74 to 0.96) but was similar between the tertiary and general oncology practices. At a prespecified 40% mortality risk threshold used to differentiate high- vs low-risk patients, observed 180-day mortality was 45.2% (95% CI, 41.3%-49.1%) in the high-risk group vs 3.1% (95%

CI, 2.9%-3.3%) in the low-risk group. Integrating the algorithm into the Eastern Cooperative Oncology Group and Elixhauser comorbidity index-based classifiers resulted in favorable reclassification (net reclassification index, 0.09 [95% CI, 0.04-0.14] and 0.23 [95% CI, 0.20-0.27], respectively). CONCLUSIONS AND RELEVANCE: In this prognostic study, an ML algorithm was feasibly integrated into the electronic health record to generate real-time, accurate predictions of short-term mortality for patients with cancer and outperformed routinely used prognostic indices. This algorithm may be used to inform behavioral interventions and prompt earlier conversations about goals of care and end-of-life preferences among patients with cancer.

Manz, C. R., et al. (2021). "Disparities in cancer prevalence, incidence, and mortality for incarcerated and formerly incarcerated patients: A scoping review." Cancer Med **10**(20): 7277-7288.

BACKGROUND: Racial and ethnic minority status, structural racism, low educational attainment, and poverty are consistently associated with cancer disparities and with higher rates of incarceration. The objective of this scoping review is to conduct a qualitative synthesis of the literature on cancer prevalence, incidence, mortality, and disparities in these outcomes for incarcerated and formerly incarcerated patients, as this literature is fragmented and heterogenous. METHODS: This scoping review included Bureau of Justice Statistics reports and searched PubMed in May 2021 for all English language studies published between 1990 and 30 April 2021, that reported on cancer prevalence, incidence, or mortality for incarcerated or formerly incarcerated individuals in the United States. RESULTS: Twenty studies were selected. Data on cancer prevalence and incidence were scarce but suggested that incarcerated and formerly incarcerated patients have a similar overall risk of cancer diagnosis as the general population, but elevated risk of certain cancers such as cervical, lung, colorectal, and hepatocellular carcinoma for which effective prevention and screening interventions exist. Cancer mortality data in state and local jails as well as prisons were robust and suggests that both incarcerated and formerly incarcerated patients have higher cancer mortality than the general population. CONCLUSIONS: Incarcerated and formerly incarcerated patients likely have a higher risk of dying from cancer than the general population, but important gaps in our knowledge about the extent and drivers of disparities for this population remain. Additional research is needed to guide interventions to reduce cancer disparities for patients experiencing incarceration.

Manz, C. R., et al. (2020). "Effect of Integrating Machine Learning Mortality Estimates With Behavioral Nudges to Clinicians on Serious Illness Conversations Among Patients With Cancer: A Stepped-Wedge Cluster Randomized Clinical Trial." JAMA Oncol **6**(12): e204759.

IMPORTANCE: Serious illness conversations (SICs) are structured conversations between clinicians and patients about prognosis, treatment goals, and end-of-life preferences. Interventions that increase the rate of SICs between oncology clinicians and patients may improve goal-concordant care and patient outcomes. OBJECTIVE: To determine the effect of a clinician-directed intervention integrating machine learning mortality predictions with behavioral nudges on motivating clinician-patient SICs. DESIGN, SETTING, AND PARTICIPANTS: This stepped-wedge cluster randomized clinical trial was conducted across 20 weeks (from June 17 to November 1, 2019) at 9 medical oncology clinics (8 subspecialty oncology and 1 general oncology clinics) within a large academic health system in Pennsylvania. Clinicians at the 2 smallest subspecialty clinics were grouped together, resulting in 8 clinic groups randomly assigned to the 4 intervention wedge periods. Included participants in the intention-to-treat analyses were 78 oncology clinicians who received SIC training and their patients (N = 14 607) who had an outpatient oncology encounter during the study period. INTERVENTIONS: (1) Weekly emails to oncology clinicians with SIC performance feedback and peer comparisons; (2) a list of up to 6 high-risk patients (>/=10% predicted risk of 180-day mortality) scheduled for the next week, estimated using a validated machine learning algorithm; and (3) opt-out text message prompts to clinicians on the patient's appointment day to consider an SIC. Clinicians in the control group received usual care consisting of weekly emails with cumulative SIC performance. MAIN OUTCOMES AND MEASURES: Percentage of patient encounters with an SIC in the intervention group vs the usual care (control) group. RESULTS: The sample consisted of 78 clinicians and 14 607 patients. The mean (SD) age of patients was 61.9 (14.2) years, 53.7% were female, and 70.4% were White. For all encounters, SICs were conducted among 1.3% in the control group and 4.6% in the intervention group, a significant difference (adjusted difference in percentage points, 3.3; 95% CI, 2.3-4.5; P < .001). Among 4124 high-risk patient encounters, SICs were conducted among 3.6% in the control group and 15.2% in the intervention group, a significant difference (adjusted difference in percentage points, 11.6; 95% CI, 8.2-12.5; P < .001). CONCLUSIONS AND RELEVANCE: In this stepped-wedge cluster randomized clinical trial, an intervention that delivered machine learning mortality predictions with behavioral

nudges to oncology clinicians significantly increased the rate of SICs among all patients and among patients with high mortality risk who were targeted by the intervention. Behavioral nudges combined with machine learning mortality predictions can positively influence clinician behavior and may be applied more broadly to improve care near the end of life. TRIAL REGISTRATION: ClinicalTrials.gov Identifier: NCT03984773.

Mao, C., et al. (2021). "[Trend analysis and prediction of colorectal cancer morbidity and mortality of residents in urban areas of Guangzhou from 1972 to 2015]." Zhonghua Yu Fang Yi Xue Za Zhi **55**(5): 640-645.

Objective: To analyze the trend of mortality and incidence of colorectal cancer among urban residents in Guangzhou from 1972 to 2015 and to predict the mortality of colorectal cancer from 2016 to 2025. Methods: The mortality data of colorectal cancer among urban residents in Guangzhou were collected from the death registration of malignant tumors of Guangzhou Health Statistics Bureau (1972-1979), Guangzhou Health Statistics (1980-2001), Guangzhou Cancer Registration Annual Report (2002-2009) and China Cancer Registration Annual Report (2010-2015). The incidence of colorectal cancer was collected from Guangzhou Cancer Registration Annual Report (2002-2009) and China Cancer Registration Annual Report (2010-2015). The incidence and mortality data of colorectal cancer coded as C18-C21 in 10th Edition of International Classification of Diseases (ICD-10) were obtained from the above data, and the demographic data were from the Guangzhou Municipal Bureau of Statistics. Joinpoint model was used to calculate the annual change percentage (APC) and average annual change percentage (AAPC) of colorectal cancer mortality and incidence among urban residents in Guangzhou from 1972 to 2015 and from 2002 to 2015. ARIMA model was used to predict colorectal cancer mortality from 2016 to 2025. Results: There were 19 309 colorectal cancer deaths among urban residents in Guangzhou from 1972 to 2015. The crude mortality rate of colorectal cancer increased from 4.33/100 000 to 24.89/100 000 (AAPC=4.2%, P<0.001). A total of 24 033 new cases of colorectal cancer were reported in Guangzhou from 2002 to 2015. The crude incidence rate of colorectal cancer increased from 22.95/100 000 to 52.81/100 000 (AAPC=6.6%, P<0.001). The mortality rate of colorectal cancer among urban residents of Guangzhou would continuously increase from 2016 to 2025 and reach 29.53/100 000 in 2025. Conclusion: The mortality rate of colorectal cancer among urban residents of Guangzhou from 1972 to 2015 and the incidence rate of colorectal cancer from 2002 to 2015 both show an upward trend. The mortality rate will increase from 2016 to 2025.

Mao, X., et al. (2021). "The Clinical Value of Pulmonary Rehabilitation in Reducing Postoperative Complications and Mortality of Lung Cancer Resection: A Systematic Review and Meta-Analysis." Front Surg **8**: 685485.

Background: Pulmonary rehabilitation is one meaningful way of improving exercise tolerance and pulmonary function. Thus, it may reduce the postoperative complications and mortality of pulmonary resection. Hence, we refreshed the data and conducted this systemic analysis. Method: We searched Pubmed, Web of Science, and EMBASE using "lung OR pulmonary" AND "operation OR resection OR surgery" AND "rehabilitation or exercise." The cut-off date was September 30, 2020. The publications were filtrated, and data were extracted from all selected studies by two reviewers. Review Manger 5.1 and the fixed or random regression model were used for calculating the pooled odds ratio (OR). Result: Finally, 13 publications were enrolled in this study. Among them, five publications reported mortality, nine reported postoperative complications, and seven reported postoperative pulmonary complications. The pooled OR of mortality was 1.32 [95% confidence interval (CI): 0.54-3.23] for the pulmonary rehabilitation group, the pooled OR of postoperative complications was 0.62 (95% CI: 0.49-0.79) for the pulmonary rehabilitation group, and the pooled OR of postoperative pulmonary complications was 0.39 (95% CI: 0.27-0.56) for the pulmonary rehabilitation group. Subgroup analysis revealed the perioperative pulmonary rehabilitation was the most important part. Conclusion: Pulmonary rehabilitation may not affect the mortality of pulmonary resection patients, however, it could decrease the number of postoperative complications, especially pulmonary complications. Perioperative pulmonary rehabilitation was the most important part of the program.

Mao, Z., et al. (2021). "Dietary Intake of Advanced Glycation End Products (AGEs) and Mortality among Individuals with Colorectal Cancer." Nutrients **13**(12).

Advanced glycation end-products (AGEs) may promote oxidative stress and inflammation and have been linked to multiple chronic diseases, including cancer. However, the association of AGEs with mortality after colorectal cancer (CRC) diagnosis has not been previously investigated. Multivariable Cox proportional hazards models were used to calculate hazard ratios and corresponding 95% confidence intervals for associations between dietary intake of AGEs with CRC-specific and all-cause mortality among 5801 participant cases diagnosed with

CRC in the European Prospective Investigation into Cancer and Nutrition study between 1993 and 2013. Dietary intakes of AGEs were estimated using country-specific dietary questionnaires, linked to an AGE database, that accounted for food preparation and processing. During a median of 58 months of follow-up, 2421 cases died (1841 from CRC). Individually or combined, dietary intakes of AGEs were not associated with all-cause and CRC-specific mortality among cases. However, there was a suggestion for a positive association between AGEs and all-cause or CRC-specific mortality among CRC cases without type II diabetes (all-cause, P(interaction) = 0.05) and CRC cases with the longest follow-up between recruitment and cancer diagnosis (CRC-specific, P(interaction) = 0.003; all-cause, P(interaction) = 0.01). Our study suggests that pre-diagnostic dietary intakes of AGEs were not associated with CRC-specific or all-cause mortality among CRC patients. Further investigations using biomarkers of AGEs and stratifying by sex, diabetes status, and timing of exposure to AGEs are warranted.

Marcelino, A. C., et al. (2021). "Race disparities in mortality by breast cancer from 2000 to 2017 in Sao Paulo, Brazil: a population-based retrospective study." BMC Cancer **21**(1): 998.

BACKGROUND: In Brazil, inequalities in access may interfere with cancer care. This study aimed to evaluate the influence of race on breast cancer mortality in the state of Sao Paulo, from 2000 to 2017, contextualizing with other causes of death. METHODS: A population-based retrospective study using mortality rates, age and race as variables. Information on deaths was collected from the Ministry of Health Information System. Only white and black categories were used. Mortality rates were age-adjusted by the standard method. For statistical analysis, linear regression was carried out. RESULTS: There were 60,940 deaths registered as breast cancer deaths, 46,365 in white and 10,588 in black women. The mortality rates for 100,000 women in 2017 were 16.46 in white and 9.57 in black women, a trend to reduction in white ($p = 0.002$), and to increase in black women ($p = 0.010$). This effect was more significant for white women ($p < 0.001$). The trend to reduction was consistent in all age groups in white women, and the trend to increase was observed only in the 40-49 years group in black women. For 'all-cancer causes', the trend was to a reduction in white ($p = 0.031$) and to increase in black women ($p < 0.001$). For 'ill-defined causes' and 'external causes', the trend was to reduce both races ($p < 0.001$). CONCLUSION: The declared race influenced mortality rates due to breast cancer in Sao Paulo. The divergences observed between white and black women also were evident in all cancer causes of death, which may indicate inequities in access to highly complex health care in our setting.

Marjerrison, N., et al. (2022). "Comparison of cancer incidence and mortality in the Norwegian Fire Departments Cohort, 1960-2018." Occup Environ Med **79**(11): 736-743.

OBJECTIVES: Elevated risk of cancer at several sites has been reported among firefighters, although with mixed findings. The purpose of this study was to calculate standardised incidence ratios (SIRs) and standardised mortality ratios (SMRs) for cancer and compare them to assess whether use of the different measures could be a source of inconsistencies in findings. METHODS: The Norwegian Fire Departments Cohort, comprising 4295 male employees who worked at 15 fire departments across Norway, was linked to health outcome registries for the period 1960-2018. SIRs and SMRs were derived using national reference rates. RESULTS: Overall, we observed elevated incidence of colon cancer (SIR, 95% CI 1.27, 1.01 to 1.58), mesothelioma (2.59, 1.12 to 5.11), prostate cancer (1.18, 1.03 to 1.34) and all sites combined (1.15, 1.08 to 1.23). Smaller, non-significant elevations were found for mortality of colon cancer (SMR, 95% CI 1.20, 0.84 to 1.67) and mesothelioma (1.66, 0.34 to 4.86), while SMR for prostate cancer was at unity. Potential errors were observed in some of the mortality data, notably for mesothelioma cases. Among those who died of cancer, 3.7% (n=14) did not have a prior diagnosis of malignancy at the same site group. CONCLUSIONS: Assessment of incidence or mortality did not greatly influence the interpretation of results. The most prominent differences in SIR and SMR appeared to be due to inconsistencies between sites of cancer diagnosis and cause of death. The difference in SIR and SMR for prostate cancer suggested a detection bias from differential screening practices.

Marklund, A., et al. (2022). "Relapse Rates and Disease-Specific Mortality Following Procedures for Fertility Preservation at Time of Breast Cancer Diagnosis." JAMA Oncol **8**(10): 1438-1446.

IMPORTANCE: Breast cancer (BC) is the most common indication for fertility preservation (FP) in women of reproductive age. Procedures for FP often include hormonal stimulation, but current data are scarce regarding whether using hormonal stimulation for FP is associated with any deterioration in BC prognosis. OBJECTIVE: To investigate the risk of disease-specific mortality and relapse in women who underwent FP with or without hormonal stimulation compared with women who did not at time of BC diagnosis. DESIGN, SETTING, AND PARTICIPANTS: This Swedish nationwide

prospective cohort study was conducted to assess the safety of hormonal and nonhormonal FP procedures indicated by BC in Sweden from January 1, 1994, through June 30, 2017. Women were identified from any of the regional FP programs located at Swedish university hospitals. A total of 425 women were found to have undergone FP, and 850 population comparators who had not undergone FP were sampled from regional BC registers and matched on age, calendar period of diagnosis, and region. Relapse-free survival was assessed in a subcohort of 241 women who underwent FP and 482 women who had not, with complete data. Nationwide demographic and health care registers provided data on outcome, disease- and treatment-related variables, and socioeconomic characteristics. Data analyses were performed between November 2021 and March 2022 and completed in June 2022. MAIN OUTCOMES AND MEASURES: Relapse and disease-specific mortality after a diagnosis of BC. RESULTS: The final study population included 1275 women (mean [SD] age, 32.9 [3.8] years) at the time of BC diagnosis. After stratification by the matching variables age, calendar period, and region, and adjustment for country of birth, education, parity at diagnosis, tumor size, number of lymph node metastases, and estrogen receptor status, disease-specific mortality was similar in women who underwent hormonal FP (adjusted hazard ratio [aHR], 0.59; 95% CI, 0.32-1.09), women who underwent nonhormonal FP (aHR, 0.51; 95% CI, 0.20-1.29), and women who were not exposed to FP (reference). In a subcohort with detailed data on relapse, adjusted rate of disease-specific mortality and relapse were also similar among the groups who underwent hormonal FP (aHR, 0.81; 95% CI, 0.49-1.37), underwent nonhormonal FP (aHR, 0.75; 95% CI, 0.35-1.62), and were not exposed to FP (reference). CONCLUSIONS AND RELEVANCE: In this cohort study, FP with or without hormonal stimulation was not associated with any increased risk of relapse or disease-specific mortality in women with BC. Results of this study provide much needed additional evidence on the safety of FP procedures in women with BC and may influence current health care practice to the benefit of young women with BC who wish to preserve their fertility.

Marrie, R. A., et al. (2021). "Cancer Incidence and Mortality Rates in Multiple Sclerosis: A Matched Cohort Study." Neurology **96**(4): e501-e512.

OBJECTIVE: To determine whether cancer risk differs in people with and without multiple sclerosis (MS), we compared incidence rates and cancer-specific mortality rates in MS and matched cohorts using population-based data sources. METHODS: We conducted a retrospective matched cohort study using population-based administrative data from Manitoba and Ontario, Canada. We applied a validated case definition to identify MS cases, then selected 5 controls without MS matched on birth year, sex, and region. We linked these cohorts to cancer registries, and estimated incidence of breast, colorectal, and 13 other cancers. For breast and colorectal cancers, we constructed Cox models adjusting for age at the index date, area-level socioeconomic status, region, birth cohort year, and comorbidity. We pooled findings across provinces using meta-analysis. RESULTS: We included 53,983 MS cases and 269,915 controls. Multivariable analyses showed no difference in breast cancer risk (pooled hazard ratio [HR] 0.92 [95% confidence interval (CI) 0.78-1.09]) or colorectal cancer risk (pooled HR 0.83 [95% CI 0.64-1.07]) between the cohorts. Mortality rates for breast and colorectal did not differ between cohorts. Bladder cancer incidence and mortality rates were higher among the MS cohort. Although the incidence of prostate, uterine, and CNS cancers differed between the MS and matched cohorts, mortality rates did not. CONCLUSION: The incidence of breast and colorectal cancers does not differ between persons with and without MS; however, the incidence of bladder cancer is increased. Reported differences in the incidence of some cancers in the MS population may reflect ascertainment differences rather than true differences.

Marrone, M. T., et al. (2021). "Lipid-Lowering Drug Use and Cancer Incidence and Mortality in the ARIC Study." JNCI Cancer Spectr **5**(5).

BACKGROUND: Lipid-lowering drugs, particularly statins, are associated with reduced incidence of certain cancers in some studies. Associations with cancer mortality are not well studied, and whether associations are similar across race is unknown. METHODS: We conducted a prospective analysis of 12 997 cancer-free participants in the Atherosclerosis Risk in Communities Study who were never users at visit 1 (1987-1989). Ever use, duration of use, and age at first use were modeled as time-dependent variables using Cox regression to estimate associations with total, obesity- and smoking-associated, bladder, breast, colorectal, lung, and prostate cancer incidence and mortality. RESULTS: We ascertained 3869 cancer cases and 1661 cancer deaths in 237 999 or more person-years. At 6 years of follow-up, 70.8% of lipid-lowering drug use was a statin. Compared with never use, ever use was associated with lower total, obesity- and smoking-associated cancer mortality and with colorectal cancer mortality (hazard ratio [HR] = 0.50, 95% confidence interval [CI] = 0.32 to 0.79) and incidence (HR = 0.69, 95% CI = 0.53 to 0.92). Inverse associations were consistent by sex and race. Shorter-term use was associated with bladder cancer incidence in men (<10

years: HR = 1.67, 95% CI = 1.02 to 2.73). First use at age 60 years or older was inversely associated with: total mortality, obesity- and smoking-associated mortality, and colorectal cancer mortality; and total incidence, obesity- and smoking-associated incidence, and breast, colorectal, and prostate cancer incidence. CONCLUSIONS: This study provides additional evidence for inverse associations between lipid-lowering drug use and cancer incidence and mortality but a positive association with bladder cancer incidence in men. Evaluation of the impact of chemoprevention strategies that include lipid-lowering drugs on population-level cancer burden is needed.

Martinez, M. E., et al. (2022). "Changes in Cancer Mortality by Race and Ethnicity Following the Implementation of the Affordable Care Act in California." Front Oncol **12**: 916167.

Although Affordable Care Act (ACA) implementation has improved cancer outcomes, less is known about how much the improvement applies to different racial and ethnic populations. We examined changes in health insurance coverage and cancer-specific mortality rates by race/ethnicity pre- and post-ACA. We identified newly diagnosed breast (n = 117,738), colorectal (n = 38,334), and cervical cancer (n = 11,109) patients < 65 years in California 2007-2017. Hazard rate ratios (HRR) and 95% confidence intervals (CI) were calculated using multivariable Cox regression to estimate risk of cancer-specific death pre-(2007-2010) and post-ACA (2014-2017) and by race/ethnicity [American Indian/Alaska Natives (AIAN); Asian American; Hispanic; Native Hawaiian or Pacific Islander (NHPI); non-Hispanic Black (NHB); non-Hispanic white (NHW)]. Cancer-specific mortality from colorectal cancer was lower post-ACA among Hispanic (HRR = 0.82, 95% CI = 0.74 to 0.92), NHB (HRR = 0.69, 95% CI = 0.58 to 0.82), and NHW (HRR = 0.90; 95% CI = 0.84 to 0.97) but not Asian American (HRR = 0.95, 95% CI = 0.82 to 1.10) patients. We observed a lower risk of death from cervical cancer post-ACA among NHB women (HRR = 0.68, 95% CI = 0.47 to 0.99). No statistically significant differences in breast cancer-specific mortality were observed for any racial or ethnic group. Cancer-specific mortality decreased following ACA implementation for colorectal and cervical cancers for some racial and ethnic groups in California, suggesting Medicaid expansion is associated with reductions in health inequity.

Martinez-Gonzalez, M. A., et al. (2022). "Effect of olive oil consumption on cardiovascular disease, cancer, type 2 diabetes, and all-cause mortality: A systematic review and meta-analysis." Clin Nutr **41**(12): 2659-2682.

BACKGROUND: Some large prospective studies on olive oil consumption and risk of chronic disease suggested protective effects. OBJECTIVE: We conducted an outcome-wide systematic review and meta-analysis of prospective cohort studies and randomized controlled trials (RCT) assessing the association between olive oil consumption and the primary risk of 4 different outcomes: cardiovascular disease (CVD), cancer, type 2 diabetes (T2D) or all-cause mortality through January 2022. METHODS: Thirty-six studies were included in the systematic review and twenty-seven studies (24 prospective cohorts and 3 different reports from one RCT) were assessed in 4 quantitative random-effects meta-analyses. They included a total of 806,203 participants with 49,223 CVD events; 1,285,064 participants with 58,892 incident cases of cancer; 680,239 participants with 13,389 incident cases of T2D; and 733,420 participants with 174,081 deaths. Olive oil consumption was most frequently measured with validated food frequency questionnaires. Studies follow-up ranged between 3.7 and 28 years. RESULTS: A 16% reduced risk of CVD (relative risk [RR]: 0.84; 95% confidence interval [CI]: 0.76 to 0.94), standardized for every additional olive oil consumption of 25 g/d was found. No significant association with cancer risk was observed (RR: 0.94; 95% CI: 0.86 to 1.03, per 25 g/d). Olive oil consumption was associated with a 22% lower relative risk of T2D (RR: 0.78; 95% CI: 0.69 to 0.87, per 25 g/d) without evidence of heterogeneity. Similarly, it was inversely associated with all-cause mortality (RR: 0.89; 95% CI: 0.85 to 0.93, per 25 g/d). Only the results for T2D were homogeneous. Specific sources of heterogeneity for the other 3 outcomes were not always apparent. CONCLUSIONS: Prospective studies supported a beneficial association of olive oil consumption with CVD, T2D and all-cause mortality, but they did not show any association with cancer risk.

Martinez-Tapia, C., et al. (2020). "The obesity paradox for mid- and long-term mortality in older cancer patients: a prospective multicenter cohort study." Am J Clin Nutr.

BACKGROUND: Overweight and obesity are associated with adverse health outcomes. However, substantial literature suggests that they are associated with longer survival among older people. This "obesity paradox" remains controversial. In the context of cancer, the association between overweight/obesity and mortality is complicated by concomitant weight loss (WL). Sex differences in the relation between BMI (in kg/m2) and survival have also been observed. OBJECTIVES: We studied whether a high BMI was associated with better survival, and whether the association differed by sex, in older patients with

cancer. METHODS: We studied patients aged >/=70 y from the ELCAPA (Elderly Cancer Patients) prospective open cohort (2007-2016; 10 geriatric oncology clinics, Greater Paris urban area). The endpoints were 12- and 60-mo mortality. We created a variable combining BMI at cancer diagnosis and WL in the previous 6 mo, and considered 4 BMI categories-underweight (BMI < 22.5), normal weight (BMI = 22.5-24.9), overweight (BMI = 25-29.9), and obesity (BMI >/= 30)-and 3 WL categories-<5% (minimal), 5% to <10% (moderate), and >/=10% (severe). Univariate and multivariate Cox proportional hazards analyses were conducted in men and women. RESULTS: A total of 2071 patients were included (mean age: 81 y; women: 48%; underweight: 30%; normal weight: 23%; overweight: 33%; obesity: 14%; predominant cancer sites: colorectal (18%) and breast (16%); patients with metastases: 49%). By multivariate analysis, obese women with WL < 5% had a lower 60-mo mortality risk than normal-weight women with WL < 5% (adjusted HR: 0.56; 95% CI: 0.37, 0.86; P = 0.012). Overweight/obese women with WL >/= 5% did not have a lower mortality risk than normal-weight women with WL < 5%. Overweight and obese men did not have a lower mortality risk, irrespective of WL. CONCLUSIONS: By taking account of prediagnosis WL, only older obese women with cancer with minimal WL had a lower mortality risk than their counterparts with normal weight.This trial was registered at clinicaltrials.gov as NCT02884375.

Masum, S., et al. (2022). "Data analytics and artificial intelligence in predicting length of stay, readmission, and mortality: a population-based study of surgical management of colorectal cancer." Discov Oncol **13**(1): 11.

Data analytics and artificial intelligence (AI) have been used to predict patient outcomes after colorectal cancer surgery. A prospectively maintained colorectal cancer database was used, covering 4336 patients who underwent colorectal cancer surgery between 2003 and 2019. The 47 patient parameters included demographics, peri- and post-operative outcomes, surgical approaches, complications, and mortality. Data analytics were used to compare the importance of each variable and AI prediction models were built for length of stay (LOS), readmission, and mortality. Accuracies of at least 80% have been achieved. The significant predictors of LOS were age, ASA grade, operative time, presence or absence of a stoma, robotic or laparoscopic approach to surgery, and complications. The model with support vector regression (SVR) algorithms predicted the LOS with an accuracy of 83% and mean absolute error (MAE) of 9.69 days. The significant predictors of readmission were age, laparoscopic procedure, stoma performed, preoperative nodal (N) stage, operation time, operation mode, previous surgery type, LOS, and the specific procedure. A BI-LSTM model predicted readmission with 87.5% accuracy, 84% sensitivity, and 90% specificity. The significant predictors of mortality were age, ASA grade, BMI, the formation of a stoma, preoperative TNM staging, neoadjuvant chemotherapy, curative resection, and LOS. Classification predictive modelling predicted three different colorectal cancer mortality measures (overall mortality, and 31- and 91-days mortality) with 80-96% accuracy, 84-93% sensitivity, and 75-100% specificity. A model using all variables performed only slightly better than one that used just the most significant ones.

Matetic, A., et al. (2022). "Prevalence, characteristics and mortality of cancer patients undergoing pericardiocentesis in the United States between 2004 and 2017." Cancer Med.

BACKGROUND: Pericardiocentesis is undertaken in patients with cancer for diagnostic and therapeutic purposes. However, there are limited data on the frequency, characteristics and mortality of patients with different cancers undergoing pericardiocentesis. METHODS: All hospitalisations of adult cancer patients (>/=18 years) in the US National Inpatient Sample between January 2004 and December 2017 were included. The cohort was stratified by discharge code of pericardiocentesis and cancer, using the International Classification of Diseases. The prevalence of pericardiocentesis, patient characteristics, cancer types and in-hospital all-cause mortality were analysed between cancer patients undergoing pericardiocentesis versus not. RESULTS: A total of 19,773,597 weighted cancer discharges were analysed, out of which 18,847 (0.1%) underwent pericardiocentesis. The most common cancer types amongst the patients receiving pericardiocentesis were lung (51.3%), haematological (15.9%), breast (5.4%), mediastinum/heart (3.2%), gastroesophageal (2.2%) and female genital cancer (1.8%), whilst 'other' cancer types were present in 20.2% patients. Patients undergoing pericardiocentesis had significantly higher mortality (15.6% vs. 4.2%, p < 0.001) compared to their counterparts. The presence of metastatic disease (aOR 2.67 95% CI 1.79-3.97), weight loss (aOR 1.48 95% CI 1.33-1.65) and coagulopathy (aOR 3.22 95% CI 1.63-6.37) were each independently associated with higher mortality in patients who underwent pericardiocentesis. CONCLUSION: Pericardiocentesis is an infrequent procedure in cancer patients and is most commonly performed in patients with lung, haematological and breast cancer. Cancer patients undergoing pericardiocentesis have increased mortality, irrespective of the underlying cancer type.

Matsueda, K., et al. (2022). "Impact of endoscopic surveillance on mortality of metachronous esophageal and head and neck cancer after esophageal endoscopic resection." J Gastroenterol Hepatol **37**(11): 2098-2104.

BACKGROUND AND AIM: As more superficial esophageal cancer (EC) patients are being treated with endoscopic resection (ER), it is important to understand the outcomes, including survival data, of patients who develop metachronous EC and head and neck cancer (HNC). We aimed to evaluate the long-term surveillance and survival outcomes of metachronous EC and HNC after esophageal ER. METHODS: This study included 627 patients who underwent ER of superficial esophageal squamous cell carcinoma from 2008 to 2016 and were generally followed by annual or biannual esophagogastroduodenoscopy up to 2019 at Osaka International Cancer Institute. Data on metachronous cancer development and causes of death were collected from an integrated database of hospital-based cancer registry and Vital Statistics of Japan. RESULTS: During a median (range) follow-up period of 67.4 (3.8-142.7) months, 230 patients (36.7%) developed 500 metachronous ECs and 126 patients (20.1%) developed 239 metachronous HNCs, post-ER of index EC. The 3-year, 5-year, and 7-year cumulative incidences were 25.8%, 36.0%, and 43.6% for metachronous EC and 10.9%, 16.0%, and 26.9% for metachronous HNC, respectively. No patients died of metachronous EC, and only seven patients (1.1%) died of metachronous HNC. The 3-year, 5-year, and 7-year disease-specific survival rates were 99.8%, 99.6%, and 98.6%, respectively. CONCLUSIONS: The incidences of metachronous EC and HNC increase with time over 5 years after esophageal ER; therefore, surveillance endoscopy should be continued over 5 years. Endoscopic surveillance is useful for survivors after esophageal ER given the high incidence and extremely low mortality of metachronous EC and HNC.

Matsunaga, M., et al. (2022). "Impact of Body Mass Index on Obesity-Related Cancer and Cardiovascular Disease Mortality; The Japan Collaborative Cohort Study." J Atheroscler Thromb **29**(10): 1547-1562.

AIM: We aimed to examine the association of obesity-related cancer and cardiovascular disease (CVD) with body mass index (BMI) and the estimated population attributable fraction in lean Asians. METHODS: We studied 102,535 participants aged 40-79 years without histories of cancer or CVD at baseline between 1988 and 2009. The cause-specific hazard ratios (csHRs) of BMI categories (<18.5, 18.5-20.9, 21.0-22.9 [reference], 23.0-24.9, 25.0-27.4, and >/= 27.5 kg/m(2)) were estimated for each endpoint. The events considered were mortalities from obesity-related cancer (esophageal, colorectal, liver, pancreatic, kidney, female breast, and endometrial cancer) and those from CVD (coronary heart disease and stroke). Population attributable fractions (PAFs) were calculated for these endpoints. RESULTS: During a 19.2-year median follow-up, 2906 died from obesity-related cancer and 4532 died from CVD. The multivariable-adjusted csHRs (95% confidence interval) of higher BMI categories (25-27.4 and >/= 27.5 kg/m(2)) for obesity-related cancer mortality were 0.93 (0.78, 1.10) and 1.18 (0.92, 1.50) in men and 1.25 (1.04, 1.50) and 1.48 (1.19, 1.84) in women, respectively. The corresponding csHRs for CVD mortality were 1.27 (1.10, 1.46) and 1.59 (1.30, 1.95) in men and 1.10 (0.95, 1.28) and 1.44 (1.21, 1.72) in women, respectively. The PAF of a BMI >/= 25 kg/m(2) for obesity-related cancer was -0.2% in men and 6.7% in women and that for CVD was 5.0% in men and 4.5% in women. CONCLUSION: A BMI >/= 25 kg/m(2) is associated with an increased risk of obesity-related cancer in women and CVD in both sexes.

Matsuo, K., et al. (2022). "Association between hysterectomy wait-time and all-cause mortality for micro-invasive cervical cancer: treatment implications during the coronavirus pandemic." Arch Gynecol Obstet **306**(1): 283-287.

Matsuo, K., et al. (2022). "Assessment of Severe Maternal Morbidity and Mortality in Pregnancies Complicated by Cancer in the US." JAMA Oncol **8**(8): 1213-1216.

This cohort study examines nationwide trends and characteristics of severe maternal morbidity and mortality among pregnant women with cancer in the US.

Matti, B., et al. (2021). "Ethnic and regional differences in the temporal trends of prostate cancer incidence and mortality in New Zealand." ANZ J Surg **91**(12): 2806-2816.

BACKGROUND: Prostate cancer (Pca) is the most frequently diagnosed cancer in New Zealand (NZ) men and the third leading cause of cancer deaths. Temporal changes in Pca incidence and mortality have not been reported despite changes in the Pca landscape. This study aims to analyse the temporal trends in Pca with focus on ethnic and regional variations. METHODS: The study cohort was identified from the NZ Cancer Registry and the mortality collection databases. Men who were diagnosed with Pca between 2000 and 2018 were included in the incidence analysis. Men who died from Pca between 2000 and 2015 were included in the mortality analysis. Other data collected were ethnicity and geographical information. Pca incidence and mortality were calculated as age-

standardized rates using the 2001 World Health Organization population. RESULTS: A total of 58 966 men were diagnosed (incidence: 105.2 per 100 000) and 14 749 men died (mortality: 49.3 per 100 000) from Pca. When compared to European men, Maori and Asian men had significantly lower Pca incidence. Mortality rates demonstrated a steady decline, which was more prominent until 2010. Maori and Pacific men had higher mortality rates when compared to European men. In most recent years, the difference in mortality is decreasing for Maori but increasing for Pacific men. There were no regional differences in mortality. CONCLUSION: Pca incidence in NZ has fluctuated over the last 20 years, while mortality rates have shown to steadily decline. Pca mortality was shown to disproportionately affect Maori and Pacific men.

Mauyenova, D., et al. (2022). "Colorectal Cancer Mortality in Kazakhstan: Spatio-Temporal Epidemiological Assessment." Asian Pac J Cancer Prev **23**(3): 953-960.

OBJECTIVE: The aim is to study the trends in colorectal cancer (CRC) mortality in Kazakhstan. METHODS: The retrospective study was done using descriptive and analytical methods of oncoepidemiology. The extensive, crude and age-specific mortality rates are determined according to the generally accepted methodology used in sanitary statistics. RESULTS: CRC mortality in Kazakhstan is considered to be increasing. Therefore, this study (for the period 2009-2018) was undertaken to retrospectively evaluate data across the country available from the central registration bureau. Age standardized data for mortality was generated and compared across age groups. It was determined that during the studied period 15,200 died of this pathology. During the studied years an average age of the dead made 69.8 years (95%CI=69.5-70.0). The average annual standardized mortality rate was 10.2 per 100,000, and in dynamics tended to decrease. Peak of mortality was noted in aged 60-84 years. Trends in age-related mortality rates had a pronounced tendency to increase in 30-34 years (T=+11.7%, R2=0.7980) and to decrease in 75-79 years (T=-16.4%, R2=0.8881). In many regions, there is a decrease in the number of deaths. During the compilation of cartograms, mortality rates were determined on the basis of standardized indicators: low - up to 8.9, average - from 8.9 to 11.5, high - above 11.5 per 100,000 for the entire population. In addition, all calculations were made taking into account age-sex differences. CONCLUSION: Trends in mortality from CRC in recent years have decreased from 11.2 to 7.7 per 100,000 of the total population, while the trend is stable (T=-3.6%, R2=0.8745). The study of regional mortality has theoretical and practical significance: monitoring and evaluation of the effectiveness of early detection and treatment of detected pathology. Health authorities should take into account the results obtained when organizing anti-cancer measures.

Maxwell, A. E., et al. (2020). "Disparities in cancer mortality in Los Angeles County, 1999-2013: an analysis comparing trends in under-resourced and affluent regions." Cancer Causes Control **31**(12): 1093-1103.

PURPOSE: While cancer mortality has declined by 27% between 1991 and 2016 in the United States, there are large disparities in cancer mortality by racial/ethnic groups, socioeconomic status and access to care. The purpose of this analysis is to compare trends in cancer mortality among regions (Service Planning Areas, SPAs) in Los Angeles (LA) County that vary with respect to racial/ethnic distribution and social determinants of health, including poverty, education and access to care. METHODS: We estimated age- and race/ethnicity-standardized mortality for lung, colorectal (CRC) and breast cancer for eight SPAs from 1999 to 2013. We calculated three recommended measures of disparities that reflect absolute, relative and between-group disparities. RESULTS: In all of LA County, statistically significant declines in age- and race/ethnicity-standardized mortality ranged from 30% for lung cancer to 20% for CRC to 15% for breast cancer. Despite some of the largest declines in the most under-resourced SPAs (South LA, East LA, South Bay), disparities between the lowest and highest mortality by SPA did not significantly change from 1999 to 2013. CONCLUSIONS: Despite significant declines in cancer mortality in LA County from 1999 to 2013, and in racial/ethnic groups, there was little progress toward reducing disparities among SPAs. Highest mortalities for the three cancers were observed in Antelope Valley, San Fernando Valley, San Gabriel Valley, South LA and East LA. Findings demonstrate the importance of examining regional differences in cancer mortality to identify areas with highest needs for interventions and policies to reduce cancer disparities.

Mazidimoradi, A., et al. (2022). "The global, regional and national epidemiology, incidence, mortality, and burden of ovarian cancer." Health Sci Rep **5**(6): e936.

BACKGROUND: Ovarian cancer has the highest mortality rate among gynecological malignancies and is associated with poor prognosis. Since the accurate assessment of the global burden along with the trend of cancers contributes to the development of policies, this study aimed to explain the incidence, mortality, and burden of ovarian cancer using the global burden of disease (GBD) 2019 study. METHODS: Epidemiological data have been collected

from the study of the GBD 2019. Data were extracted globally for 204 countries and groups based on a socio-demographic index (SDI), WHO regions, continents, World Bank regions, and 22 GBD regions. RESULTS: In 2019, a total of 294,422 new cases of ovarian cancer were reported. The highest age-standardized incidence rate (ASIR) was reported in areas with higher SDI, World high-income countries, continental Europe, and then America. In GBD regions, the highest age-standardized incidence is in Central Europe. In 2019, a total of 198,412 deaths due to ovarian cancer were reported. The highest ASR death is related to countries with high SDI and the World Bank high-income countries. In 2019, adjusted years of life with disabilities (DALYs) due to ovarian cancer were reported to be 5,359,737, of which 5,205,660 were related to lost years of life (YLLs), and 154,077 were related to years of life with disabilities (YLDs). CONCLUSIONS: In 2019, the highest age-standardized incidence of ovarian cancer, ASR death, and DALYs ASR belong to the high SDI countries. Designing interventions based on risk factors as well as providing preventive approaches to reduce the risk of this cancer, improving the treatment of ovarian cancer, and using appropriate and invasive treatments are recommended.

McCarty, M. F., et al. (2021). "Age-adjusted mortality from pancreatic cancer increased NINE-FOLD in japan from 1950 to 1995 - Was a low-protein quasi-vegan diet a key factor in their former low risk?" Med Hypotheses **149**: 110518.

During the last half of the twentieth century, age-adjusted mortality from pancreatic cancer in Japan rose about nine-fold in both sexes. Well-characterized risk factors such as smoking, obesity/metabolic syndrome, and heavy alcohol use appear to explain only a modest part of this rise. It is proposed that a diet relatively low in protein, and particularly low in animal protein, was a key determinant of the low risk for pancreatic cancer in mid-century Japan. It is further proposed that pancreatic acinar cells, owing to their extraordinarily high rate of protein synthesis, are at high risk for ER stress; that such stress plays a fundamental role in the induction of most pancreatic cancers; and that low-protein diets help to offset such stress by modulating activities of the kinases GCN2 and mTORC1 while increasing autocrine and systemic production of fibroblast growth factor 21. This model appears to clarify the role of various risk factors and protective factors in pancreatic cancer induction. A vegan or quasi-vegan low-protein diet may have broader potential for decreasing risk for a range of common "Western" cancers.

Moik, F., et al. (2021). "Hemostatic Biomarkers and Venous Thromboembolism Are Associated With Mortality and Response to Chemotherapy in Patients With Pancreatic Cancer." Arterioscler Thromb Vasc Biol **41**(11): 2837-2847.

OBJECTIVE: Pancreatic cancer activates coagulation and increases risk of venous thromboembolism (VTE). We aimed at characterizing the association of hemostatic biomarkers and VTE with mortality and chemotherapy response. APPROACH AND RESULTS: Pancreatic cancer patients (N=145) were included in a prospective, observational cohort study (CATS [Vienna Cancer and Thrombosis Study]). Hemostatic biomarkers (D-dimer, extracellular vesicle-tissue factor activity, prothrombin fragment 1+2, fibrinogen, factor VIII, PAI-1 [plasminogen activator inhibitor 1], sP-selectin [soluble P-selectin], thrombin generation assay) were measured at inclusion. The impact of VTE on overall survival/progression-free survival (OS/PFS) was evaluated by multistate modeling. The association of biomarkers with OS was analyzed by Cox-regression and with PFS and disease control rate in patients initiating palliative chemotherapy (n=95) by Cox-regression and logistic regression. Multivariable analysis included stage, grade, sex, age, performance status, VTE (time-dependent), vascular infiltration/compression, and tumor marker levels (carbohydrate-antigen 19-9, carcinoembryonic antigen). VTE occurrence was associated with shorter OS (transition hazard ratio, 3.40 [95% CI, 2.05-5.64]) and shorter PFS (transition hazard ratio, 2.10 [1.16-3.79]). Median post-VTE OS/PFS in months was 5.5 [2.2-6.5] and 3.0 [1.5-3.9], compared with 13.4 [9.7-16.6] and 7.5 [5.9-9.8] in patients without VTE (both P<0.001). D-dimer, extracellular vesicle-tissue factor activity, PAI-1, and sP-selectin were associated with increased mortality (hazard ratio per doubling, 1.27 [1.00-1.61]; 1.63 [1.14-2.36]; 1.25 [1.06-1.47]; 1.52 [1.05-2.20]). In patients initiating palliative chemotherapy, higher D-dimer predicted shorter PFS (hazard ratio per doubling, 1.27 [1.01-1.60]) and lower disease control rate (odds ratio per doubling, 0.59 [0.36-0.98]). CONCLUSIONS: VTE diagnosis is associated with shorter OS and PFS. Higher baseline levels of D-dimer, extracellular vesicle-tissue factor activity, PAI-1, and sP-selectin were independently prognostic for increased mortality, and D-dimer predicted response to palliative chemotherapy.

Moke, D. J., et al. (2021). "A Population-Based Analysis of 30-Year Mortality among Five-Year Survivors of Adolescent and Young Adult Cancer: The Roles of Primary Cancer, Subsequent Malignancy, and Other Health Conditions." Cancers (Basel) **13**(16).

Despite an aggregate 5-year survival of 85%, many adolescents and young adults (AYAs, 15-39 years old) treated for cancer die prematurely decades later. To develop a more complete understanding of this problem, particularly the role of specific subsequent malignant neoplasms (SMNs), we used the SEER-9 registry to analyze causes of death (COD: Primary cancer, SMN, non-malignant conditions) among 162,317 AYAs diagnosed with first cancer between 1975-2012 and surviving 5 or more years. Cumulative mortality, attributable mortality, standardized mortality ratios (SMRs), and adjusted hazard ratios were determined for each cancer site and COD. At 30 years, cumulative mortality due to primary cancer was matched by that due to all other causes (12.8% 95% CI [12.5%, 13.0%] for primary cancer versus 12.8% [12.5%, 13.1%] for all other causes combined) in the combined cohort, and was overtaken by non-malignant conditions in Hodgkin lymphoma, testicular, cervical/uterine, and thyroid cancers. Overall, SMNs accounted for 20% of malignant deaths, the most common being lung/bronchus (25.6%), colorectal/liver/biliary/pancreas (19.1%), and breast (10.2%). For non-malignant conditions, excess risk was noted overall (SMR 1.37, 95% CI [1.34, 1.40]) and for infectious (1.97 [1.85, 2.10]), renal (1.85 [1.60, 2.13]), cardio/cerebrovascular (1.38 [1.33, 1.43]), and suicide (1.15 [1.04, 1.27]). Racial minorities were at significantly higher risk across all COD. Safer therapy, longitudinal monitoring, and primary/secondary preventive strategies are needed to reduce late mortality in this vulnerable population.

Molassiotis, A., et al. (2021). "Organized breast cancer screening not only reduces mortality from breast cancer but also significantly decreases disability-adjusted life years: analysis of the Global Burden of Disease Study and screening programme availability in 130 countries." ESMO Open **6**(3): 100111.

BACKGROUND: Multiple studies over the past 4 decades have shown the significant benefit of breast cancer screening (BCS) in reducing mortality rates from breast cancer (BC). However, significant debate exists about the role of BCS in this regard, with some studies also showing no benefit in terms of mortality along with issues such as overdiagnosis, health care utilisation costs, psychological distress or overtreatment. To date, no BCS study has focused on disability. Hence the aim of this study is to evaluate the relative contribution of BCS approaches to age-standardized mortality and disability-adjusted life years (DALYs) rates along with other related risk factors, from a country-level perspective. PATIENTS AND METHODS: This study created a country-dataset by merging information from the Global Burden of Disease study regarding female age-standardized BC mortality, DALYs rates and other risk factors with the BCS programme availability at the national or regional level (versus no or only pilot such programme), BCS type (mammography, digital screening, breast self-examination and clinical breast examination) and other BCS-related information among 130 countries. Mixed-effect multilevel regression models were run to examine the associations of interest. RESULTS: The most important factor predictive of lower mortality was the more advanced type of BCS programme availability [mammography: -4.16, 95% CI -6.76 to -1.55; digital mammography/ultrasound: -3.64, 95% CI -6.59 to -0.70] when compared with self- or clinical breast examinations. High levels of low-density lipoprotein cholesterol (LDL-c) and smoking were also related to higher mortality and DALYs from BC. In terms of BC DALYs, BCS had a 21.9 to 22.3-fold increase in the magnitude of effect compared with that in terms of mortality. Data on mortality and DALYs in relation to BCS programmes were also calculated for high-, middle- and low-income countries. CONCLUSIONS: These data further support the positive effects of BCS in relation to age-standardized BC mortality rates, and for the first time show the impact of BCS on DALYs too. Additional factors, such as diabetes, high levels of LDL-c or smoking seemed to be related to BC mortality and disability, and could be considered as additional components of possible interventions to be used alongside BCS to optimize the BCS benefit on patients.

Molina-Montes, E., et al. (2021). "The Role of Diet, Alcohol, BMI, and Physical Activity in Cancer Mortality: Summary Findings of the EPIC Study." Nutrients **13**(12).

Evidence on the impact of diet, alcohol, body-mass index (BMI), and physical activity on mortality due to cancer and other cancer-related outcomes is still scarce. Herein, we reviewed the contribution of the European Prospective Investigation into Cancer and Nutrition (EPIC) study to the current state of the art on the role of these factors in cancer mortality. We identified 45 studies using a rapid systematic review methodology. Dietary factors associated with reduced cancer mortality included raw vegetable intake; dietary fiber intake; the Mediterranean diet; other dietary scores; other diet patterns including low meat eaters, vegetarians/vegans, or fish eaters; dietary intake (or biomarkers) of some vitamins (e.g., vitamin D, vitamin K2, or Vitamin C); and intake of lignans. Physical activity and following healthy lifestyle recommendations also reduced cancer mortality risk. In contrast, dietary factors associated with higher cancer mortality risk included poor diet quality, consumption of alcohol and soft drinks including juice, and, to a lesser extent, intake of some fatty acids. Excess weight

and obesity also increased the risk of cancer mortality. The EPIC study holds valuable information on diet and lifestyle factors and offers a unique opportunity to identify key diet-related factors for cancer mortality prevention.

Moller, A., et al. (2022). "Travel vaccines are strongly associated to reduced mortality in prostate cancer patients - a real effect or residual confounding?" Vaccine **40**(27): 3797-3801.

Repurposing of existing drugs and vaccines for diseases that they were not originally intended for is a promising research field. Recently there has been evidence that oral cholera vaccine might be used in the treatment of inflammatory disease and some common cancers. Specifically, Ji et al showed that the administration of cholera vaccine after a prostate cancer diagnosis reduced prostate cancer specific mortality rates by almost 50%. In a cohort of men from Stockholm, Sweden, with more detailed cancer data and a higher coverage of exposure to vaccine, we replicated these findings using a marginal structural Cox model. We showed that administration of cholera vaccine after prostate cancer diagnosis is associated with a significant reduction in mortality (HR 0.46, 95% CI 0.31-0.69, p-value 0.0001) even after adjusting for all known confounders. However, the same effect (or even stronger) could be seen for several other traveling vaccines and malaria prophylaxis. Therefore, we conclude that this effect is most likely due to a healthy traveler bias and is an example of residual confounding.

Monlezun, D. J., et al. (2021). "TAVR and cancer: machine learning-augmented propensity score mortality and cost analysis in over 30 million patients." Cardiooncology **7**(1): 25.

INTRODUCTION: Cardiovascular disease (CVD) and cancer are the top mortality causes globally, yet little is known about how the diagnosis of cancer affects treatment options in patients with hemodynamically compromising aortic stenosis (AS). Patients with cancer often are excluded from aortic valve replacement (AVR) trials including trials with transcatheter AVR (TAVR) and surgical AVR (SAVR). This study looks at how cancer may influence treatment options and assesses the outcome of patients with cancer who undergo SAVR or TAVR intervention. Additionally, we sought to quantitate and compare both clinical and cost outcomes for patients with and without cancer. METHODS: This population-based case-control study uses the most recent year available National Inpatient Sample (NIS (2016) from the United States Department of Health and Human Services' Agency for Healthcare Research and Quality (AHRQ). Machine learning augmented propensity score adjusted multivariable regression was conducted based on the likelihood of undergoing TAVR versus medical management (MM) and TAVR versus SAVR with model optimization supported by backward propagation neural network machine learning. RESULTS: Of the 30,195,722 total hospital admissions, 39,254 (0.13%) TAVRs were performed, with significantly fewer performed in patients with versus without cancer even in those of comparable age and mortality risk (23.82% versus 76.18%, $p < 0.001$) despite having similar hospital and procedural mortality. Multivariable regression in patients with cancer demonstrated that mortality was similar for TAVR, MM, and SAVR, though LOS and cost was significantly lower for TAVR versus MM and comparable for TAVR versus SAVR. Patients with prostate cancer constituted the largest primary cancer among TAVR patients including those with metastatic disease. There were no significant race or geographic disparities for TAVR mortality. DISCUSSION: Comparison of aortic valve intervention in patients with and without cancer suggests that interventions are underutilized in the cancer population. This study suggests that patients with cancer including those with metastasis have similar inpatient outcomes to patients without cancer. Further, patients who have symptomatic AS and those with higher risk aortic valve disease should be offered the benefit of intervention. Modern techniques have reduced intervention-related adverse events, provided improved quality of life, and appear to be cost effective; these advantages should not necessarily be denied to patients with co-existing cancer.

Monlezun, D. J., et al. (2022). "Artificial Intelligence-Augmented Propensity Score, Cost Effectiveness and Computational Ethical Analysis of Cardiac Arrest and Active Cancer with Novel Mortality Predictive Score." Medicina (Kaunas) **58**(8).

Background and objectives: Little is known about outcome improvements and disparities in cardiac arrest and active cancer. We performed the first known AI and propensity score (PS)-augmented clinical, cost-effectiveness, and computational ethical analysis of cardio-oncology cardiac arrests including left heart catheterization (LHC)-related mortality reduction and related disparities. Materials and methods: A nationally representative cohort analysis was performed for mortality and cost by active cancer using the largest United States all-payer inpatient dataset, the National Inpatient Sample, from 2016 to 2018, using deep learning and machine learning augmented propensity score-adjusted (ML-PS) multivariable regression which informed cost-effectiveness and ethical analyses. The Cardiac Arrest Cardio-Oncology Score (CACOS) was then created for the above population and validated.

The results informed the computational ethical analysis to determine ethical and related policy recommendations. Results: Of the 101,521,656 hospitalizations, 6,656,883 (6.56%) suffered cardiac arrest of whom 61,300 (0.92%) had active cancer. Patients with versus without active cancer were significantly less likely to receive an inpatient LHC (7.42% versus 20.79%, p < 0.001). In ML-PS regression in active cancer, post-arrest LHC significantly reduced mortality (OR 0.18, 95%CI 0.14-0.24, p < 0.001) which PS matching confirmed by up to 42.87% (95%CI 35.56-50.18, p < 0.001). The CACOS model included the predictors of no inpatient LHC, PEA initial rhythm, metastatic malignancy, and high-risk malignancy (leukemia, pancreas, liver, biliary, and lung). Cost-benefit analysis indicated 292 racial minorities and $2.16 billion could be saved annually by reducing racial disparities in LHC. Ethical analysis indicated the convergent consensus across diverse belief systems that such disparities should be eliminated to optimize just and equitable outcomes. Conclusions: This AI-guided empirical and ethical analysis provides a novel demonstration of LHC mortality reductions in cardio-oncology cardiac arrest and related disparities, along with an innovative predictive model that can be integrated within the digital ecosystem of modern healthcare systems to improve equitable clinical and public health outcomes.

Montoya-Gonzalez, M. C., et al. (2021). "Incidence, mortality and survival of endometrial cancer in Manizales, Colombia 2003-2017." Rev Peru Med Exp Salud Publica **38**(4): 562-568.

OBJECTIVE. To estimate the incidence, mortality and five-year survival of endometrial carcinoma in Manizales for the period 2003-2017. MATERIALS AND METHODS. Observational, retrospective, population-based study, descriptive in scope. Incidence and mortality rates were adjusted by the direct method using the Segi world population as reference. Passive and active follow-up of the cases was carried out until completing 60 months or until the follow-up closing date. Survival was estimated using Kaplan-Meier functions and Cox models. RESULTS. 210 incident cases were observed in a population of 214.928 women. The average age at diagnosis was 61 years. The most frequent histological type was endometrioid, well differentiated. Most of the patients were affiliated to the contributory health insurance scheme and belonged to the middle socioeconomic level. The age-adjusted incidence rate was 5.7 new cases per 100,000 woman-years. Seventy-five deaths were identified, with greater mortality between 65-69 and 75-79 age groups. Overall survival was 95.1% at 12 months and 83.8% at 60 months. Statistically significant differences were found in survival in favor of epithelial histology, early stages at the time of diagnosis, and age at diagnosis less than 60 years. CONCLUSIONS. Manizales follows the global pattern of rise in the age-adjusted incidence rate. Mortality is like that reported in other countries in the region. In Manizales, endometrial cancer survival was higher in patients with early diagnosis, less than 60 years of age, and with endometrioid histology.

Moore, J., et al. (2022). "Oncotype DX Risk Recurrence Score and Total Mortality for Early-Stage Breast Cancer by Race/Ethnicity." Cancer Epidemiol Biomarkers Prev **31**(4): 821-830.

BACKGROUND: Oncotype DX recurrence score (ODX RS) is a prognostic biomarker for early-stage, node-negative, estrogen receptor-positive (ER+) breast cancer. Whether test uptake, associated factors, and the test's prognostic values differ by race/ethnicity is unknown. METHODS: From the National Cancer Database, 2010-2014, we identified 227,259 early-stage ER+, node-negative breast cancer cases. Logistic regression was used to examine ODX RS uptake and associated factors among non-Hispanic White (White), non-Hispanic Black (Black), Hispanic, and Asian American patients. Cox regression was used to estimate hazard ratios (HR) and 95% confidence intervals (CI) for overall mortality with ODX RS by race/ethnicity. RESULTS: White patients were more likely to receive an ODX RS test compared with Black, Hispanic, and Asian American patients (36.7%, 32.8%, 31.6%, and 35.5%, respectively; $P < 0.001$). Disparities persisted after adjustments for demographics, clinical characteristics, and access-to-care, with rate ratios of 0.87 (95% CI, 0.85-0.88), 0.82 (95% CI, 0.80-0.85), and 0.89 (95% CI, 0.87-0.92), respectively, for Black, Hispanic, and Asian American compared with White patients. Black patients had higher proportions of high-risk scores (>/=26) compared with White, Hispanic, and Asian American patients (19.1%, 14.0%, 14.2%, and 15.6%, respectively; $P < 0.0001$). ODX RS was predictive for total mortality across all races/ethnicities, particularly younger patients (<50). No significant race/ethnicity interactions were observed. CONCLUSIONS: Although ODX RS uptake and risk distribution varied by race/ethnicity, ODX RS was prognostic for mortality across groups. IMPACT: These findings emphasize the importance of developing strategies to increase ODX RS uptake among racial/ethnic minorities and call for more investigations on potential racial/ethnic differences in breast cancer biology. See related commentary by Wang et al., p. 704.

Moore, J. X., et al. (2022). "Exploring racial disparities on the association between allostatic load and cancer

mortality: A retrospective cohort analysis of NHANES, 1988 through 2019." SSM Popul Health **19**: 101185.

BACKGROUND: Several studies suggest that chronic stress may be associated with increased risk of cancer mortality. Our study sought to determine the association between allostatic load (AL), a measure of cumulative stress, and risk of cancer death; and whether these associations varied by race/ethnicity. METHODS: We performed retrospective analysis using National Health and Nutrition Examination Survey (NHANES) years 1988 through 2010 linked with the National Death Index through December 31, 2019. We fit Fine & Gray Cox proportional hazards models to estimate sub-distribution hazard ratios (SHRs) of cancer death between high and low AL status (models adjusted for age, sociodemographics, and comorbidities). RESULTS: In fully adjusted models, high AL was associated with a 14% increased risk of cancer death (adjusted (SHR): 1.14, 95% CI: 1.04-1.26) among all participants and a 18% increased risk of cancer death (SHR:1.18, 95% CI: 1.03-1.34) among Non-Hispanic White (NH-White) adults. When further stratified by age (participants aged <40 years), high AL was associated with a 80% increased risk (SHR: 1.80, 95% CI: 1.35-2.41) among all participants; a 95% increased risk (SHR: 1.95, 95% CI: 1.22-3.12) among NH-White adults; a 2-fold (SHR: 2.06, 95% CI: 1.27-3.34) increased risk among Non-Hispanic Black (NH-Black) adults; and a 36% increased risk among Hispanic adults (SHR: 1.36, 95% CI: 0.70-2.62). CONCLUSIONS: Overall, the risk of cancer death was associated with high AL; however, when stratified among NH-Black and Hispanic adults this association was slightly attenuated. IMPACT: High AL is associated with increased risk of overall cancer death, and future studies should delineate the association between AL and cancer-specific mortality to better understand the causal mechanisms between cumulative stress and cancer.

Moss, J. L., et al. (2020). "Persistent Poverty and Cancer Mortality Rates: An Analysis of County-Level Poverty Designations." Cancer Epidemiol Biomarkers Prev **29**(10): 1949-1954.

BACKGROUND: Cancer mortality is higher in counties with high levels of (current) poverty, but less is known about associations with persistent poverty. Persistent poverty counties (with >/=20% of residents in poverty since 1980) face social, structural, and behavioral challenges that may make their residents more vulnerable to cancer. METHODS: We calculated 2007 to 2011 county-level, age-adjusted, and overall and type-specific cancer mortality rates (deaths/100,000 people/year) by persistent poverty classifications, which we contrasted with mortality in counties experiencing current poverty (>/=20% of residents in poverty according to 2007-2011 American Community Survey). We used two-sample t tests and multivariate linear regression to assess mortality by persistent poverty, and compared mortality rates across current and persistent poverty levels. RESULTS: Overall cancer mortality was 179.3 [standard error (SE) = 0.55] deaths/100,000 people/year in nonpersistent poverty counties and 201.3 (SE = 1.80) in persistent poverty counties (12.3% higher, $P < 0.0001$). In multivariate analysis, cancer mortality was higher in persistent poverty versus nonpersistent poverty counties for overall cancer mortality as well as for several type-specific mortality rates: lung and bronchus, colorectal, stomach, and liver and intrahepatic bile duct (all $P < 0.05$). Among counties experiencing current poverty, those counties that were also experiencing persistent poverty had elevated mortality rates for all cancer types as well as lung and bronchus, colorectal, breast, stomach, and liver and intrahepatic bile duct (all $P < 0.05$). CONCLUSIONS: Cancer mortality was higher in persistent poverty counties than other counties, including those experiencing current poverty. IMPACT: Etiologic research and interventions, including policies, are needed to address multilevel determinants of cancer disparities in persistent poverty counties.

Motsuku, L., et al. (2021). "Colorectal cancer incidence and mortality trends by sex and population group in South Africa: 2002-2014." BMC Cancer **21**(1): 129.

BACKGROUND: South Africa (SA) has experienced a rapid transition in the Human Development Index (HDI) over the past decade, which had an effect on the incidence and mortality rates of colorectal cancer (CRC). This study aims to provide CRC incidence and mortality trends by population group and sex in SA from 2002 to 2014. METHODS: Incidence data were extracted from the South African National Cancer Registry and mortality data obtained from Statistics South Africa (STATS SA), for the period 2002 to 2014. Age-standardised incidence rates (ASIR) and age-standardised mortality rates (ASMR) were calculated using the STATS SA mid-year population as the denominator and the Segi world standard population data for standardisation. A Joinpoint regression analysis was computed for the CRC ASIR and ASMR by population group and sex. RESULTS: A total of 33,232 incident CRC cases and 26,836 CRC deaths were reported during the study period. Of the CRC cases reported, 54% were males and 46% were females, and among deaths reported, 47% were males and 53% were females. Overall, there was a 2.5% annual average percentage change (AAPC) increase in ASIR from 2002 to 2014 (95% CI: 0.6-4.5, p-value < 0.001). For ASMR overall, there was 1.3% increase from 2002 to 2014 (95% CI: 0.1-2.6, p-value

< 0.001). The ASIR and ASMR among population groups were stable, with the exception of the Black population group. The ASIR increased consistently at 4.3% for black males (95% CI: 1.9-6.7, p-value < 0.001) and 3.4% for black females (95% CI: 1.5-5.3, p-value < 0.001) from 2002 to 2014, respectively. Similarly, ASMR for black males and females increased by 4.2% (95% CI: 2.0-6.5, p-value < 0.001) and 3.4% (, 95%CI: 2.0-4.8, p-value < 0.01) from 2002 to 2014, respectively. CONCLUSIONS: The disparities in the CRC incidence and mortality trends may reflect socioeconomic inequalities across different population groups in SA. The rapid increase in CRC trends among the Black population group is concerning and requires further investigation and increased efforts for cancer prevention, early screening and diagnosis, as well as better access to cancer treatment.

Moubadder, L., et al. (2022). "Drivers of racial, regional, and socioeconomic disparities in late-stage breast cancer mortality." Cancer **128**(18): 3370-3382.

BACKGROUND: The authors identified tumor, treatment, and patient characteristics that may contribute to differences in breast cancer (BC) mortality by race, rurality, and area-level socioeconomic status (SES) among women diagnosed with stage IIIB-IV BC in Georgia. METHODS: Using the Georgia Cancer Registry, 3084 patients with stage IIIB-IV primary BC (2013-2017) were identified. Cox proportional hazards regression was used to calculate the hazard ratios (HRs) and 95% confidence intervals (CIs) comparing mortality among non-Hispanic Black (NHB) versus non-Hispanic White (NHW), residents of rural versus urban neighborhoods, and residents of low- versus high-SES neighborhoods by tumor, treatment, and patient characteristics. The mediating effects of specific characteristics on the association between race and BC mortality were estimated. RESULTS: Among the study population, 41% were NHB, 21% resided in rural counties, and 72% resided in low SES neighborhoods. The authors observed mortality disparities by race (HR, 1.27; 95% CI, 1.13, 1.41) and rurality (HR, 1.14; 95% CI, 1.00, 1.30), but not by SES (HR, 1.04; 95% CI, 0.91, 1.19). In the stratified analyses, racial disparities were the most pronounced among women with HER2 overexpressing tumors (HR, 2.30; 95% CI, 1.53, 3.45). Residing in a rural county was associated with increased mortality among uninsured women (HR, 2.25; 95% CI, 1.31, 3.86), and the most pronounced SES disparities were among younger women (<40 years: HR, 1.46; 95% CI, 0.88, 2.42). CONCLUSIONS: There is considerable variation in racial, regional, and socioeconomic disparities in late-stage BC mortality by tumor, treatment, and patient characteristics.

Moura, A. R., et al. (2020). "Trends in the incidence and mortality of colorectal cancer in a brazilian city." BMC Res Notes **13**(1): 560.

OBJECTIVES: This study was conducted to analyze the trends in colorectal cancer (CRC) incidence and mortality in the city of Aracaju, Sergipe State, Brazil, between 1996 and 2015 with Joinpoint Regression Program 4.7.0.0 and to identify the geographical distribution of CRC in the municipality. RESULTS: A total of 1322 cases of CRC and 467 CRC-related deaths during the study period were included. In total, 40% of the incident cases and 43% of the deaths occurred in men, while 60% of the incident cases and 57% of the deaths occurred in women. Males who were 20 to 44 years old had the most significant trend in growth. Among women, those in the group aged 45 to 64 years had the highest observed annual percent change (APC). In both sexes, mortality was stable. Regarding the geographic distribution, there were constant hotspots in the northeast region of the municipality. This study showed a significant increase in incidence, mainly in young men between 20 and 44 years of age, but stable mortality in Aracaju.

Moura, L., et al. (2022). "Does Abdominal Obesity Increase All-Cause, Cardiovascular Disease, and Cancer Mortality Risks in Older Adults? A 10-Year Follow-Up Analysis." Nutrients **14**(20).

There is insufficient evidence on the impact of abdominal obesity (AO) on mortality in older adults. Therefore, the objective to analyze the 10-year impact of AO, assessed using different diagnostic criteria, on all-cause, cardiovascular disease (CVD), and cancer mortality in older adults. In this prospective cohort study of older adults (>/=60 years), sociodemographic, lifestyle, clinical history, laboratory test, and anthropometric data were analyzed. The considered were used for AO diagnostic: waist circumference (WC) of >/=88 cm for women and >/=102 cm for men; WC of >/=77.8 cm for women and >/=98.8 cm for men; and increased waist-to-hip ratio (WHR), being the highest tertile of distribution by sex. Multivariate Cox regression and Kaplan-Meier analyses were performed. A total of 418 individuals, with an average age of 70.69 +/- 7.13 years, participated in the study. In the analysis adjusted for sex and age, WHR was associated with a high risk of all-cause mortality (p = 0.044). Both cutoff points used for the WC were associated with an increased CVD mortality risk. None of the AO parameters were associated with cancer mortality. An increased WHR was associated to a higher all-cause mortality risk factor, while an increased WC was a risk factor for a higher CVD mortality in older adults.

Mubarik, S., et al. (2020). "A multi-country comparison of stochastic models of breast cancer mortality with P-splines smoothing approach." BMC Med Res Methodol **20**(1): 299.

BACKGROUND: Precise predictions of incidence and mortality rates due to breast cancer (BC) are required for planning of public health programs as well as for clinical services. A number of approaches has been established for prediction of mortality using stochastic models. The performance of these models intensely depends on different patterns shown by mortality data in different countries. METHODS: The BC mortality data is retrieved from the Global burden of disease (GBD) study 2017 database. This study include BC mortality rates from 1990 to 2017, with ages 20 to 80+ years old women, for different Asian countries. Our study extend the current literature on Asian BC mortality data, on both the number of considered stochastic mortality models and their rigorous evaluation using multivariate Diebold-Marino test and by range of graphical analysis for multiple countries. RESULTS: Study findings reveal that stochastic smoothed mortality models based on functional data analysis generally outperform on quadratic structure of BC mortality rates than the other lee-carter models, both in term of goodness of fit and on forecast accuracy. Besides, smoothed lee carter (SLC) model outperform the functional demographic model (FDM) in case of symmetric structure of BC mortality rates, and provides almost comparable results to FDM in within and outside data forecast accuracy for heterogeneous set of BC mortality rates. CONCLUSION: Considering the SLC model in comparison to the other can be obliging to forecast BC mortality and life expectancy at birth, since it provides even better results in some cases. In the current situation, we can assume that there is no single model, which can truly outperform all the others on every population. Therefore, we also suggest generating BC mortality forecasts using multiple models rather than relying upon any single model.

Nadkarni, A. R., et al. (2021). "Mortality in Cancer Patients With COVID-19 Who Are Admitted to an ICU or Who Have Severe COVID-19: A Systematic Review and Meta-Analysis." JCO Glob Oncol **7**: 1286-1305.

PURPOSE: There are scarce data to aid in prognostication of the outcome of critically ill cancer patients with COVID-19. In this systematic review and meta-analysis, we investigated the mortality of critically ill cancer patients with COVID-19. METHODS: We searched online databases and manually searched for studies in English that reported on outcomes of adult cancer patients with COVID-19 admitted to an intensive care unit (ICU) or those with severe COVID-19 between December 2019 and October 2020. Risk of bias was assessed by the Modified Newcastle-Ottawa Scale. The primary outcome was all-cause mortality. We also determined the odds of death for cancer patients versus noncancer patients, as also outcomes by cancer subtypes, presence of recent anticancer therapy, and presence of one or more comorbidities. Random-effects modeling was used. RESULTS: In 28 studies (1,276 patients), pooled mortality in cancer patients with COVID-19 admitted to an ICU was 60.2% (95% CI, 53.6 to 6.7; I(2) = 80.27%), with four studies (7,259 patients) showing higher odds of dying in cancer versus noncancer patients (odds ratio 1.924; 95% CI, 1.596 to 2.320). In four studies (106 patients) of patients with cancer and severe COVID-19, pooled mortality was 59.4% (95% CI, -39.4 to 77.5; I(2) = 72.28%); in one study, presence of hematologic malignancy was associated with significantly higher mortality compared with nonhematologic cancers (odds ratio 1.878; 95% CI, 1.171 to 3.012). Risk of bias was low. CONCLUSION: Most studies were reported before the results of trials suggesting the benefit of dexamethasone and tocilizumab, potentially overestimating mortality. The observed mortality of 60% in cancer patients with COVID-19 admitted to the ICU is not prohibitively high, and admission to the ICU should be considered for selected patients (registered with PROSPERO, CRD42020207209).

Nascimento, W., et al. (2021). "Muscle-strengthening activities and cancer incidence and mortality: a systematic review and meta-analysis of observational studies." Int J Behav Nutr Phys Act **18**(1): 69.

BACKGROUND: Physical activity has been associated with reduced risk of seven types of cancer. It remains unclear, however, whether muscle-strengthening activities also reduce cancer incidence and mortality. METHODS: PubMed, Embase, Web of Science and Scopus were searched from inception to March 2020. Summary hazard ratio (HR) and 95% confidence intervals (CI) were estimated using random-effects models. RESULTS: Twelve studies (11 cohorts; 1 case-control), 6 to 25 years of follow-up, including 1,297,620 participants, 32,196 cases and 31,939 deaths, met inclusion criteria. Muscle-strengthening activities were associated with a 26% lower incidence of kidney cancer (HR for high vs low levels of muscle-strengthening activities: 0.74; 95% CI 0.56 to 0.98; I(2) 0%; 2 studies), but not with incidence of other 12 types of cancer. Muscle-strengthening activities were associated with lower total cancer mortality: HRs for high vs low levels of muscle-strengthening activities was 0.87 (95% CI 0.73 to 1.02; I(2) 58%; 6 studies); and HR for >/=2 times/week vs < 2 times/week of muscle-strengthening activities was 0.81 (95% CI 0.74 to 0.87; I(2) 0%; 4 studies). Regarding the weekly

duration of muscle-strengthening activities, HR for total cancer mortality were 0.91 (95% CI 0.82 to 1.01; I(2) 0%; 2 studies) for 1-59 min/week and 0.98 (95% CI 0.89 to 1.07; I(2) 0%) for >/=60 min/week vs none. Combined muscle-strengthening and aerobic activities (vs none) were associated with a 28% lower total cancer mortality (HR 0.72; 95% CI 0.53 to 0.98; I(2) 85%; 3 studies). CONCLUSIONS: Muscle-strengthening activities were associated with reduced incidence of kidney cancer and total cancer mortality. Combined muscle-strengthening and aerobic activities may provide a greater reduction in total cancer mortality.

Nash, R., et al. (2022). "Understanding gastrointestinal cancer mortality disparities in a racially and geographically diverse population." Cancer Epidemiol **77**: 102110.

BACKGROUND: Gastrointestinal (GI) cancers represent a diverse group of diseases. We assessed differences in geographic and racial disparities in cancer-specific mortality across subtypes, overall and by patient characteristics, in a geographically and racially diverse US population. METHODS: Clinical, sociodemographic, and treatment characteristics for patients diagnosed during 2009-2014 with colorectal cancer (CRC), pancreatic cancer, hepatocellular carcinoma (HCC), or gastric cancer in Georgia were obtained from the Surveillance, Epidemiology, and End Results Program database. Patients were classified by geography (rural or urban county) and race and followed for cancer-specific death. Multivariable Cox proportional hazards models were used to calculate stratified hazard ratios (HR) and 95% confidence intervals (CIs) for associations between geography or race and cancer-specific mortality. RESULTS: Overall, 77% of the study population resided in urban counties and 33% were non-Hispanic Black (NHB). For all subtypes, NHB patients were more likely to reside in urban counties than non-Hispanic White patients. Residing in a rural county was associated with an overall increased hazard of cancer-specific mortality for HCC (HR = 1.15, 95% CI = 1.02-1.31), pancreatic (HR = 1.11, 95% CI = 1.03-1.19), and gastric cancer (HR = 1.17, 95% CI = 1.03-1.32) but near-null for CRC. Overall racial disparities were observed for CRC (HR = 1.18, 95% CI = 1.11-1.25) and HCC (HR = 1.12, 95% CI = 1.01-1.24). Geographic disparities were most pronounced among HCC patients receiving surgery. Racial disparities were pronounced among CRC patients receiving any treatment. CONCLUSION: Geographic disparities were observed for the rarer GI cancer subtypes, and racial disparities were pronounced for CRC. Treatment factors appear to largely drive both disparities.

Nasirzadeh, N., et al. (2022). "Risk Assessment of Silicosis and Lung Cancer Mortality associated with Occupational Exposure to Crystalline Silica in Iran." J Res Health Sci **22**(2): e00550.

BACKGROUND: Exposure to crystalline silica has long been identified to be associated with lung diseases. Therefore, the present study aimed to assess the risk of silicosis and lung cancer associated with occupational exposure to crystalline silica in Iran. STUDY DESIGN: It is a systematic review study. METHODS: Different databases were searched, and the Cochrane method was used for the systematic review. Thereafter, cumulative exposure to crystalline silica (mg/m3-y) was calculated in every industry. The relative risk of death from silicosis was performed using Mannetje's method. Based on the geometric mean of exposure, the lung cancer risk of exposure to crystalline silica was also calculated. RESULTS: As evidenced by the results, worker's exposure to silica ranged from a geometric mean of 0.0212- 0.2689 mg/m3 (Recommended standard by the American Conference of Governmental Industrial Hygienists (ACGIH) was 0.025 mg/m3), which is generally higher than the occupational exposure limit recommended by National Institute for Occupational Safety and Health (NIOSH), ACGIH, and occupational exposure limits. The relative risk of silicosis was in the range of 1 to 14 per 1000 people, and the risk of lung cancer in workers ranged from 13-137 per 1000 people. CONCLUSION: Since workers are at considerable risk of cancer due to exposure to silica in Iran, exposure control programs need to be implemented in workplaces to decrease the concentration of silica.

Nasrazadani, A., et al. (2022). "Breast cancer mortality as a function of age." Aging (Albany NY) **14**(3): 1186-1199.

BACKGROUND: Incidence of breast cancer (BC) in US women continues to increase with age as the strongest risk factor. We aimed to compare clinical, pathological and sociological variables associated to BC diagnosis, as well as the relative mortality rates of BC patients compared to the general US population. METHODS: We performed a retrospective, single-institution study evaluating 52,509 patients diagnosed with unilateral BC at the University of Pittsburgh Medical Center (UPMC) between 1990-2020. Primary outcome was death from any cause with cancer recurrence as a secondary outcome, evaluated for 4 age groups: 20-44, 45-55, 56-69, and 70-90. A dataset of expected mortality for women in the general population over a 10-year period was constructed using the Surveillance, Epidemiology, and End Results (SEER) Program. Observed vs. expected mortality and standardized mortality ratios (SMR) for each age group were calculated. RESULTS: Youngest patients with

BC demonstrated the highest SMR at 10-year follow-up from time of diagnosis compared to the general US population (SMR 9.68, 95% CI: 8.99to 10.42), and remained highest compared to other age groups when analysis was limited to Stage 0/1 disease (10-year SMR 3.11, 95% CI: 2.54 to 3.76). SMRs decreased with increasing age at diagnosis with an SMR <1.0 in patients diagnosed with stage 0/1 at ages 70-90 at 5-year follow-up. CONCLUSIONS: Younger BC patients have the highest SMR which declines gradually with age. In the elderly, lower stage 0/1 SMR's are found compared to the general population, suggesting the possibility of an associated protective effect.

Naumann, R. W., et al. (2021). "The impact of opportunistic salpingectomy on ovarian cancer mortality and healthcare costs: a call for universal insurance coverage." Am J Obstet Gynecol **225**(4): 397 e391-397 e396.

BACKGROUND: Opportunistic salpingectomy at the time of hysterectomy or as an alternative to bilateral tubal ligation may reduce the incidence of ovarian cancer, because it has been demonstrated that most serous ovarian cancers begin in the fallopian tubes. However, salpingectomy at the time of sterilization is not always financially covered by third-party payers, and this represents a barrier to adoption. Routine salpingectomy has become more common but is not always practiced at the time of hysterectomy. OBJECTIVE: This study aimed to determine the impact of opportunistic salpingectomy as an alternative tubal ligation and routine salpingectomy at the time of hysterectomy on ovarian cancer mortality and overall cost. STUDY DESIGN: An 8-state Markov state transition model was constructed, including hysterectomy, tubal ligation, and ovarian cancer. Transition probabilities were informed by previously reported population data and include age-adjusted rates of elective sterilization and hysterectomy. This model was used to predict ovarian cancer incidence and the cost effectiveness of opportunistic salpingectomy. Testing of this model suggested that it accurately predicted overall life expectancy and closely predicted the rate of hysterectomy in the population. The model may underestimate the rate of tubal sterilization, making it conservative with respect to the benefits of salpingectomy. RESULTS: The recursive Markov model was run from ages 20 to 85 years in 1-year intervals with a half step correction and included age-adjusted rates of tubal ligation, hysterectomy (with and without oophorectomy), and ovarian cancer. The model predicts that opportunistic salpingectomy at the time of tubal ligation will reduce ovarian cancer mortality by 8.13%. Opportunistic salpingectomy at the time of hysterectomy will reduce ovarian cancer mortality by 6.34% for a combined decrease of 14.5%. Both strategies are cost effective when considering only the cost of the opportunistic salpingectomy. The excess cost of opportunistic salpingectomy at the time of tubal ligation was $433.91 with an incremental cost-effective ratio of $6401 per life-year and $5469 per quality-adjusted life year gained when adjusting for ovarian cancer with a utility of 0.64. The incremental cost-effective ratio for opportunistic salpingectomy during hysterectomy at a cost of $124.70 was $2006 per life-year and $1667 per quality-adjusted life year. When considering the impact of ovarian cancer prevention with respect to the cost of ovarian cancer treatment, opportunistic salpingectomy may produce a substantial healthcare savings. Utilizing a 3% discount rate, it is estimated that the total savings for universal salpingectomy could be as high as $445 million annually in the United States. A sensitivity analysis around the benefit of opportunistic salpingectomy suggests that this procedure will be cost effective even if salpingectomy provides only a modest reduction in the risk of ovarian cancer. CONCLUSION: It is estimated that universal opportunistic salpingectomy may prevent 1854 deaths per year from ovarian cancer and may reduce healthcare costs. Given these data, universal opportunistic salpingectomy should be considered at the time of tubal ligation and hysterectomy and covered by third-party payers.

Naylor, K. L., et al. (2021). "Comparison of All-Cause Mortality Between Canadian Kidney Transplant Recipients and Patients With Cancer: A Population-Based Cohort Study." Can J Kidney Health Dis **8**: 20543581211056234.

BACKGROUND: Understanding rates of mortality in kidney transplant recipients relative to other common diseases can enhance our understanding of the mortality burden in kidney transplant recipients. OBJECTIVE: To compare the survival probability in Canadian female and male kidney transplant recipients with patients with common cancers (female: breast, colorectal, lung, or pancreas; male: prostate, colorectal, lung, or pancreas) in a contemporary population. DESIGN: Population-based cohort study using linked administrative health care databases. SETTING: Ontario, Canada. PATIENTS: A total of 6888 incident kidney transplant recipients (median age was 50 and 51 years in females and males, respectively) and a total of 532 452 incident patients with cancer (median age range 60 to 72 years across cancer types) from 1997 to 2015. MEASUREMENTS: All-cause mortality. METHODS: The survival of study participants was described using the Kaplan-Meier product limit estimator. The rate of survival was compared between kidney transplant recipients and patients with cancer using extended Cox regression with a Heaviside

function. RESULTS: Kidney transplant recipients had a higher survival probability compared with all cancer types. For example, male kidney transplant recipients had a 5-year survival probability of 89.6% (95% confidence interval [CI]: 88.6%-90.5%) compared with 83.3% (95% CI: 83.1%-83.5%) in patients with prostate cancer, and 14.0% (95% CI: 13.7%-14.3%), 56.1% (95% CI: 55.7%-56.5%), and 9.1% (95% CI: 8.5%-9.7%) in patients with lung, colorectal, and pancreas cancer, respectively. After presenting survival probabilities by age at cohort entry and after adjusting for clinical characteristics, similar results were found with a few exceptions. Unlike the unadjusted analysis, in the adjusted analysis males with prostate cancer had a significantly higher survival compared with kidney transplant recipients and females with breast cancer had higher survival compared with kidney transplant recipients at 2+ years of follow-up. In a subpopulation of the cohort who had information available on cancer stage (ie, stages 1-4), we generally found similar results to our primary analysis with kidney transplant recipients having a higher survival probability compared with each cancer stage. However, female kidney transplant recipients had a lower survival probability compared with females with stage 1 breast cancer, whereas male kidney transplant recipients had a lower survival probability compared with males with stage 1 to 3 prostate cancer. LIMITATIONS: External generalizability, residual confounding, and cancer stage could only be provided for a subpopulation. CONCLUSION: Mortality in kidney transplant recipients is lower than in patients with several cancer types. These results improve our understanding of the mortality burden in this population and reaffirm kidney transplantation as a good treatment option for end-stage kidney disease but also highlight the continuing need to improve posttransplant survival. TRIAL REGISTRATION: This is not applicable as this is a population-based cohort study and not a clinical trial.

Nazer, L., et al. (2022). "All-cause mortality in cancer patients treated for sepsis in intensive care units: a systematic review and meta-analysis." Support Care Cancer **30**(12): 10099-10109.

PURPOSE: Sepsis is a common complication in patients with cancer, but studies evaluating the outcomes of critically ill cancer patients with sepsis on a global scale are limited. We aimed to summarize the existing evidence on mortality rates in this patient population. METHODS: Prospective and retrospective observational studies evaluating critically ill adult cancer patients with sepsis, severe sepsis, and/or septic shock were included. Studies published from January 2010 to September 2021 that reported at least one mortality outcome were retrieved from MEDLINE (Ovid), Embase (Ovid), and Cochrane databases. Study selection, bias assessment, and data collection were performed independently by two reviewers, and any discrepancies were resolved by a third reviewer. The risk of bias was assessed using the Newcastle-Ottawa scale. We calculated pooled intensive care unit (ICU), hospital, and 28/30-day mortality rates. The heterogeneity of the data was tested using the chi-square test, with a P value < 0.10 indicating significant heterogeneity. RESULTS: A total of 5464 citations were reviewed, of which 10 studies met the inclusion criteria; these studies included 6605 patients. All studies had a Newcastle-Ottawa scale score of 7 or higher. The mean patient age ranged from 51.4 to 64.9 years. The pooled ICU, hospital, and 28/30 day mortality rates were 48% (95% CI, 43- 53%; I(2) = 80.6%), 62% (95% CI, 58-67%; I(2) = 0%), and 50% (95% CI, 38- 62%; I(2) = 98%), respectively. Substantial between-study heterogeneity was observed. CONCLUSION: Critically ill cancer patients with sepsis had poor survival, with a hospital mortality rate of about two-thirds. The substantial observed heterogeneity among studies could be attributed to variability in the criteria used to define sepsis as well as variability in treatment, the severity of illness, and care across settings. Our results are a call to action to identify strategies that improve outcomes for cancer patients with sepsis.

Nduma, B. N., et al. (2022). "Geographical Distribution of Pancreatic Cancer in the State of Mississippi by Incidence and Mortality From 2003 to 2019." Cureus **14**(11): e31605.

BACKGROUND: Pancreatic cancer can be a very debilitating disease. In the USA and around the world, pancreatic cancer is among the causes of cancer-related deaths. This study aims to highlight mortality and incidence rates of pancreatic cancer by geographic location. METHODS: The study area is the state of Mississippi with a targeted time period between 2003 and 2019. The Mississippi Cancer Registry is the source of data for this study. The subject under investigation was divided into two phases. The first phase involved analyzing data on the incidence rate while the second phase entailed data analysis of the pancreatic cancer mortality rate in Mississippi. In both phases, the focus was on three categories of geographic locations in Mississippi, which include public health districts, the regional cancer coalitions in the state, and the interplay between rural and urban locations. Descriptive and inferential statistical approaches with graphical techniques and tabulations were utilized in data presentation. RESULTS: The results of this study demonstrate there are variations in the incidence rates of pancreatic cancer by geographic location in Mississippi. In the data analysis of the Mississippi public health districts, the worst-hit areas include the

rural communities in the rural-urban regional analysis, the Delta region among the cancer coalition regions, and the Central District (incidence rates) and North District (mortality rates). CONCLUSION: In Mississippi, there is a need for aggressive community-based participation and education. This approach will help improve screening and early detection of pancreatic cancer. Healthcare intake should be boosted and geared toward a reduction in mortality rates. To minimize disparities that eventually lead to differences in disease incidence and mortality from different locations, legislative and non-legislative authorities should advocate for equitable distribution of healthcare resources. An understanding of the geographic distribution of pancreatic cancer in a state will aid in the designation of specific primary prevention measures targeted in the worst-hit communities.

Niksic, M., et al. (2021). "The role of multimorbidity in short-term mortality of lung cancer patients in Spain: a population-based cohort study." BMC Cancer **21**(1): 1048.

AIM: Chronic diseases often occur simultaneously and tend to be associated with adverse health outcomes, but limited research has been undertaken to understand their role in lung cancer mortality. Therefore, this study aims to describe the prevalence and patterns of having one (comorbidity) or >/= 2 chronic diseases (multimorbidity) among lung cancer patients in Spain, and to examine the association between comorbidity or multimorbidity and short-term mortality risk at six months after cancer diagnosis. METHODS: In this population-based cohort study, data were drawn from two Spanish population-based cancer registries, Girona and Granada, and electronic health records. We identified 1259 adult lung cancer patients, diagnosed from 1st January 2011 to 31st December 2012. We identified the most common patterns of individual comorbidities and their pairwise correlations. We used a flexible parametric modelling approach to assess the overall short-term mortality risk 6 months after cancer diagnosis by levels of comorbidity after adjusting for age, sex, smoking status, province of residence, surgery, cancer stage, histology, and body mass index. RESULTS: We found high prevalence of comorbidity in lung cancer patients, especially among the elderly, men, those diagnosed with advanced-stage tumours, smokers, and obese patients. The most frequent comorbidities were chronic obstructive pulmonary disease (36.6%), diabetes (20.7%) and heart failure (16.8%). The strongest pairwise correlation was the combination of heart failure with renal disease ($r = 0.20$, $p < 0.01$), and heart failure with diabetes ($r = 0.16$, $p < 0.01$). Patients with either one or two or more comorbidities had 40% higher overall mortality risk than those without comorbidities (aHR for comorbidity: 1.4, 95%CI: 1.1-1.7; aHR for multimorbidity: 1.4, 95%CI: 1.1-1.8), when relevant confounding factors were considered. CONCLUSIONS: The presence of comorbid diseases, rather than the number of comorbidities, was associated with increasing the risk of short-term lung cancer mortality in Spain. Comorbidity was a consistent and independent predictor of mortality among lung cancer patients, six months after diagnosis. The most common comorbid conditions were age-, obesity- and tobacco-related diseases. Our findings highlight the need to develop targeted preventive interventions and more personalised clinical guidelines to address the needs of lung cancer patients with one or more comorbidities in Spain.

Nimptsch, K., et al. (2022). "Pre-diagnostic C-reactive protein concentrations, CRP genetic variation and mortality among individuals with colorectal cancer in Western European populations." BMC Cancer **22**(1): 695.

BACKGROUND: The role of elevated pre-diagnostic C-reactive protein (CRP) concentrations on mortality in individuals with colorectal cancer (CRC) remains unclear. METHODS: We investigated the association between pre-diagnostic high-sensitivity CRP concentrations and CRP genetic variation associated with circulating CRP and CRC-specific and all-cause mortality based on data from 1,235 individuals with CRC within the European Prospective Investigation into Cancer and Nutrition cohort using multivariable-adjusted Cox proportional hazards regression. RESULTS: During a median follow-up of 9.3 years, 455 CRC-specific deaths were recorded, out of 590 deaths from all causes. Pre-diagnostic CRP concentrations were not associated with CRC-specific (hazard ratio, HR highest versus lowest quintile 0.92, 95% confidence interval, CI 0.66, 1.28) or all-cause mortality (HR 0.91, 95% CI 0.68, 1.21). Genetic predisposition to higher CRP (weighted score based on alleles of four CRP SNPs associated with higher circulating CRP) was not significantly associated with CRC-specific mortality (HR per CRP-score unit 0.95, 95% CI 0.86, 1.05) or all-cause mortality (HR 0.98, 95% CI 0.90, 1.07). Among four investigated CRP genetic variants, only SNP rs1205 was significantly associated with CRC-specific (comparing the CT and CC genotypes with TT genotype, HR 0.54, 95% CI 0.35, 0.83 and HR 0.58, 95% CI 0.38, 0.88, respectively) and all-cause mortality (HR 0.58, 95% CI 0.40, 0.85 and 0.64, 95% CI 0.44, 0.92, respectively). CONCLUSIONS: The results of this prospective cohort study do not support a role of pre-diagnostic CRP concentrations on mortality in individuals with CRC. The observed associations with rs1205 deserve further scientific attention.

Ningarhari, M., et al. (2022). "Benefits of tailored hepatocellular carcinoma screening in patients with cirrhosis on cancer-specific and overall mortality: A modeling approach." Hepatol Commun **6**(10): 2964-2974.

To validate cancer screening programs, experts recommend estimating effects on case fatality rates (CFRs) and cancer-specific mortality. This study evaluates hepatocellular carcinoma (HCC) screening in patients with cirrhosis for those outcomes using a modeling approach. We designed a Markov model to assess 10-year HCC-CFR, HCC-related, and overall mortality per 100,000 screened patients with compensated cirrhosis. The model evaluates different HCC surveillance intervals (none, annual [12 months], semiannual [6 months], or quarterly [3 months]) and imaging modalities (ultrasound [US] or magnetic resonance imaging [MRI]) in various annual incidences (0.2%, 0.4%, or 1.5%). Compared to no surveillance, 6-month US reduced the 10-year HCC-CFR from 77% to 46%. With annual incidences of 0.2%, 0.4%, and 1.5%, the model predicted 281, 565, and 2059 fewer HCC-related deaths, respectively, and 187, 374, and 1356 fewer total deaths per 100,000 screened patients, respectively. Combining alpha-fetoprotein screening to 6-month US led to 32, 63, and 230 fewer HCC-related deaths per 100,000 screened patients for annual incidences of 0.2%, 0.4%, and 1.5%, respectively. Compared to 6-month US, 3-month US reduced cancer-related mortality by 14%, predicting 61, 123, and 446 fewer HCC-related deaths per 100,000 screened patients with annual incidences of 0.2%, 0.4%, and 1.5%, respectively. Compared to 6-month US, 6-month MRI (-17%) and 12-month MRI (-6%) reduced HCC-related mortality. Compared to 6-month US, overall mortality reductions ranged from -0.1% to -1.3% when using 3-month US or MRI. A US surveillance interval of 6 months improves HCC-related and overall mortality compared to no surveillance. A shorter US interval or using MRI could reduce HCC-CFR and HCC-related mortality, with a modest effect on overall mortality.

Niroomand, E., et al. (2022). "Impact of Medicaid Expansion on Incidence and Mortality from Gastric and Esophageal Cancer." Dig Dis Sci.

BACKGROUND AND AIMS: Individuals in Medicaid expanded states have increased access to treatment for medical conditions and other health care resources. Esophageal and gastric cancer are associated with several modifiable risk factors (e.g. smoking, drinking, Helicobacter pylori infection). The impact of Medicaid expansion on these cancers incidence and mortality remains uninvestigated. METHODS: We evaluated the association between Medicaid expansion and gastric and esophageal cancer incidence and mortality in adults aged 25-64. We employed an observational design using a difference-in-differences method with state level data, from 2010 to 2017. Annual, age-adjusted gastric and esophageal cancer incidence and mortality rates, from the CDC Wonder Database, were analyzed. Rates were adjusted for by several socio-demographic factors. RESULTS: Expansion and non-expansion states were similar in percent Hispanic ethnicity and female gender. The non-expansion states had significantly higher proportion of Black race, diabetics, obese persons, smokers, and those living below the federal poverty line. Adjusted analyses demonstrate that expansion states had significantly fewer new cases of gastric cancer: - 1.6 (95% CI 0.2-3.5; P = 0.08) per 1,000,000 persons per year. No significant association was seen between Medicaid expansion and gastric cancer mortality (0.46 [95% CI - 0.08 to 0.17; P = 0.46]) and esophageal cancer incidence (0.8 [95% CI - 0.08 to 0.24; P = 0.33]) and mortality (1.0 [95% CI - 0.06 to 0.26; P = 0.21]) in multivariable analyses. CONCLUSION: States that adopted Medicaid expansion saw a decrease in gastric cancer incidence when compared to states that did not expand Medicaid. Though several factors may influence gastric cancer incidence, this association is important to consider during health policy negotiations.

Nishikawa, T., et al. (2021). "Prognostic Effect of Incidental Pulmonary Embolism on Long-Term Mortality in Cancer Patients." Circ J.

BACKGROUND: The effect of incidental pulmonary embolism (PE) on long-term prognosis in cancer patients is unclear. This study assessed the characteristics of cancer and venous thromboembolism (VTE) and the effect of incidental PE identified by oncologists on long-term survival of patients with cancer.Methods and Results:This single-center, retrospective, cohort study used hospital-based cancer registry data from the Osaka International Cancer Institute linked with electronic medical records and administrative data from Japan's Diagnosis Procedure Combination Per-diem Payment System. Overall, 15,689 cancer patients underwent contrast-enhanced thoracic computed tomography during 2010-2018. After excluding patients with missing data, symptomatic patients, or patients with suspected PE, 174 with incidental PE (PE+ group) and 13,197 with no PE (PE- group) were identified. The total incidence of incidental PE was 1.3%. No deaths from thrombotic events were identified in the PE+ group. Both groups were adjusted for cancer- and VTE-related characteristics using inverse probability weighting. After adjusting for immortal time bias in the PE+ group, Kaplan-Meier analysis revealed that all-cause

mortality was higher in the PE+ group (hazard ratio, 2.26; 95% confidence interval, 1.53-3.33). A Cox proportional hazard model revealed that metastatic cancer and a history of curative treatment were significant prognostic factors, whereas central PE and residual proximal deep vein thrombosis were not. CONCLUSIONS: Incidental PE in cancer patients indicates poorer prognosis. Cancer-related but not thrombosis-related factors determine prognosis.

Nishiyama, H., et al. (2022). "Low apolipoprotein A1 was associated with increased risk of cancer mortality in patients following percutaneous coronary intervention: A 10-year follow-up study." Int J Cancer **151**(9): 1482-1490.

Previous studies showed that elevated apolipoprotein A1 (ApoA1) and high-density lipoprotein cholesterol (HDL-C) predicted reduced risk of cardiovascular-related (CV) mortality in patients following percutaneous coronary intervention (PCI). Nevertheless, as the association between ApoA1 and cancer mortality in this population has been rarely addressed, our study aimed to evaluate prognostic impact of ApoA1 on multiple types of cancer mortality after PCI. This is a retrospective analysis of a single-center prospective registry database of patients who underwent PCI between 2000 and 2018. The present study enrolled 3835 patients whose data of serum ApoA1 were available and they were divided into three groups according to the tertiles of the preprocedural level of ApoA1. The outcome measures were total, gastrointestinal, and lung cancer mortalities. The median and range of the follow-up period between the index PCI and latest follow-up were 5.9 and 0-17.8 years, respectively. Consequently, Kaplan-Meier analyses showed significantly higher rates of the cumulative incidences of total, gastrointestinal, and lung cancer mortality in the lowest ApoA1 tertile group compared to those in the highest. In contrast, there were no significant differences in all types of cancer mortality rates in the groups divided by the tertiles of HDL-C. Multivariable Cox proportional hazard regression analysis adjusted by cancer-related prognostic factors, such as smoking status, identified the elevated ApoA1 as an independent predictor of decreased risk of total and gastrointestinal cancer mortalities. Our study demonstrates the prognostic implication of preprocedural ApoA1 for predicting future risk of cancer mortality in patients undergoing PCI.

Njor, S. H., et al. (2022). "Colorectal cancer mortality after randomized implementation of FIT-based screening - a nationwide cohort study." J Med Screen **29**(4): 241-248.

OBJECTIVE: Evidence of reduction in colorectal cancer (CRC) mortality following CRC screening based on the faecal immunochemical test (FIT) is insufficient. This study aimed to analyse if CRC mortality was reduced after implementing FIT-based screening. SETTING: The Danish national CRC screening programme. METHODS: This nationwide cohort study included residents aged 50-71 years invited to the prevalence round of the screening programme. Invitation order was decided by randomising on birth month; the first two birth months to be invited were classified as invited and the five last were classified as not-yet-invited and given a pseudo invitation data. Follow-up was from (pseudo)invitation date until 31 December 2017, emigration or death. Relative risk (RR) of CRC death was calculated with 95% confidence intervals (CIs). RESULTS: A total of 897,812 residents were included (29% invited and 71% not-yet-invited). The median follow-up was 3.3 years. The RR of CRC death at end of follow-up was 0.83 (95% CI 0.66; 1.03) among those invited to screening compared with those not yet invited. For men aged 60-71 years, this RR was 0.68 (95% CI 0.49; 0.94). For those participating in screening compared with a similar group of not-yet-invited residents, the RR was 0.71 (95% CI 0.46-1.08). For male participants aged 60-71 years, this RR was 0.49 (95% CI 0.27-0.89). For women and men aged 50-59 years, RRs were small and statistically non-significant. CONCLUSION: This nationwide study showed that even within a median follow-up of only 3.3 years, implementing FIT-based CRC screening reduced CRC mortality among older men.

Nnorom, S. O., et al. (2022). "Color or money?: The impact of socioeconomic status and race/ethnicity on breast cancer mortality." Am J Surg **224**(6): 1403-1408.

BACKGROUND: Although the incidence of breast cancer is highest in White women, Black women die at a higher rate. Our aim was to compare the relative association between race/ethnicity and socioeconomic status on breast cancer mortality. METHODS: We identified female breast cancer patients diagnosed between 2007 - 2011 and followed through 2016 in the SEER database. Patients were grouped into socioeconomic quartiles by a prosperity index. The primary outcome of interest was 5-year cancer-specific survival. RESULTS: A total of 286,520 patients were included. Five-year survival was worst for Black women compared to other races/ethnicities in each socioeconomic quartile. When compared to White women in the lowest quartile, Black women in the lowest quartile, 2nd quartile, and 3rd quartile experienced the lowest 5-year survival rates (Hazard ratio 1.33, 1.23, 1.20; $P < 0.01$). CONCLUSION:

Regarding cancer mortality, only in the most prosperous quartile do Black women achieve a similar outcome to the poorest quartile White women.

Nobel, T. B., et al. (2020). "Disparities in mortality-to-incidence ratios by race/ethnicity for female breast cancer in New York City, 2002-2016." Cancer Med **9**(21): 8226-8234.

BACKGROUND: Racial disparities in New York City (NYC) breast cancer incidence and mortality rates have previously been demonstrated. Disease stage at diagnosis and mortality-to-incidence ratio (MIR) may present better measures of differences in screening and treatment access. Racial/ethnic trends in NYC MIR have not previously been assessed. METHODS: Mammogram rates were compared using the NYC Community Health Survey, 2002-2014. Breast cancer diagnosis, stage, and mortality were from the New York State Cancer Registry, 2000-2016. Primary outcomes were MIR, the ratio of age-adjusted mortality to incidence rates, and stage at diagnosis. Joinpoint regression analysis identified significant trends. RESULTS: Mammogram rates in 2002-2014 among Black and Latina women ages 40 and older (79.9% and 78.4%, respectively) were stable and higher than among White (73.6%) and Asian/Pacific-Islander women (70.4%) ($P < .0001$). There were 82 733 incident cases of breast cancer and 16 225 deaths in 2000-2016. White women had the highest incidence, however, rates among Black, Latina, and Asian/Pacific Islander women significantly increased. Black and Latina women presented with local disease (Stage I) less frequently (53.2%, 57.6%, respectively) than White (62.5%) and Asian/Pacific-Islander women (63.0%). Black women presented with distant disease (Stage IV) more frequently than all other groups (Black 8.7%, Latina 5.8%, White 6.0%, and Asian 4.2%). Black women had the highest breast cancer mortality rate and MIR (Black 0.25, Latina 0.18, White 0.17, and Asian women 0.11). CONCLUSIONS: More advanced disease at diagnosis coupled with a slower decrease in breast cancer mortality among Black and Latina women may partially explain persistent disparities in MIR especially prominent among Black women. Assessment of racial/ethnic differences in screening quality and access to high-quality treatment may help identify areas for targeted interventions to improve equity in breast cancer outcomes.

Nocera, L., et al. (2022). "Tumor Stage and Substage Predict Cancer-specific Mortality After Nephrectomy for Nonmetastatic Renal Cancer: Histological Subtype-specific Validation." Eur Urol Focus **8**(1): 182-190.

BACKGROUND: For patients with nonmetastatic renal cell carcinoma (nmRCC) treated with nephrectomy, prediction of cancer-specific mortality (CSM) by T stage and substage has not been validated for the separate histological subtypes. OBJECTIVE: To investigate the ability of pathological T stage and substage to predict CSM for patients with clear-cell, papillary, or chromophobe nmRCC treated with nephrectomy. DESIGN, SETTING, AND PARTICIPANTS: Using the SEER database for 2004-2016, we identified 87 149 patients with T1-4 N0/X M0 nmRCC treated with nephrectomy for the clear-cell (65 715; 75.4%), papillary (14 587; 16.7%), or chromophobe (6847; 7.9%) histological subtype. OUTCOME MEASUREMENTS AND STATISTICAL ANALYSIS: Kaplan-Meier plots and Cox regression models were used to estimate CSM. RESULTS AND LIMITATIONS: For all three histological subtypes, patients with T1a-T3a disease exhibited more favorable CSM than patients with T3b-T4 RCC. For clear-cell RCC, there were clinically meaningful and statistically significant differences for virtually all intergroup comparisons among T1a-T3a stages. For papillary T1a-T3a RCC, clinically meaningful differences disappeared, although the statistical significance remained. For chromophobe T1a-T3a RCC, no clinically meaningful or statistically significant differences were observed. For all three histological subtypes, patients with T3b-T4 RCC exhibited virtually uniformly unfavorable CSM, with no clinically meaningful intergroup CSM differences. CONCLUSION: The use of T stage and substage for stratification of patients with nmRCC treated with nephrectomy revealed differences in CSM among T1a-T3a cases, but not T3b-T4. The magnitude of the CSM difference was greatest for clear-cell, intermediate for papillary, and marginal for chromophobe RCC. PATIENT SUMMARY: For patients with kidney cancer, the stage of their disease assessed after surgery on the affected kidney can predict how likely they are to die from their cancer. This prediction varies for different subtypes of kidney cancer.

Nogawa, K., et al. (2022). "Renal tubular dysfunction and cancer mortality in the Japanese general population living in cadmium-non-contaminated areas." J Appl Toxicol **42**(9): 1458-1466.

The relationship between cadmium exposure, exposure-related renal tubular dysfunction, and mortality have been reported, mainly in the residents of Cd-contaminated areas in Japan. The aim of this study was to establish the cause-effect relationship between renal tubular dysfunction and cancer mortality in the general population in non-contaminated areas. A 19-year cohort study was conducted in 1110 men and 1703 women in 1993 or 1994, who lived in three cadmium-non-contaminated areas. Mortality risk ratios of urinary beta2-microglobulin (beta2MG) and N-acetyl-beta-glucosaminidase (NAG) for all malignant neoplasms

and specific cancers were estimated using the Fine and Gray competing risks regression model. Significant hazard ratios (HRs) for liver and pancreas cancer were observed for NAG (liver: HR corresponding to an increase of 1 IU/g cr, 1.10, 95%CI, 1.02-1.19, pancreas: HR, 1.10, 95%CI, 1.02-1.19) in men. In women, a negative HR was observed for NAG (lung cancer: HR 0.80, 95% CI, 0.67-0.96) and for beta2MG (all malignant neoplasms: HR, 0.97, 95% CI, 0.93-1.00). The present study indicated that renal tubular dysfunction was significantly related to mortality in the general population of cadmium-non-contaminated areas in Japan.

Nohara-Shitama, Y., et al. (2021). "Differential impacts of 24 hour urinary sodium excretion on cardiovascular diseases or cancer mortality in a general population." J Cardiol **78**(4): 334-340.

BACKGROUND: Elevated blood pressure is a major risk factor for cardiovascular (CV) disease. But the effects of sodium intake or excretion on CV mortality are uncertain. The present study aimed to investigate the association between 24 h urinary sodium excretion, as a marker of dietary salt intake, and CV or cancer mortality in a healthy Japanese population using 24 hurine collection. METHODS: The baseline study was conducted in 1980. A total of 1291 participants aged 21 to 85 years, underwent health check-ups, which included blood chemistry measurements and the collection of 24 h urine samples. Enrolled 1291 participants were followed up for 27.5 years, in whom the final follow-up rate was 95.8%. Cox proportional hazards regression models were used to assess the association between 24 h urinary sodium excretion and CV or cancer mortality. RESULTS: The mean 24 h urinary sodium excretion was 5.80 +/- 2.28 g/day. There were 631 deaths: 153 (27%) from cancer, 142 (26%) from CV disease. In the Cox proportional hazard regression model after adjustment for confounding factors, systolic and diastolic blood pressures, and uric acid were positively associated with CV mortality, and the 24 h urinary sodium and potassium excretions were inversely associated with CV mortality ($p < 0.05$). On the other hand, there were no association between 24 h urinary sodium excretions and cancer mortality. We divided the urinary sodium excretions levels into quartiles. After adjustment for confounding factors, the hazard ratio of CV mortality in the highest quartile of 24 h urinary sodium excretion versus the lowest was 0.46 ($p < 0.05$). The cumulative survival rate for CV death was significantly decreased in the lowest quartile compared with the other higher groups. CONCLUSIONS: We found that impacts of 24 h sodium excretion on CV and cancer mortalities were much different in the general population.

Nopel-Dunnebacke, S., et al. (2022). "Causes of mortality in elderly UICC stage III colon cancer (CC) patients--Tumor-related death and competing risks from the German AIO colorectal study group Colopredict Plus (CPP) registry." Cancer Med **11**(8): 1735-1744.

BACKGROUND: Colon cancer (CC) is a disease of elderly patients (pts.) with a median age of 73 years (yrs.). Lack of data about the effects of adjuvant chemotherapy (ACT) is caused by underrepresentation of this clinically relevant cohort in interventional trials. We analyzed real-world data from the German CPP registry with regard to a possible benefit of ACT in elderly (70+ yrs.) versus younger pts. (50 to <70 yrs.) taking cause-specific deaths into account. METHODS: We analyzed the effect of age and ACT on overall survival (OS) and cause-specific death of stage III pts. using Cox regression. RESULTS: In total, 1558 pts. were analyzed and follow-up was 24.6 months. 62.6% of the elderly received ACT whereas 91.1% of younger pts. ($p < 0.001$). Oxaliplatin combinations were significantly less often given to older than younger pts. (38.8% vs. 88.9%; $p < 0.001$). Mean Charlson comorbidity score was significantly lower in pts. that received ACT (0.61) than in those without ACT (1.16; $p < 0.001$). ACT was an independent positive prognostic factor for cancer-related death in elderly pts. even in pts. 75+ yrs. No significant difference in the effect of ACT could be observed between age groups (interaction: cancer-specific death HR = 1.7948, $p = 0.1079$; death of other cause HR = 0.7384, $p = 0.6705$). CONCLUSION: ACT was an independent positive prognostic factor for OS. There may be a cohort of elderly with less co-morbidities who benefit from ACT.

Nordestgaard, A. T. (2022). "Causal relationship from coffee consumption to diseases and mortality: a review of observational and Mendelian randomization studies including cardiometabolic diseases, cancer, gallstones and other diseases." Eur J Nutr **61**(2): 573-587.

PURPOSE: High coffee consumption is associated with low risk of mortality and morbidity, but the causality remains unclear. This review aims to discuss findings from observational studies on coffee consumption in context of Mendelian randomization studies. METHODS: The PubMed database was searched for all Mendelian randomization studies on coffee consumption and corresponding observational studies. RESULTS: High coffee consumption is associated with low risk of all-cause and cardiovascular mortality in observational studies (HRs of 0.85-0.90 vs. no/low consumers), with no support of causality in Mendelian randomization studies. Moderate/high consumption is associated with low risk of cardiometabolic diseases, including ischemic heart

disease (HRs of 0.85-0.90 vs. no/low consumption), stroke (HRs of approximately 0.80 vs. no/low consumption), type 2 diabetes (HRs of approximately 0.70 vs. no/low consumption) and obesity in observational studies, but not in Mendelian randomization studies. High consumption is associated with low risk of endometrial cancer and melanoma and high risk of lung cancer in observational studies, but with high risk of colorectal cancer in Mendelian randomization studies. In observational and Mendelian randomization studies, high coffee consumption is associated with low risk of gallstones (HRs of 0.55-0.70 for high vs. no/low self-reported and 0.81 (0.69-0.96) for highest vs. lowest genetic consumption). CONCLUSION: High coffee consumption is associated with low risk of mortality, cardiometabolic diseases, some cancers and gallstones in observational studies, with no evidence to support causality from Mendelian randomization studies for most diseases except gallstones.

Oliveira, J. C. S., et al. (2022). "Incidence and Mortality by the Main Types of Cancer in the City of Cuiaba, Mato Grosso, Between the Years of 2008 and 2016." Rev Bras Epidemiol **25**(Supl 1): e220011.

OBJECTIVE: To analyze the temporal trend of the incidence and mortality rate for prostate, breast, colorectal, lung, cervical, stomach and laryngeal cancer among residents in the city of Cuiaba between 2008 and 2016. METHODS: Time series study with data from the Mortality Information System and the Population-Based Cancer Registry. Stratified by sex, the proportional distribution of new cases and deaths by age group and the cancer incidence and mortality rates standardized by the world population were calculated. Linear regression was used and the annual percentage change (APC) was estimated. RESULTS: In males, most new cases and deaths, for the main types of cancer, occurred among those aged 50 years or older, and the incidence rate of prostate cancer showed a tendency to decrease in the period (APC=-4.33%). For females, the proportion of new cases and deaths, due to breast and cervical cancer, were more frequent among women aged 50 years or younger, and lung, stomach and colorectal cancer among women aged 50 years or older. The incidence rate of breast cancer showed an increasing trend (APC=3.60%). For both sexes, the mortality rate remained stable. CONCLUSION: The incidence rate trend varied between sexes, an increase was observed for breast cancer among women and a reduction for prostate cancer among men. The mortality rate for the main types of cancer was stable.

Oliveira, M. M., et al. (2021). "Esophageal Cancer Mortality in Brazil: A Time-Series Analysis from the Global Burden of Disease Study." Arq Gastroenterol **58**(1): 100-106.

BACKGROUND: In the world, around 450,000 new cases of esophageal cancer are diagnosed each year. OBJECTIVE: To evaluate the trend of esophageal cancer mortality rates in Brazil between 1990-2017. METHODS: A time series study using data on mortality from esophageal cancer in residents >/=30 years in Brazil from 1990 to 2017. Data was estimated by the Global Burden of Disease (GBD) study and analyzed according to sex, age group and federal unit of Brazil. The standardized rates according to age were calculated by the direct method using the standard GBD world population. Annual average percentage change and 95% confidence interval (95% CI) were calculated for mortality by Joinpoint regression. RESULTS: The age-standardized mortality rate in males was 20.6 in 1990 and 17.6/100,000 in 2017, increasing according to age, being 62.4 (1990) and 54.7 (2017) for >/=70 years. In women, the age-standardized mortality rate was 5.9 in 1990 and 4.2/100,000 in 2017. There was a reduction in mortality rates in all age groups and both sexes with great variation among the states. CONCLUSION: Despite the high mortality rates for esophageal cancer in Brazil, the trend was decreasing, but with regional differences. Mortality was around four times higher in men.

Oliveira, N. P. D., et al. (2021). "Spatial distribution of advanced stage diagnosis and mortality of breast cancer: Socioeconomic and health service offer inequalities in Brazil." PLoS One **16**(2): e0246333.

Breast cancer presents high incidence and mortality rates, being considered an important public health issue. Analyze the spatial distribution pattern of late stage diagnosis and mortality for breast cancer and its correlation with socioeconomic and health service offer-related population indicators. Ecological study, developed with 161 Intermediate Region of Urban Articulation (IRUA). Mortality data were collected from the Mortality Information System (MIS). Tumor staging data were extracted from the Hospital Cancer Registry (HCR). Socioeconomic variables were obtained from the Atlas of Human Development in Brazil; data on medical density and health services were collected from the National Registry of Health Institutions (NRHI) and Supplementary National Health Agency. Global Moran's Index and Local Indicator of Spatial Association (LISA) were utilized to verify the existence of territorial clusters. Multivariate analysis used models with global spatial effects. The proportion of late stage diagnosis of breast cancer was 39.7% (IC 39.4-40.0). The mean mortality rate for breast cancer, adjusted by the standard world population was 10.65 per 100,000 women (+/- 3.12).

The proportion of late stage diagnosis presented positive spatial correlation with Gini's Index (p = 0.001) and negative with the density of gynecologist doctors (p = 0.009). The adjusted mortality rates presented a positive spatial correlation with the Human Development Index (p<0.001) and density of gynecologist doctors (p<0.001). Socioeconomic and health service offer-related inequalities of the Brazilian territory are determinants of the spatial pattern of breast cancer morbimortality in Brazil.

Olschewski, P., et al. (2021). "Associations between Weather, Air Quality and Moderate Extreme Cancer-Related Mortality Events in Augsburg, Southern Germany." Int J Environ Res Public Health **18**(22).

While many authors have described the adverse health effects of poor air quality and meteorological extremes, there remain inconsistencies on a regional scale as well as uncertainty about the single and joint effects of atmospheric predictors. In this context, we investigated the short-term impacts of weather and air quality on moderate extreme cancer-related mortality events for the urban area of Augsburg, Southern Germany, during the period 2000-2017. First, single effects were uncovered by applying a case-crossover routine. The overall impact was assessed by performing a Mann-Whitney U testing scheme. We then compared the results of this procedure to extreme noncancer-related mortality events. In a second step, we found periods with contemporaneous significant predictors and carried out an in-depth analysis of these joint-effect periods. We were interested in the atmospheric processes leading to the emergence of significant conditions. Hence, we applied the Principal Component Analysis to large-scale synoptic conditions during these periods. The results demonstrate a strong linkage between high-mortality events in cancer patients and significantly above-average levels of nitrogen dioxide (NO(2)) and particulate matter (PM(2.5)) during the late winter through spring period. These were mainly linked to northerly to easterly weak airflow under stable, high-pressure conditions. Especially in winter and spring, this can result in low temperatures and a ground-level increase and the accumulation of air pollution from heating and traffic as well as eastern lateral advection of polluted air. Additionally, above-average temperatures were shown to occur on the days before mortality events from mid-summer through fall, which was also caused by high-pressure conditions with weak wind flow and intense solar radiation. Our approach can be used to analyse medical data with epidemiological as well as climatological methods while providing a more vivid representation of the underlying atmospheric processes.

Pader, J., et al. (2021). "Estimates of future cancer mortality attributable to modifiable risk factors in Canada." Can J Public Health **112**(6): 1069-1082.

OBJECTIVES: Modifiable lifestyle, environmental, and infectious risk factors associated with cancer impact both cancer incidence and mortality at the population level. Most studies estimating this burden focus on cancer incidence. However, because these risk factors are associated with cancers of disparate mortality rates, the burden associated with cancer incidence could differ from cancer mortality. Therefore, estimating the cancer mortality attributable to these risk factors provides additional insight into cancer prevention. Here, we estimated future cancer deaths and the number of avoidable deaths in Canada due to modifiable risk factors. METHODS: The projected cancer mortality data came from OncoSim, a web-based microsimulation tool. These data were applied to the methodological framework that we previously used to estimate the population attributable risks and the potential impact fractions of modifiable risk factors on Canadian cancer incidence. RESULTS: We estimated that most cancer deaths will be attributed to tobacco smoking with an average of 27,900 deaths annually from 2024 to 2047. If Canada's current trends in excess body weight continue, cancer deaths attributable to excess body weight would double from 2786 deaths in 2024 to 5604 deaths in 2047, becoming the second leading modifiable cause of cancer death. Applying targets to reduce these risk factors, up to 34,600 cancer deaths could be prevented from 2024 to 2047. CONCLUSION: Our simulated results complement our previous findings on the cancer incidence burden since decreasing the overall burden of cancer will be accelerated through a combination of decreasing cancer incidence and improving survival outcomes through improved treatments.

Pak, S., et al. (2022). "Incidence and mortality projections for major cancers among Korean men until 2034, with a focus on prostate cancer." Investig Clin Urol **63**(2): 175-183.

PURPOSE: The Korean population is rapidly aging, and the cancer burden is expected to change significantly. This study aimed to generate projections of incidence and mortality of major cancers among men in Korea until 2034, with a special focus on prostate cancer. MATERIALS AND METHODS: Cancer incidence data from 1999 to 2016 were obtained from the Korea National Cancer Incidence Database. Mortality data were obtained from Statistics Korea. The most common cancers among Korean men (stomach, colorectum, liver, lung and prostate) were analyzed. To predict the future trends of these cancers, the age-period-cohort method was conducted and extrapolated up to 2034. RESULTS: In Korean men,

prostate cancer was the fourth most commonly diagnosed cancer in 2016. Based on newly diagnosed cases, the leading cancer site in the year 2034 is expected to be the lung, and the prostate is expected to be the second most frequently diagnosed cancer among Korean men. Age-standardized incidence rates of the most common cancers in men, except prostate cancer, are expected to decrease until 2034. Lung cancer is projected to remain the most common cause of cancer-related mortality until 2034, and the highest estimated change in cancer deaths is expected to be for prostate cancer. CONCLUSIONS: In Korea, the incidence and mortality of prostate cancer is expected to increase markedly in the period up to 2034, particularly in older men. Concerted efforts in screening, diagnosis, and treatment strategies should be considered by healthcare planners and providers.

Pal, L., et al. (2022). "Health and economic gain attributable to the introduction of the World Health Organization's drinking water standard on arsenic level in Hungary: A nationwide retrospective study on cancer occurrence and ischemic heart disease mortality." Sci Total Environ **851**(Pt 2): 158305.

The World Health Organization (WHO) estimates that 140 million individuals are at risk from consumption of drinking water containing arsenic at concentrations above the WHO guideline value of 10 mug/l. Arsenic mitigation is considered to be the most effective way to prevent arsenic related diseases. After joining the European Union, Hungary implemented a Drinking Water Quality Improvement Programme (DWQIP) to reduce levels of arsenic in drinking water below the WHO guideline value. But what impact did this have on health? We estimated the change in lifetime excess skin, lung, and bladder cancer risks and mortality from ischaemic heart disease (IHD) associated with chronic arsenic intake among those exposed before (2004-2007) and after (2014-2017) the implementation of DWQIP. A population-based risk assessment approach was used to assess lifetime excess cancer risk applying two scenarios for lung and bladder cancers. The economic benefits of the DWQIP were estimated by the combination of cost of illness and value per statistical life methods. Compared to the period before the DWQIP, its implementation was associated with a significant reduction in arsenic in drinking water [median: 3.0 mug/l interquartile range (IQR): 1.5-12.0 mug/l to median: 2.15 mug/l IQR: 1.0-5.79 mug/l]. The two scenarios were estimated to be associated with 225.2 and 35.9 fewer cancer cases each year. The number of annually prevented IHD deaths was estimated to be 88.9. It was estimated that the benefits of the DWQIP will outweigh its costs. We conclude that reducing arsenic levels in drinking water to 10.0 mug/l resulted in significant health and economic benefits. Our study goes beyond the existing research, offering both new insights into the impact of arsenic mitigation and providing a methodological template for similar studies in the many parts of the world that have yet to reduce arsenic exposure.

Palacios, D. A., et al. (2021). "Does Reduced Renal Function Predispose to Cancer-specific Mortality from Renal Cell Carcinoma?" Eur Urol **79**(6): 774-780.

BACKGROUND: Recent publications have reported an association between increased renal cancer-specific mortality (CSM) and reduced renal function "below safety limits," and advocated for partial nephrectomy (PN) even for potentially aggressive/complex tumors. We hypothesize that this association may be related to confounding factors rather than a consequence of functional differences. OBJECTIVE: To assess whether there is an independent association between preoperative estimated glomerular filtration rate (eGFR) or new baseline eGFR (NB-GFR) and CSM in patients undergoing PN or radical nephrectomy (RN). DESIGN, SETTING, AND PARTICIPANTS: A single-center retrospective review was performed. All clinically and pathologically confirmed T1-T3a/N0/M0 renal cancer patients undergoing PN/RN (1999-2008, n = 1605) with adequate functional/oncological data were included. OUTCOME MEASUREMENTS AND STATISTICAL ANALYSIS: The primary endpoint was CSM. Secondary endpoints were cancer recurrence (CR) and all-cause mortality (ACM). Cox regression analyses investigated endpoints and predictive factors. RESULTS AND LIMITATIONS: The median age was 60 yr and 64% of patients were male. Comorbidities included hypertension (60%), cardiovascular disease (19%), diabetes (21%), and chronic kidney disease (22%). PN was performed in 954 patients (59%). The median preoperative eGFR and NB-GFR were 80 and 60 ml/min/1.73 m(2), respectively. Median tumor diameter was 3.6 cm (interquartile range [IQR] = 2.4, 5.5); 70% of tumors were clear cell and 40% were of high grade. Pathology revealed pT1-2/N0/M0 and pT3a/N0/M0 in 81% and 19%, respectively. The median follow-up among survivors was 11.5 yr (IQR = 4, 14). Cancer-specific survival, recurrence-free survival, and overall survival were 94%, 88%, and 73% at 10 yr, respectively. On multivariable analysis, increased age (hazard ratio [HR] = 1.03, p = 0.04), increased tumor size (HR = 1.24, p < 0.01), tumor grade 3/4 (HR = 3.17, p < 0.01), and clear-cell histology (HR = 2.92, p < 0.01) were associated with increased hazard of CSM. Neither preoperative eGFR nor NB-GFR was significantly associated with CSM or CR (all p > 0.1), while an increased preoperative eGFR was associated with reduced hazard of ACM (HR = 0.87, p < 0.01). Limitations include retrospective

design and a potential selection bias. CONCLUSIONS: Our data do not support oncological protection of greater preservation of renal function and confirm that unfavorable oncological outcomes for localized RCC are mostly associated with aggressive tumor characteristics. PATIENT SUMMARY: We did not find an association between greater preservation of renal function and oncological outcomes for kidney cancer.

Palencia, L., et al. (2020). "Socio-economic inequalities on cancer mortality in nine European areas: The effect of the last economic recession." Cancer Epidemiol **69**: 101827.

BACKGROUND: The effect of inequalities aggravated by economic recessions in the mortality rates of certain diseases has been previously described. In this study, we analyzed the relationship between socio-economic deprivation and cancer mortality. We focused on lung, colon, prostate, and breast cancers in nine European urban areas over three periods: two before (2000-2003 and 2004-2008) and one after (2009-2014) the onset of the 2008 financial crisis. METHODS: This is an ecological study of trends. The units of analysis were small areas within nine European urban areas. We used a composite deprivation index as a socio-economic indicator. As a mortality indicator, we used the smoothed standardized mortality ratio, calculated using the hierarchical Bayesian model proposed by Besag, York and Mollie. To analyze the evolution of socio-economic inequalities, we fitted an ecological regression model that included the socio-economic indicator, the period of time, and the interaction between these terms. RESULTS: In men, socio-economic inequalities in all-cancer and lung cancer mortality were observed in most of the cities studied, but did not increase after the onset of the economic crisis. In women, only two cities (Stockholm and London) showed socio-economic inequalities in all-cancer and lung cancer mortality; there was also no increase in inequalities. CONCLUSIONS: Our results did not validate our hypothesis that inequalities increase in times of crisis. However, they emphasize the importance of socio-economic measurements for understanding mortality inequalities, and can be used to inform prevention strategies and help plan local health programs aimed at reducing health inequalities.

Palmer, C. R., et al. (2021). "Association between vitamin K(1) intake and mortality in the Danish Diet, Cancer, and Health cohort." Eur J Epidemiol **36**(10): 1005-1014.

Reported associations between vitamin K(1) and both all-cause and cause-specific mortality are conflicting. The 56,048 participants from the Danish Diet, Cancer, and Health prospective cohort study, with a median [IQR] age of 56 [52-60] years at entry and of whom 47.6% male, were followed for 23 years, with 14,083 reported deaths. Of these, 5015 deaths were CVD-related, and 6342 deaths were cancer-related. Intake of vitamin K(1) (phylloquinone) was estimated from a food-frequency questionnaire (FFQ), and its relationship with mortality outcomes was investigated using Cox proportional hazards models. A moderate to high (87-192 microg/d) intake of vitamin K(1) was associated with a lower risk of all-cause [HR (95%CI) for quintile 5 vs quintile 1: 0.76 (0.72, 0.79)], cardiovascular disease (CVD)-related [quintile 5 vs quintile 1: 0.72 (0.66, 0.79)], and cancer-related mortality [quintile 5 vs quintile 1: 0.80 (0.75, 0.86)], after adjusting for demographic and lifestyle confounders. The association between vitamin K(1) intake and cardiovascular disease-related mortality was present in all subpopulations (categorised according to sex, smoking status, diabetes status, and hypertension status), while the association with cancer-related mortality was only present in current/former smokers (p for interaction = 0.002). These findings suggest that promoting adequate intakes of foods rich in vitamin K(1) may help to reduce all-cause, CVD-related, and cancer-related mortality at the population level.

Pan, B., et al. (2022). "Association of soft drink and 100% fruit juice consumption with all-cause mortality, cardiovascular diseases mortality, and cancer mortality: A systematic review and dose-response meta-analysis of prospective cohort studies." Crit Rev Food Sci Nutr **62**(32): 8908-8919.

Sugar-sweetened beverages (SSBs), artificially sweetened beverages (ASBs), and 100% fruit juices are frequently consumed and have been documented that they could lead to serious disease burden. However, inconsistent evidence on the association between SSBs, ASBs, and 100% fruit juices consumption and mortality have been presented. PubMed, Embase, Web of Science, Cochrane Central Register of Controlled Trials, and PsycINFO were systematically searched. We conducted a random-effects meta-analysis and dose-response meta-analysis to assess the association and calculated the pooled hazard ratio with 95% confidence interval. And we evaluated the certainty of evidence using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach. Thirteen studies with 1,539,127 participants proved eligible. An SSB-consumption increase per 250 mL/day was associated with a 4% greater risk of all-cause mortality (5 more per 1000 persons; low certainty) and 8% greater risk of cardiovascular disease mortality (3 more per 1000 persons; low certainty). ASB-consumption increase per 250 mL/day demonstrated a 4% greater risk of all-cause mortality (5 more per 1000 persons; low

certainty) and 4% greater risk of cardiovascular disease mortality (2 more per 1000 persons; low certainty). The association of SSBs and ASBs with cancer mortality was not significant, with a very low certainty of evidence. There was evidence of a linear dose-response association between SSB intake and cancer mortality, as well as between ASB intake and all-cause mortality and cancer mortality. We observed a non-linear dose-response association between ASB intake and CVD mortality and SSB intake and all-cause and CVD mortality. Low certainty of evidence demonstrated that per 250 mL/day consumption increase in SSBs and ASBs had a small impact on all-cause and cardiovascular disease mortality but not on cancer mortality. The association of 100% fruit juice consumption with all-cause and cardiovascular disease mortality was uncertain.

Pan, D., et al. (2022). "Mortality of early treatment for radiation-induced brain necrosis in head and neck cancer survivors: A multicentre, retrospective, registry-based cohort study." EClinicalMedicine **52**: 101618.

BACKGROUND: The evidence of early treatment for radiation-induced brain necrosis (RN) in head and neck cancer survivors remains insufficient. This study aimed to determine whether early anti-RN treatment was associated with lower mortality. METHODS: In this cohort study, we utilized data from the Study in Radiotherapy-related Nervous System Complications (NCT03908502) and Hong Kong Cancer Registry. We included consecutive patients who had received radiotherapy (RT) for head and neck cancers and had subsequently developed RN between Jan 8, 2005 and Jan 19, 2020. Patients who had tumor progression before the diagnosis of RN, underwent surgical brain necrosis lesions resection before corticosteroids and/or bevacizumab treatment, had intracranial metastases before the diagnosis of RN, lacked follow-up data, or had a follow-up period of less than three months were excluded. Individual-level data were extracted from electronic medical records of the above-mentioned registries. The primary outcome was all-cause death. The vital status of each patient was confirmed through a standardized telephone interview. We compared patients who received early treatment (initiating bevacizumab or corticosteroids treatment within three months after RN diagnosis) with patients who did not (following a "watch-and-wait" policy). FINDINGS: Of 641 eligible patients, 451 patients (70.4%) received early treatment after RN diagnosis and 190 patients (29.6%) did not. Overall, 112 patients (17.5%) died, of whom 73 (16.2%) in the early treatment group and 39 (20.5%) in the watch-and-wait group, during a median follow-up of 3.87 years. The early treatment group showed a lower risk of all-cause death compared with the watch-and-wait group after adjusting for age, sex, absence or presence of neurological symptoms at baseline, RN lesion features on brain magnetic resonance imaging, history of stroke, prior tumor-related characteristics (TNM stage, RT dose and techniques, and chemotherapy), and the time interval from RT to RN (HR 0.48, 95%CI 0.30 to 0.77; p = 0.0027), and extensive sensitivity analyses yielded similar results. There was no significant difference in the effect of early treatment on post-RN survival among subgroups stratified by presence or absence of neurological symptoms at diagnosis (p for interaction=0.41). INTERPRETATION: Among head and neck cancer survivors with RN, initiating treatment early after RN diagnosis is associated with a lower risk of all-cause mortality as compared with following the watch-and-wait policy, irrespective of whether patients exhibit symptoms or not. Further prospective randomised studies would be needed to validate our findings since the observational study design might lead to some potential confounding. In the absence of data from randomised trials, our study will have an important implication for clinicians regarding the optimal timing of treatment for RN, and provides the foundation and supporting data for future trials on this topic. FUNDING: National Natural Science Foundation of China (81925031, 81820108026, 81872549, 81801229, 82003389), the Science and Technology Program of Guangzhou (202007030001), Young Teacher Training Program of Sun Yat-sen University (20ykpy106), Key-Area Research and Development Program of Guangdong Province (2018B030340001), the National Medical Research Council Singapore Clinician Scientist Award (NMRC/CSA-INV/0027/2018, CSAINV20nov-0021), the Duke-NUS Oncology Academic Program Goh Foundation Proton Research Programme, NCCS Cancer Fund, the Kua Hong Pak Head and Neck Cancer Research Programme, and the National Research Foundation Clinical Research Programme Grant (NRF-CRP17-2017-05).

Pan, K., et al. (2021). "Low-fat dietary pattern and breast cancer mortality by metabolic syndrome components: a secondary analysis of the Women's Health Initiative (WHI) randomised trial." Br J Cancer **125**(3): 372-379.

BACKGROUND: In the Women's Health Initiative (WHI) dietary modification (DM) randomised trial, the low-fat dietary intervention reduced deaths from breast cancer (P = 0.02). Extending these findings, secondary analysis examined dietary intervention influence on breast cancer mortality by metabolic syndrome (MS) components. METHODS: In total, 48,835 postmenopausal women with no prior breast cancer were randomised to a low-fat dietary intervention or comparison groups. Four MS

components were determined at entry in 45,833 participants: (1) high waist circumference, (2) high blood pressure, (3) high cholesterol and (4) diabetes history. Forest plots of hazard ratios (HRs) were generated with P-values for interaction between randomisation groups and MS component score. Primary outcome was death from breast cancer by metabolic syndrome score. RESULTS: HRs and 95% confidence intervals (CI) for dietary intervention influence on death from breast cancer were with no MS components (n = 10,639), HR 1.09, 95% CI 0.63-1.87; with 1-2 MS components (n = 30,948), HR 0.80, 95% CI 0.62-1.02; with 3-4 MS components (n = 4,246), HR 0.31, 95% CI 0.14-0.69 (interaction P = 0.01). CONCLUSIONS: While postmenopausal women with 3-4 MS components were at higher risk of death from breast cancer, those randomised to a low-fat dietary intervention more likely had reduction in this risk. REGISTRY: ClinicalTrials.gov (NCT00000611).

Pan, K., et al. (2020). "Protein Intake by Source and Breast Cancer Incidence and Mortality: The Women's Health Initiative." JNCI Cancer Spectr **4**(6): pkaa101.

BACKGROUND: Prior studies of dietary protein intake and breast cancer have been mixed and were limited by dietary self-report measurement error. METHODS: Biomarker-calibrated total protein intake and estimated vegetable protein and animal protein intake were determined from baseline food frequency questionnaires in 100 024 Women's Health Initiative participants. Associations between total, animal, and vegetable protein intake and breast cancer incidence, deaths from breast cancer, and deaths after breast cancer were estimated using Cox proportional hazards regression. Breast cancers were verified by medical record review and survival outcomes enhanced by National Death Index queries. All statistical tests were 2-sided. RESULTS: After 14 years of follow-up, there were 6340 incident breast cancers, 764 deaths from breast cancer, and 2059 deaths after breast cancer. In multivariable analyses, higher calibrated total protein intake was not associated with breast cancer incidence or deaths from or after breast cancer. Vegetable protein intake was associated with statistically significantly lower breast cancer incidence (hazard ratio [HR] = 0.98, 95% confidence interval [CI] = 0.96 to 0.99, P (trend) = .006) and statistically significantly lower risk of death after breast cancer (HR = 0.93, 95% CI = 0.91 to 0.97, P (trend) < .001) but not with deaths from breast cancer. In contrast, higher animal protein intake was associated with statistically significantly higher breast cancer incidence (HR = 1.03, 95% CI = 1.01 to 1.06, P (trend) = .02) but not with deaths from or after breast cancer. CONCLUSIONS: Calibrated total protein intake was not associated with breast cancer incidence or mortality. Higher vegetable protein intake was associated with lower breast cancer incidence and lower risk of death after breast cancer. Higher animal protein intake was associated with higher breast cancer incidence.

Panin, S. I., et al. (2022). "[Perforated peptic ulcer in patients with cancer: prediction of postoperative morbidity and mortality]." Khirurgiia (Mosk)(7): 12-18.

OBJECTIVE: To analyze treatment outcomes and approaches to predicting the postoperative morbidity and mortality in patients with perforated ulcers and cancer. MATERIAL AND METHODS: A non-randomized trial included 194 patients. The first group enrolled 45 (23%) patients with perforated ulcers and concomitant cancer who underwent at the oncology center; the second group included 149 (77%) patients with perforated ulcers and no cancer who underwent surgery in general surgical hospitals. Organ-sparing procedures prevailed (40 (88.9%) and 138 (92.6%) cases, respectively). Resections were performed in 5 (11.1%) and 11 (7.4%) patients respectively. Analyzing the factors affecting treatment outcomes, we studied crude (COR) and adjusted (AOR) odds ratios. ROC-analysis was used to assess diagnostic significance of the models for prognosis of morbidity and mortality. RESULTS: Length of hospital-stay was 10 (range 9-14) and 8 (range 7-9) days respectively. Postoperative complications (Clavien-Dindo grading system) occurred in 18 (40%) in 37 (24.8%) patients, respectively. According to multivariate analysis, predictors of complications in patients of the first group were treatment with NSAIDs/glucocorticoids and Charlson-Deyo index >3. Sensitivity of this model was 82.4%, specificity - 75.0%. Postoperative mortality was 15.6% (n=7) and 7.4% (n=11) respectively. According to multivariate analysis, predictors of mortality were age over 65 years and more than 5 chemotherapeutic courses. Sensitivity of the model was 85.7%, specificity - 97.4%. CONCLUSION: The stratified approach makes it possible to improve prediction of postoperative morbidity and mortality in patients with perforated ulcers.

Panunzio, A., et al. (2022). "Effect of positive surgical margins at radical prostatectomy on cancer-specific mortality in high/very high-risk prostate cancer patients with Gleason Grade Group 4-5." Prostate.

BACKGROUND: The effect of positive surgical margins (PSM) on cancer specific mortality (CSM) in high/very high-risk (HR/VHR) prostate cancer (PCa) with aggressive Gleason Grade Group (GGG) is unknown. We tested PSM effect on CSM in this setting, in addition to testing of radiotherapy (RT) benefit in PSM patients. METHODS: We relied on

Surveillance, Epidemiology, and End Results database (2010-2015), focusing on HR/VHR patients with exclusive GGG 4-5 at radical prostatectomy (RP). Kaplan-Meier plots and multivariable Cox regression models tested the relationship between PSM and CSM. Moreover, the effect of RT on CSM was explored in PSM patients. RESULTS: Of 3383 HR/VHR patients, 15.1% (n = 511) exhibited PSM. Patients with PSM harbored higher rates of GGG 5 (60.1% vs. 50.9%, p < 0.001), pathologic tumor stage T3a (69.1% vs. 45.2%, p < 0.001) and lymph node involvement (14.1% vs. 9.4%, p < 0.001), relative to patients without PSM. PSM rates decreased over time (2010-2015) from 16.0% to 13.6%. Seven-year CSM-free survival rates were 91.6% versus 95.7% in patients with and without PSM, respectively. In multivariable Cox regression models, PSM was an independent predictor of CSM (hazard ratio = 1.6, p = 0.040) even after adjustment for age, prostate specific antigen, pathologic tumor stage and lymph node status. Finally, in PSM patients, RT delivery did not reduce CSM in either univariable or multivariable Cox regression models. CONCLUSIONS: In HR/VHR PCa patients with exclusive GGG 4-5, PSM at RP adversely affect survival. Moreover, RT has no protective effect on CSM. In consequence, lowest possible PSM rates are crucial in such patients.

Panunzio, A., et al. (2022). "Cancer specific mortality in patients with collecting duct vs. clear cell renal carcinoma." Cancer Epidemiol **82**: 102297.

BACKGROUND: Collecting duct carcinoma (CDC) is biologically more aggressive than clear cell renal cell carcinoma (ccRCC). We tested for differences in cancer specific mortality (CSM) rates according to CDC vs. ISUP (International Society of Urological Pathology) 4 ccRCC histological subtype. We hypothesized that the survival disadvantage still applies, even after most detailed adjustments. METHODS: Within Surveillance, Epidemiology, and End Results database (2004-2018), we identified 380 CDC vs. 6273 ISUP 4 ccRCC patients of all stages. Propensity score matching (age, sex, race/ethnicity, T, N, and M stages, nephrectomy, and systemic therapy status), Kaplan-Meier plots and multivariable Cox regression models were used. RESULTS: All 380 CDC were matched (1:2) with 760 ISUP4 ccRCC patients. Prior to matching CDC patients exhibited higher rates of lymph node invasion (37.6 % vs. 14.7 %, p < 0.001), and of distant metastases (40.8 % vs. 30.4 %, p < 0.001). Systemic therapy rates were higher in CDC (29.5 % vs. 20.5 %, p < 0.001). However, nephrectomy rates were higher in ISUP4 ccRCC patients (97.5 % vs. 84.7 %, p < 0.001). After matching, in multivariable Cox regression models addressing CSM, CDC was associated with a HR of 1.5 (p < 0.001) in the overall population vs. 1.9 (p = 0.014) in stage I-II vs. 1.4 (p = 0.022) in stage III vs. 1.6 in stage IV (p < 0.001), relative to ISUP4 ccRCC. CONCLUSION: CDC patients exhibited 40-90 % higher CSM than their ISUP4 ccRCC counterparts in the overall analysis, as well as in stage specific analyses. The CSM disadvantage applies despite higher rates of systemic therapy in CDC patients.

Pathirana, T., et al. (2022). "Trends in Prostate Specific Antigen (PSA) testing and prostate cancer incidence and mortality in Australia: A critical analysis." Cancer Epidemiol **77**: 102093.

BACKGROUND: Population trends in PSA testing and prostate cancer incidence do not perfectly correspond. We aimed to better understand relationships between trends in PSA testing, prostate cancer incidence and mortality in Australia and factors that influence them. METHODS: We calculated and described standardised time trends in PSA tests, prostate biopsies, treatment of benign prostatic hypertrophy (BPH) and prostate cancer incidence and mortality in Australia in men aged 45-74, 75-84, and 85 + years. RESULTS: PSA testing increased from its introduction in 1989 to a peak in 2008 before declining in men aged 45-84 years. Prostate biopsies and cancer incidence fell from 1995 to 2000 in parallel with decrease in trans-urethral resections of the prostate (TURP) and, latterly, changes in pharmaceutical management of BPH. After 2000, changes in biopsies and incidence paralleled changes in PSA screening in men 45-84 years, while in men >/=85 years biopsy rates stabilised, and incidence fell. Prostate cancer mortality in men aged 45-74 years remained low throughout. Mortality in men 75-84 years gradually increased until mid 1990s, then gradually decreased. Mortality in men >/= 85 years increased until mid 1990s, then stabilised. CONCLUSION: Age specific prostate cancer incidence largely mirrors PSA testing rates. Most deviation from this pattern may be explained by less use of TURP in management of BPH and consequent less incidental cancer detection in TURP tissue specimens. Mortality from prostate cancer initially rose and then fell below what it was when PSA testing began. Its initial rise and fall may be explained by a possible initial tendency to over-attribute deaths of uncertain cause in older men with a diagnosis of prostate cancer to prostate cancer. Decreases in mortality rates were many fold smaller than the increases in incidence, suggesting substantial overdiagnosis of prostate cancer after introduction of PSA testing.

Patti, M. G. and F. A. Herbella (2021). "Predicting Mortality Rates After Esophagectomy for Cancer." JAMA Surg **156**(9): 845-846.

Paulozzi, L. J., et al. (2021). "A Disparity beneath a Paradox: Cancer Mortality among Young Hispanic Americans in the US-Mexico Border Region." J Racial Ethn Health Disparities **8**(6): 1556-1562.

The age-adjusted mortality rate for cancer in the US Hispanic population is two thirds that of the non-Hispanic white population, probably because of differences in smoking rates. We aimed to determine whether Hispanic white (HW) cancer mortality in the US-Mexico Border Region was also lower than that of the non-Hispanic white (NHW) border population, particularly in the younger population less likely to develop smoking-related cancer. We obtained age-adjusted cancer mortality rates from 1999 to 2017 for the 44 border counties, the four US-Mexico border states, and the rest of the US. We obtained cancer incidence rates for 1999-2016 from state registries. We stratified rates by age group, ethnicity, border state, urbanization, and cancer site. Age-adjusted border cancer mortality rates were 139.1/100,000 in the HW and 171.4 in the NHW populations, a ratio of 0.8. HW mortality rates were higher than NHW rates only for the 0-34 age group. State-specific HW cancer incidence rates for people 0-34 years old were 77%-80% of NHW rates. We also calculated mortality-incidence ratios (MIR) for the 0-34 population. Border mortality-incidence ratios were higher in the HW population. HW rates exceeded NHW rates for all cancer sites except skin cancer. The HW cancer disparity is due to poorer survival in the HW population, which might be due to limited access to prevention and treatment in a medically underserved area. Mortality among young border Hispanic residents might be reduced through efforts to improve insurance coverage and increase access to medical providers .

Pedersen, R. N., et al. (2022). "Mortality After Late Breast Cancer Recurrence in Denmark." J Clin Oncol **40**(13): 1450-1463.

PURPOSE: Late breast cancer (BC) recurrence (ie, >/= 10 years after primary diagnosis) may have a more favorable prognosis than earlier recurrence. We investigated the risk of BC death after late recurrence, identified prognostic factors, and compared survival after early and late recurrence. METHODS: Using the Danish Breast Cancer Group and other nationwide databases, we identified women with early or late BC recurrence during 2004-2018, who were alive 6 months after recurrence. We followed them until BC death, death from other causes, emigration, 10 years, or December 31, 2018, whichever came first. We calculated mortality rates (MRs) per 1,000 person-years (PY) and cumulative BC mortality, for early versus late recurrence, and by characteristics of the primary tumor and the late recurrence. Using Cox regression, we calculated adjusted hazard ratios (HRs) for BC death, accounting for death from other causes as competing risks. RESULTS: Among 2,004 patients with late recurrence, 721 died of BC with a median survival time of 10 years (MR = 84.8 per 1,000 PY; 10-year cumulative mortality = 50%). Among 1,528 patients with early recurrence, 1,092 BC deaths occurred with a median survival time of 4 years (MR = 173.9 per 1,000 PY; 10-year cumulative mortality = 72%). We observed a lower hazard of BC-specific death among patients who developed late compared with early recurrence (hazard ratio = 0.72; 95% CI, 0.62 to 0.85). Advanced stage at primary diagnosis, distant metastases, adjuvant treatment for locoregional recurrence, and systemic treatment for distant recurrence were associated with increased mortality after late recurrence. Breast-conserving surgery at primary diagnosis, locoregional recurrence, and surgery for recurrence were associated with lower mortality after late recurrence. CONCLUSION: Patients with late recurrence had more favorable prognosis than patients with early recurrence. The localization of recurrent disease was the main prognostic factor for BC death.

Pedrazzoli, S. (2022). "Surgical treatment of pancreatic cancer: Currently debated topics on morbidity, mortality, and lymphadenectomy." Surg Oncol **45**: 101858.

This review will examine several aspects of pancreatic surgery. Over the past twenty years, the need for a standardized postoperative complication report after resective pancreatic surgery has led to the definition both of a postoperative complication severity score, a postoperative pancreatic fistula (POPF) severity grading, a fistula risk score (FRS) and a postoperative morbidity index to establish the burden of complications. Unfortunately, three problems have hindered the success of standardization: first, the failure to define a minimum postoperative follow-up period that needs to be reported; second, the lack of a clear definition of POPF-related morbidity and mortality; third, the often-incomplete reporting of postoperative complications. The debate on the extent of lymphadenectomy to associate to pancreaticoduodenectomy started in the late 1980s when, based on retrospective studies, Japanese surgeons reported better survival after extended" than after "standard" lymphadenectomy. Subsequently, eight prospective randomized controlled trials showed that "extended" lymphadenectomy offers no advantage over "standard" lymphadenectomy. Several consensus conference and reviews tried to define the optimal extent of lymphadenectomy to be associated to pancreaticoduodenectomy and distal pancreatectomy (DP). At least nineteen lymph nodes (LN) are required

for optimal tumor staging, but eleven LN are considered the minimum to prevent under staging. There is no general agreement about aborting PD in LN16-positive patients; some authors perform PD in fit patients. Based on retrospective studies, a significant increase of R0 resections, a decrease of recurrence rate, a decrease of local recurrence rate and an increase of median or overall disease-free survival were reported after mesopancreas excision.

Pei, J., et al. (2022). "Worldwide trends in cervical cancer incidence and mortality." Cancer **128**(5): 1141.

Peltomaa, A. I., et al. (2022). "Inverse Association between Statin Use and Cancer Mortality Relates to Cholesterol Level." Cancers (Basel) **14**(12).

Statins have been associated with a decreased cancer mortality. However, cholesterol level as such may modify the risk of cancer death. To clarify the complex interplay between statins, cholesterol level, and cancer mortality, we conducted a comprehensive analysis to separate the effects of cholesterol level and statin medication on cancer mortality. Our study population consisted of 16,924 men participating in the Finnish Randomized Study of Screening for Prostate Cancer with at least one cholesterol measurement during follow-up (1996-2017). Cox proportional regression was used to estimate hazard ratios. In total, 1699 cancer deaths were observed during the median follow-up of 19 years. When statins' association with the risk of cancer death was estimated without adjustment for cholesterol level, statin use was associated with a lowered cancer mortality (HR 0.87; 95% CI 0.79-0.97) compared to non-users. However, with further adjustment for total cholesterol level, statin use was no longer associated with a lower cancer mortality (HR 1.08; 95% CI 0.97-1.20). Upon stratified analysis, statin use was associated with a decreased cancer mortality only if the total cholesterol level decreased after the initiation of statin use (HR 0.66; 95% CI 0.58-0.76). The inverse association between statin use and cancer mortality is limited to men with a reduction in total cholesterol level after the commencement of statins, i.e., statin use is associated with a lowered cancer mortality only if the total cholesterol level decreases. This suggests that the effect of statin use on cancer mortality relates to the decreased total cholesterol level.

Peng, Q. and X. Ren (2021). "Mapping of Female Breast Cancer Incidence and Mortality Rates to Socioeconomic Factors Cohort: Path Diagram Analysis." Front Public Health **9**: 761023.

OBJECTIVES: Breast cancer is the leading cause of death in women around the world. Its occurrence and development have been linked to genetic factors, living habits, health conditions, and socioeconomic factors. Comparisons of incidence and mortality rates of female breast cancer are useful approaches to define cancer-related socioeconomic disparities. METHODS: This was a retrospective observational cohort study on breast cancer of women in several developed countries over 30 years. Effects of socioeconomic factors were analyzed using a path diagram method. RESULTS: We found a positive, significant association of public wealth on incidence and mortality of breast cancer, and the path coefficients in the structural equations are -0.51 and -0.39, respectively. The unemployment rate (UR) is critical and the path coefficients are all 0.2. The path coefficients of individual economic wealth to the rates of breast cancer are 0.18 and 0.27, respectively. CONCLUSION: The influence of social pressure on the incidence and mortality of breast cancer was not typical monotonous. The survival rate of breast cancer determined by the ratio of mortality rate to incidence rate showed a similar pattern with socioeconomic factors.

Pera, M., et al. (2022). "Machine Learning Risk Prediction Model of 90-day Mortality After Gastrectomy for Cancer." Ann Surg **276**(5): 776-783.

OBJECTIVE: To develop and validate a risk prediction model of 90-day mortality (90DM) using machine learning in a large multicenter cohort of patients undergoing gastric cancer resection with curative intent. BACKGROUND: The 90DM rate after gastrectomy for cancer is a quality of care indicator in surgical oncology. There is a lack of well-validated instruments for personalized prognosis of gastric cancer. METHODS: Consecutive patients with gastric adenocarcinoma who underwent potentially curative gastrectomy between 2014 and 2021 registered in the Spanish EURECCA Esophagogastric Cancer Registry database were included. The 90DM for all causes was the study outcome. Preoperative clinical characteristics were tested in four 90DM predictive models: Cross Validated Elastic regularized logistic regression method (cv-Enet), boosting linear regression (glmboost), random forest, and an ensemble model. Performance was evaluated using the area under the curve by 10-fold cross-validation. RESULTS: A total of 3182 and 260 patients from 39 institutions in 6 regions were included in the development and validation cohorts, respectively. The 90DM rate was 5.6% and 6.2%, respectively. The random forest model showed the best discrimination capacity with a validated area under the curve of 0.844 [95% confidence interval (CI): 0.841-0.848] as compared with cv-Enet (0.796, 95% CI: 0.784-0.808), glmboost (0.797, 95% CI: 0.785-0.809), and ensemble model (0.847, 95% CI: 0.836-0.858) in the development

cohort. Similar discriminative capacity was observed in the validation cohort. CONCLUSIONS: A robust clinical model for predicting the risk of 90DM after surgery of gastric cancer was developed. Its use may aid patients and surgeons in making informed decisions.

Perea, L. M. E., et al. (2021). "Mortality from oral and oropharyngeal cancer: age-period-cohort effect, Brazil, 1983-2017." Rev Saude Publica **55**: 72.

OBJECTIVE: Estimate the effect of age, period, and birth cohort on mortality from oral and oropharyngeal cancer in Brazil and its macro-regions. METHODS: Deaths from oral and oropharyngeal cancer from 1983 to 2017 were analyzed. The Poisson regression model was applied, using estimable functions proposed by Holford. RESULTS: From 1983 to 2017, 142,634 deaths from oral and oropharyngeal cancer were registered in Brazil, 81% among men, and the South and Southeast regions had the highest rates. The most significant period effects were observed in male mortality in the Southeast and Central-West regions for the 2003-2007 reference period. In the North, Northeast, and Central-West regions, an increased risk of mortality was observed in the most recent male cohorts. In the North region, the most significant risk identified was for men born during 1973-1977 (RR = 1.47; 95%CI 1.05-2.08); in the Northeast, for men born during 1988-1992 (RR = 2.77; 95%CI 1.66-4.63); and in the Central-West, for women born during 1973-1977 (RR = 2.01; 95%CI 1.19-3.39). In the Southeast and South regions, the most recent cohorts had lower mortality rates. The lowest risk in the Southeast region was observed in the male cohort born during 1978-1982 (RR = 0.53; 95%CI 0.45-0.62) and 1983-1987 in the South region (RR = 0.25; 95%CI 0.12-0.54). CONCLUSIONS: Age had a significant effect on mortality from oral and oropharyngeal cancer in all regions. In the North, Northeast, and Central-West regions, an increase in risk was observed in the most recent cohorts, while in the South and Southeast regions, these cohorts presented a lower risk when compared to the older cohorts.

Perea, L. M. E., et al. (2022). "Approaches to the problem of nonidentifiability in the age-period-cohort models in the analysis of cancer mortality: a scoping review." Eur J Cancer Prev **31**(1): 93-103.

Aiming to detect age, period and cohort effects in cancer mortality, age-period-cohort models (APC) can be applied to distinguish these effects. The main difficulty with adjusting an APC model involving age, period and cohort factors is the linear relationship between them, leading to a condition known as the 'nonidentifiability problem'. Many methods have been developed by statisticians to solve it, but there is not a consensus. All these existing methods, with their advantages and disadvantages, create confusion when choosing which one of them should be implemented. In this context, the present scoping review intends not to show all methods developed to avoid the nonidentifiability problem on APC models but to show which of them are, in fact, applied in the literature, especially in the cancer mortality studies. A search strategy was made to identify evidence on MEDLINE (PubMed), Scopus, EMBASE, Science Direct and Web of Science. A total of 46 papers were analyzed. The main methods found were: Holford's method (n = 14; 30%), ntrinsic estimator (n = 10; 22%), Osmond & Gardner method n = 8; 17%), Carstensen (n = 6;13%), Bayesian approach (n = 6;13%) and others (n = 2; 5%). Even with their limitations, all methods have beneficial applications. However, the decision to use one or another method seemed to be more related to an observed geographic pattern.

Perea, L. M. E., et al. (2022). "Oral and oropharyngeal cancer mortality in Brazil, 1983-2017: Age-period-cohort analysis." Oral Dis **28**(1): 97-107.

AIM: To estimate the effect of age, period, and birth cohort on mortality from oral and oropharyngeal cancer in Brazil. METHODS: Deaths due to oral and oropharyngeal cancer from 1983 to 2017 were analyzed. The effect of age, period, and cohort was calculated using the Poisson regression model. RESULTS: Between 1983 and 2017, 142,634 deaths were recorded from oral and oropharyngeal cancer in Brazil, 54% from oropharyngeal cancer. The male sex contributed to 81% of the deaths. The average mortality rate for men was 4.5 deaths per 100,000 inhabitants, and for women, it was 0.9 deaths per 100,000 inhabitants. There was a strong effect of age on mortality rates from oral and oropharyngeal cancer. The risk increases from 40 years of age in men and 55 years of age in women. An overall period effect was observed. The 2000 period showed the greatest risk when compared to the 1985 period in men. In women, the period of highest risk was 2010. The cohorts born between 1958 and 1962 had a higher risk of death. CONCLUSIONS: The period effect is mainly attributed to mortality from oropharyngeal cancer. Most significant values regarding the effect on the cohort groups were observed in female mortality from oral cancer.

Perez-Cornago, A., et al. (2020). "Examination of potential novel biochemical factors in relation to prostate cancer incidence and mortality in UK Biobank." Br J Cancer **123**(12): 1808-1817.

BACKGROUND: Although prostate cancer is a leading cause of cancer death, its aetiology is not well understood. We aimed to identify novel biochemical

factors for prostate cancer incidence and mortality in UK Biobank. METHODS: A range of cardiovascular, bone, joint, diabetes, renal and liver-related biomarkers were measured in baseline blood samples collected from up to 211,754 men at recruitment and in a subsample 5 years later. Participants were followed-up via linkage to health administrative datasets to identify prostate cancer cases. Hazard ratios (HRs) and 95% confidence intervals were calculated using multivariable-adjusted Cox regression corrected for regression dilution bias. Multiple testing was accounted for by using a false discovery rate controlling procedure. RESULTS: After an average follow-up of 6.9 years, 5763 prostate cancer cases and 331 prostate cancer deaths were ascertained. Prostate cancer incidence was positively associated with circulating vitamin D, urea and phosphate concentrations and inversely associated with glucose, total protein and aspartate aminotransferase. Phosphate and cystatin-C were the only biomarkers positively and inversely, respectively, associated with risk in analyses excluding the first 4 years of follow-up. There was little evidence of associations with prostate cancer death. CONCLUSION: We found novel associations of several biomarkers with prostate cancer incidence. Future research will examine associations by tumour characteristics.

Perez-de-Acha, A., et al. (2022). "All-Cause Mortality Risk Prediction in Older Adults with Cancer: Practical Approaches and Limitations." Curr Oncol Rep **24**(11): 1377-1385.

PURPOSE OF REVIEW: The prediction of all-cause mortality is an important component of shared decision-making across the cancer care continuum, particularly in older adults with limited life expectancy, for whom there is an increased risk of over-diagnosis and treatment. RECENT FINDINGS: Currently, several international societies recommend the use of all-cause mortality risk prediction tools when making decisions regarding screening and treatment in geriatric oncology. Here, we review some practical aspects of the utilization of those tools and dissect the characteristics of those most employed in geriatric oncology, highlighting both their advantages and their limitations.

Pes, G. M., et al. (2021). "Spatial Association between Gastric Cancer Mortality and Goiter in Sardinia." Asian Pac J Cancer Prev **22**(1): 105-110.

BACKGROUND: Gastric cancer (GC) is the third leading cause of cancer mortality worldwide. The incidence of GC varies between countries according to exposure to different risk factors. Hypothyroidism has been suggested as a potential GC risk factor. In Sardinia, Italy, the prevalence of endemic goiter is high and GC mortality is unevenly distributed. This ecological study aimed to investigate GC mortality and its relationship with hypothyroidism, adjusting for potential confounders. METHODS: The spatial association between GC mortality and goiter (a proxy of hypothyroidism), diet, stature and pastoralism (a proxy of Helicobacter pylori infection), available at the aggregated level, was modelled in the island's 377 municipalities, separately by sex, using geographically weighted regression (GWR). RESULTS: The GC standardized mortality ratio ranged from 0.0 to 10.4 across municipalities. A hotspot of GC mortality was detected in the central mountainous area of Sardinia among males, positively associated with goiter (GWR estimate 0.213 +/- 0.122), and the practice of sheep–rearing (GWR estimate 0.127 +/- 0.080), whereas a negative association with the diet score (GWR estimate 0.032 +/- 0.034), and null for stature were found. No significant associations were found in females. CONCLUSION: Within the limitations of ecological studies goiter prevalence was an independent predictor of GC mortality in males.

Petermann-Rocha, F., et al. (2021). "Nonlinear Associations Between Cumulative Dietary Risk Factors and Cardiovascular Diseases, Cancer, and All-Cause Mortality: A Prospective Cohort Study From UK Biobank." Mayo Clin Proc **96**(9): 2418-2431.

OBJECTIVE: To develop a score from cumulative dietary risk factors and examine its nonlinear associations with cardiovascular disease (CVD) and cancer incidence and mortality, as well as all-cause mortality. PATIENTS AND METHODS: There were 422,702 participants from UK Biobank included in this prospective study. Cumulative dietary risk factors were represented using a score ranging from 0 (healthiest) to 9 (least healthy). This was derived from 9 food items based on current UK guidelines using baseline data. Associations between the cumulative score and health outcomes were investigated using nonlinear penalized cubic splines fitted in Cox proportional hazard models. Follow-up was conducted until June 2020 for mortality, and for incidence, up to June 2020 in England and March 2017 in Wales and Scotland. RESULTS: The median follow-up period was 9.0 years for incidence outcomes and 9.3 years for mortality outcomes. Each 1-point increment in the cumulative dietary risk factors score was associated with higher risk for incidence and mortality of the outcomes studied. The highest risks were identified for mortality due to heart failure (8.0% higher), CVD, and ischemic heart disease (both 7.0% higher). In addition, a higher diet score accounted for 18.8% of all deaths, 4.47% of incident cases of CVD, 25.5% of CVD deaths, 7.7% of incident cancers, and 18.2% of all cancer deaths. CONCLUSION: Our

findings show that dietary risk factors contributed to a large proportion of CVD and cancer events, as well as deaths, among those who did not meet most dietary recommendations.

Pham, J., et al. (2021). "Excess mortality and undertreatment in elderly lung cancer patients: treatment nihilism in the modern era?" ERJ Open Res **7**(2).

Treatment of elderly patients with lung cancer is significantly hindered by concerns about treatment tolerability, toxicity and limited clinical trial data in the elderly; potentially giving rise to treatment nihilism amongst clinicians. This study aims to describe survival in elderly patients with lung cancer and explore potential causes for excess mortality. Patients diagnosed with lung cancer in the Victorian Lung Cancer Registry between 2011-2018 were analysed (n=3481). Patients were age-categorised and compared using Cox-regression modelling to determine mortality risk, after adjusting for confounding. Probability of being offered cancer treatments was also determined, further stratified by disease stage. The eldest patients (>/=80 years old) had significantly shorter median survival compared with younger age groups (<60 years: 2.0 years; 60-69 years: 1.5 years; 70-79 years: 1.6 years; >/=80 years: 1.0 years; p<0.001). Amongst those diagnosed with stage 1 or 2 lung cancer, there was no significant difference in adjusted-mortality between age groups. However, in those diagnosed with stage 3 or 4 disease, the eldest patients had an increased adjusted-mortality risk of 28% compared with patients younger than 60 years old (p=0.005), associated with markedly reduced probability of cancer treatment, after controlling for sex, performance status, comorbidities and histology type (OR 0.24, compared with <60 years old strata; p<0.001). Compared to younger patients, older patients with advanced-stage lung cancer have a disproportionately higher risk of mortality and lower likelihood of receiving cancer treatments, even when performance status and comorbidity are equivalent. These healthcare inequities could be indicative of widespread treatment nihilism towards elderly patients.

Pichardo, M. S., et al. (2022). "Adherence to the American Cancer Society Guidelines on nutrition and physical activity for cancer prevention and obesity-related cancer risk and mortality in Black and Latina Women's Health Initiative participants." Cancer **128**(20): 3630-3640.

BACKGROUND: Although adherence to the American Cancer Society (ACS) Guidelines on Nutrition and Physical Activity for Cancer Prevention associates with lower risk of obesity-related cancer (ORC) incidence and mortality, evidence in Black and Latina women is limited. This association was examined in Black and Latina participants in the Women's Health Initiative (WHI). METHODS: Semi-Markov multistate model examined the association between ACS guideline adherence and ORC incidence and mortality in the presence of competing events, combined and separately, for 9301 Black and 4221 Latina postmenopausal women. Additionally, ACS guideline adherence was examined in a subset of less common ORCs and potential effect modification by neighborhood socioeconomic status and smoking. RESULTS: Over a median of 11.1, 12.5, and 3.7 years of follow-up for incidence, nonconditional mortality, and conditional mortality, respectively, 1191 ORCs (Black/Latina women: 841/269), 1970 all-cause deaths (Black/Latina women: 1576/394), and 341 ORC-related deaths (Black/Latina women: 259/82) were observed. Higher ACS guideline adherence was associated with lower ORC incidence for both Black (cause-specific hazard ratio [CSHR](highvs.low) : 0.72; 95% CI, 0.55-0.94) and Latina (CSHR(highvs.low) : 0.58, 95% CI, 0.36-0.93) women; but not conditional all-cause mortality (Black hazard ratio [HR](highvs.low) : 0.86; 95% CI, 0.53-1.39; Latina HR(highvs.low) : 0.81; 95% CI, 0.32-2.06). Higher adherence was associated with lower incidence of less common ORC (P(trend) = .025), but conditional mortality events were limited. Adherence and ORC-specific deaths were not associated and there was no evidence of effect modification. CONCLUSIONS: Adherence to the ACS guidelines was associated with lower risk of ORCs and less common ORCs but was not for conditional ORC-related mortality. LAY SUMMARY: Evidence on the association between the American Cancer Society Guidelines on Nutrition and Physical Activity for Cancer Prevention and cancer remains scarce for women of color. Adherence to the guidelines and risk of developing one of 13 obesity-related cancers among Black and Latina women in the Women's Health Initiative was examined. Women who followed the lifestyle guidelines had 28% to 42% lower risk of obesity-related cancer. These findings support public health interventions to reduce growing racial/ethnic disparities in obesity-related cancers.

Pidsley, R., et al. (2022). "Comprehensive methylome sequencing reveals prognostic epigenetic biomarkers for prostate cancer mortality." Clin Transl Med **12**(10): e1030.

BACKGROUND: Prostate cancer is a clinically heterogeneous disease with a subset of patients rapidly progressing to lethal-metastatic prostate cancer. Current clinicopathological measures are imperfect predictors of disease progression. Epigenetic changes are amongst the earliest molecular changes in tumourigenesis. To find new prognostic

biomarkers to enable earlier intervention and improved outcomes, we performed methylome sequencing of DNA from patients with localised prostate cancer and long-term clinical follow-up. METHODS: We used whole-genome bisulphite sequencing (WGBS) to comprehensively map and compare DNA methylation of radical prostatectomy tissue between patients with lethal disease (n = 7) and non-lethal (n = 8) disease (median follow-up 19.5 years). Validation of differentially methylated regions (DMRs) was performed in an independent cohort (n = 185, median follow-up 15 years) using targeted multiplex bisulphite sequencing of candidate regions. Survival was assessed via univariable and multivariable analyses including clinicopathological measures (log-rank and Cox regression models). RESULTS: WGBS data analysis identified cancer-specific methylation patterns including CpG island hypermethylation, and hypomethylation of repetitive elements, with increasing disease risk. We identified 1420 DMRs associated with prostate cancer-specific mortality (PCSM), which showed enrichment for gene sets downregulated in prostate cancer and de novo methylated in cancer. Through comparison with public prostate cancer datasets, we refined the DMRs to develop an 18-gene prognostic panel. Applying this panel to an independent cohort, we found significant associations between PCSM and hypermethylation at EPHB3, PARP6, TBX1, MARCH6 and a regulatory element within CACNA2D4. Strikingly in a multivariable model, inclusion of CACNA2D4 methylation was a better predictor of PCSM versus grade alone (Harrell's C-index: 0.779 vs. 0.684). CONCLUSIONS: Our study provides detailed methylome maps of non-lethal and lethal prostate cancer and identifies novel genic regions that distinguish these patient groups. Inclusion of our DNA methylation biomarkers with existing clinicopathological measures improves prognostic models of prostate cancer mortality, and holds promise for clinical application.

Pierre-Victor, D., et al. (2021). "Prostate Cancer Incidence and Mortality Following a Negative Biopsy in a Population Undergoing PSA Screening." Urology **155**: 62-69.

OBJECTIVE: Transrectal ultrasound guided biopsy for diagnostic workup for prostate cancer (PCa) has a substantial false negative rate. We sought to estimate PCa incidence and mortality following negative biopsy in a cohort of men undergoing prostate cancer screening. SUBJECTS AND METHODS: The Prostate, Lung, Colorectal and Ovarian (PLCO) cancer screening trial randomized participants 55-74 years to an intervention vs control arm. Intervention arm men received annual prostate-specific antigen (PSA) tests for 6 years and digital rectal exams (DRE) for 4 years. We examined the cohort of men with a positive PSA (> 4 ng/mL) or DRE screen followed within one year by a negative biopsy. PCa incidence and mortality rates from time of first negative biopsy were analyzed as a function of PSA level at diagnosis and other factors. Cumulative incidence and mortality rates accounting for competing risk were estimated. Multivariate proportional hazards regression was utilized to estimate hazard ratios (HRs) of PCa outcomes by PSA level, controlling for age and race. RESULTS: The negative biopsy cohort included 2855 men. Median (25th/75th) age at biopsy was 65 (61/69) years; biopsies occurred between 1994 and 2006. Median (25/75th) follow-up was 13.2 (6.5/16.8) years for incidence and 16.6 (12.3/19.2) years for mortality. 740 PCa cases were diagnosed, with 33 PCa deaths. Overall 20-year cumulative PCa incidence and mortality rates were 26.4% (95% CI: 24.8-28.1) and 1.2% (95% CI: 0.9-1.7), respectively. HRs for PCa incidence and mortality increased significantly with increasing PSA. CONCLUSION: The mortality rate from PCa through 20 years following a negative biopsy is low.

Pierre-Victor, D., et al. (2021). "Other and All-Cause Mortality among Men Diagnosed with Prostate Cancer in the PLCO Trial." J Urol **205**(5): 1372-1378.

PURPOSE: Men with prostate cancer have high cause-specific survival, and most deaths are from other causes. This study aimed to investigate other and all-cause mortality in a large cancer screening cohort. MATERIALS AND METHODS: From the PLCO (Prostate, Lung, Colorectal and Ovarian) Cancer Screening Trial cohort, we selected men diagnosed with prostate cancer from 1994-2014. We examined other and all-cause survival by prostate cancer risk level, defined as the D'Amico categories for localized disease (low, intermediate and high risk) plus nonlocalized disease. We developed 3 Cox proportional hazards models to assess the relationship between risk level and survival. Model I controlled for age, race, study arm and diagnosis year. Model II additionally controlled for other demographic and medical history factors. Model III additionally controlled for initial treatment. RESULTS: Of 76,672 men in PLCO and 10,859 prostate cancer cases, 9,248 (85.2%) had known prostate cancer risk level (mean+/-SD age 70.4+/-6.2 years). Median followup time from diagnosis was 10.8 years (IQR 6.8-15.0). Of 3,318 deaths 81% were from other causes. Compared to the low risk group, other-cause mortality HRs were 1.13 (95% CI 1.04-1.23), 1.35 (95% CI 1.21-1.50) and 1.63 (95% CI 1.35-1.97) for intermediate risk, high risk and advanced disease, respectively, in model II. Model III HRs were similar to model II except for advanced disease, where the HR decreased to 1.35. CONCLUSIONS: Other-cause survival was greater in

lower vs higher risk disease, even after controlling for lifestyle characteristics and comorbidities. Further research is needed to identify factors contributing to this higher other-cause mortality to help mitigate the risk.

Pinato, D. J., et al. (2022). "Vaccination against SARS-CoV-2 protects from morbidity, mortality and sequelae from COVID19 in patients with cancer." Eur J Cancer **171**: 64-74.

BACKGROUND: Although SARS-CoV-2 vaccines immunogenicity in patients with cancer has been investigated, whether they can significantly improve the severity of COVID-19 in this specific population is undefined. METHODS: Capitalizing on OnCovid (NCT04393974) registry data we reported COVID-19 mortality and proxies of COVID-19 morbidity, including post-COVID-19 outcomes, according to the vaccination status of the included patients. RESULTS: 2090 eligible patients diagnosed with COVID-19 between 02/2020 and 11/2021 were included, of whom 1930 (92.3%) unvaccinated, 91 (4.4%) fully vaccinated and 69 (3.3%) partially vaccinated. With the exception of a higher prevalence of patients from the UK (p = 0.0003) and receiving systemic anticancer therapy at COVID-19 diagnosis (p = 0.0082) among fully vaccinated patients, no demographics/oncological features were associated with vaccination status. The 14-days case fatality rate (CFR) (5.5% vs 20.7%, p = 0.0004) and the 28-days CFR (13.2% vs 27.4%, p = 0.0028) demonstrated a significant improvement for fully vaccinated patients in comparison with unvaccinated patients. The receipt of prior full vaccination was also associated with reduced symptomatic COVID-19 (79.1% vs 88.5%, p = 0.0070), need of COVID-19 oriented therapy (34.9% vs 63.2%, p < 0.0001), complications from COVID-19 (28.6% vs 39.4%, p = 0.0379), hospitalizations due to COVID-19 (42.2% vs 52.5%, p = 0.0007) and oxygen therapy requirement (35.7% vs 52%, p = 0.0036). Following Inverse Probability Treatment Weighting (IPTW) procedure no statistically significant difference according to the vaccination status was confirmed; however, all COVID-19 related outcomes were concordantly in favour of full vaccination. Among the 1228 (58.8%) patients who underwent a formal reassessment at participating centres after COVID-19 resolution, fully vaccinated patients experienced less sequelae than unvaccinated patients (6.7% vs 17.2%, p = 0.0320). CONCLUSIONS: This analysis provides initial evidence in support of the beneficial effect of SARS-CoV-2 vaccines against morbidity and mortality from COVID-19 in patients with cancer.

Pinchas-Mizrachi, R., et al. (2022). "Disparities in Breast Cancer Mortality Rates in Israel among Urban and Rural Women." Int J Environ Res Public Health **19**(23).

Breast cancer is a leading cause of death. There are a number of risk factors for breast cancer mortality including parity, age, ethnicity, genetic history, and place of residence. This study examined the disparities in breast cancer-related mortality rates among women from urban areas compared to rural areas in Israel. This was a retrospective, follow-up study on mortality from breast cancer among 894,608 Israeli women born between the years of 1940 and 1960. Data was collected from the Israeli Central Bureau of Statistics, the Population Authority, the Education Ministry, and the Health Ministry. Over 80% of women lived in urban areas. A higher incidence of mortality from breast cancer in Israel was found among urban women compared to rural women (1047.8/100,000 compared to 837/100,000, respectively). Even after adjusting for sociodemographic variables, higher mortality rates were found among women from urban areas in Israel compared to women from rural areas in Israel. It is believed that environmental factors can partially explain the geographic variation of breast cancer incidence, and that breast cancer incidence is likely a complex interaction between genetic, environmental, and health factors.

Pinchas-Mizrachi, R., et al. (2021). "Predictors of respiratory cancer-related mortality for Jews and Arabs in Israel." SSM Popul Health **14**: 100783.

BACKGROUND: Respiratory cancers, including lung, tracheal and bronchus cancers, are a leading cause of cancer-related mortality in Israel; however, incidence can differ among demographic groups. Despite the importance of sociodemographic characteristics and the interactions between them to incidence and mortality, this topic is understudied. This study analyzes sociodemographic disparities by sex and ethnicity among Jews and Arabs to understand cancer outcome differences stratified by SES, marital status, and number of children as potential contextual factors. METHODS: This retrospective cohort study analyzed respiratory cancer-related mortality rates among Israelis born between 1940 and 1960 over 21-years. The follow up period was between January 1, 1996 and 12.31.2016. Mortality rates for Jews and Arabs were calculated. Using a Cox Regression, a multivariate model was constructed to determine the association between ethnicity and respiratory cancer mortality. The study population was then divided into four groups, by sex and ethnicity, to determine the association between marital status, number of children, and SES with respiratory cancer mortality for each subgroup. RESULTS: The overall mortality rate was 0.6%. Arabs had higher mortality rates compared to Jews, even after

adjusting for demographic factors including age, sex and SES (Adjusted Hazard Ratio (AHR) = 1.442, 99% confidence intervals (CI) = 1.354,1.546). Among men, a higher mortality rate was found among Arabs (AHR = 1.383, 99%CI = 1.295,1.477), while among women, Arabs had lower mortality rates (AHR = 0.469, 99%CI = 0.398,0.552). Significant mortality rate differences were observed by ethnicity and sex for each sociodemographic variable. CONCLUSIONS: This study highlights the importance and implications of understanding differences in respiratory cancer mortality between Jews and Arabs, a minority group in Israel, and is relevant for minority groups in general. There is a need to tailor interventions for these groups, based on differing underlying causes and contextual factors for these cancers. Cancer outcomes among these groups should also be studied separately, by sex, to better understand them.

Pinheiro, L. C., et al. (2022). "Social determinants of health and cancer mortality in the Reasons for Geographic and Racial Differences in Stroke (REGARDS) cohort study." Cancer **128**(1): 122-130.

BACKGROUND: Social determinants of health (SDOHs) cluster together and can have deleterious impacts on health outcomes. Individually, SDOHs increase the risk of cancer mortality, but their cumulative burden is not well understood. The authors sought to determine the combined effect of SDOH on cancer mortality. METHODS: Using the Reasons for Geographic and Racial Differences in Stroke (REGARDS) cohort, the authors studied 29,766 participants aged 45+ years and followed them 10+ years. Eight potential SDOHs were considered, and retained SDOHs that were associated with cancer mortality (P < .10) were retained to create a count (0, 1, 2, 3+). Cox proportional hazard models estimated associations between the SDOH count and cancer mortality through December 31, 2017, adjusting for confounders. Models were age-stratified (45-64 vs 65+ years). RESULTS: Participants were followed for a median of 10.6 years (interquartile range [IQR], 6.5, 12.7 years). Low education, low income, zip code poverty, poor public health infrastructure, lack of health insurance, and social isolation were significantly associated with cancer mortality. In adjusted models, among those <65 years, compared to no SDOHs, having 1 SDOH (adjusted hazard ratio [aHR], 1.39; 95% CI, 1.11-1.75), 2 SDOHs (aHR, 1.61; 95% CI, 1.26-2.07), and 3+ SDOHs (aHR, 2.09; 95% CI, 1.58-2.75) were associated with cancer mortality (P for trend <.0001). Among individuals 65+ years, compared to no SDOH, having 1 SDOH (aHR, 1.16; 95% CI, 1.00-1.35) and 3+ SDOHs (aHR, 1.26; 95% CI, 1.04-1.52) was associated with cancer mortality (P for trend = .032). CONCLUSIONS: A greater number of SDOHs were significantly associated with an increased risk of cancer mortality, which persisted after adjustment for confounders.

Ratjen, I., et al. (2021). "Post-diagnostic reliance on plant-compared with animal-based foods and all-cause mortality in omnivorous long-term colorectal cancer survivors." Am J Clin Nutr **114**(2): 441-449.

BACKGROUND: Plant-rich diets are associated with lower cardiometabolic risks and longer survival in the general population, but their association with mortality in cancer survivors is still unclear. OBJECTIVES: We aimed to examine the associations of 3 postdiagnostic plant-based diet indices with all-cause mortality in omnivorous long-term colorectal cancer (CRC) survivors. METHODS: Diet was assessed with FFQs at a median of 6 years after diagnosis in 1404 CRC survivors (56% male; median age, 69 years) in a Northern German prospective cohort study. An overall, a healthful plant-based, and an unhealthful plant-based diet index were derived by scoring intakes of animal foods reversely and intakes of healthy (whole grains, vegetables, fruits, legumes, nuts, oils, tea/coffee) and less healthy plant foods (refined grains, fruit juices, sugar-sweetened beverages, potatoes, sweets/desserts) positively or reversely, depending on the index. Vital status follow-up was conducted via population registries. Cox proportional hazards regression was applied to estimate HRs for all-cause mortality according to plant-based diet adherence. RESULTS: Within 7 years (median) after diet assessment, 204 deaths occurred. The overall plant-based diet index displayed a significant, inverse association with all-cause mortality (HR per 10-point increase in diet index, 0.72; 95% CI, 0.57-0.91). Although not statistically significant, higher healthful plant-based diet scores showed a strong tendency towards lower mortality (HR, 0.82; 95% CI, 0.67-1.01). The unhealthful plant-based diet index was associated with higher mortality, but lost statistical significance after multivariable adjustment (HR, 1.19; 95% CI, 0.96-1.48). A subgroup analysis revealed that the tendency towards a positive association of the unhealthful plant-based diet with mortality was restricted to less physically active individuals (<95 metabolic equivalent of task hours/week). CONCLUSIONS: An overall plant-based diet was inversely associated with all-cause mortality in long-term CRC survivors. However, more research is needed to further disentangle the impacts of different qualities of plant-based diets on cancer survivors' health.

Ray, E. M., et al. (2022). "Incidence of Severe Acute Respiratory Syndrome Coronavirus 2 and Subsequent Mortality in a Multisite Cohort of Patients With Cancer

in the CancerLinQ Discovery Database." JCO Oncol Pract **18**(8): e1265-e1277.

PURPOSE: Understanding risks for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection and subsequent mortality among patients with cancer may help inform treatment decisions during the COVID-19 pandemic. METHODS: CancerLinQ is an electronic health record database from US oncology practices. We identified a cohort of patients with malignancy and 2+ encounters at CancerLinQ practices in the 12 months before the study period (January 1, 2020-January 31, 2021). We identified a SARS-CoV-2 subcohort as having a positive SARS-CoV-2 test or International Classification of Diseases, 10th Revision, code. We examined predictors of SARS-CoV-2 infection and mortality including sex, race, ethnicity, age, malignancy type, and prior therapy. Unadjusted and adjusted incidence rate ratios (aIRRs) and 95% CIs were estimated from Poisson regression models for SARS-CoV-2 infections and mortality. RESULTS: The cancer cohort included 629,128 patients, and the SARS-CoV-2 subcohort included 12,300 patients. Higher incidence of SARS-CoV-2 was seen among patients who were male (incidence rate ratio [IRR], 1.14; 95% CI, 1.10 to 1.18), Black (IRR, 1.48; 95% CI, 1.41 to 1.56), Hispanic (IRR, 2.02; 95% CI, 1.91 to 2.14), age < 50 years (IRR, 1.34; 95% CI, 1.26 to 1.42), with hematologic malignancies (IRR, 1.07; 95% CI, 1.02 to 1.12), and with recent chemotherapy (IRR, 1.30, 95% CI, 1.22 to 1.40). In the adjusted analysis, higher incidence was seen in patients who were male (aIRR, 1.17; 95% CI, 1.13 to 1.21), Hispanic (aIRR, 2.01; 95% CI, 1.88 to 2.14), and with recent chemotherapy (aIRR, 1.17; 95% CI, 1.09 to 1.25). There were 182 all-cause deaths within the SARS-CoV-2 subcohort. Higher mortality was seen among patients who were male (IRR, 1.39; 95% CI, 1.04 to 1.86), unknown race (IRR, 2.64; 95% CI, 1.42 to 4.91), other/unknown ethnicity (IRR, 1.99; 95% CI, 1.20 to 3.29), age 60-69 years (IRR, 2.76; 95% CI, 1.23 to 6.19), age 70-79 years (IRR, 5.28; 95% CI, 2.42 to 11.5), age 80+ years (IRR, 7.31; 95% CI, 3.31 to 16.1), or with recent chemotherapy (IRR, 1.52, 95% CI, 1.01 to 2.29). In the adjusted analysis, higher mortality was seen with increased age and receipt of chemotherapy. CONCLUSION: Patients with increased risk of SARS-CoV-2 infection must balance the competing risks of their cancer diagnosis/treatment and SARS-CoV-2 infection.

Recuero-Diaz, J. L., et al. (2022). "Treatment and intention-to-treat propensity score analysis to evaluate the impact of video-assisted thoracic surgery on 90-day mortality after anatomical resection for lung cancer." Eur J Cardiothorac Surg **62**(3).

OBJECTIVES: The aim of this study was to know the treatment effect of video-assisted thoracic surgery (VATS) on 90-day mortality after anatomical lung resection based on a nationwide cohort. METHODS: This is a multicentre prospective cohort of 2721 anatomical resections for lung cancer from December 2016 to March 2018. Treatment and intention-to-treat (ITT) analyses were performed after inverse probability score weighting and different propensity score matching algorithms. Covariate balance was assessed by standardized mean differences. The estimators reported were the average treatment effect, the average treatment effect on the treated and odds ratios after conditional logistic models with 95% confidence intervals. The unconfoundedness assumption was evaluated by sensitivity analysis for average treatment effect (c-dependence) and average treatment effect on the treated (Gamma). RESULTS: VATS was the initial approach in 1911 patients (70.2%), though 273 cases (14.3%) had to be converted to thoracotomy. Ninety-day mortality rates were: treatment analysis (VATS 1.16% vs open 3.9%, P < 0.001), ITT analysis (VATS 1.78% vs open 3.36%, P = 0.012). After inverse probability score weighting and propensity score matching, in the treatment analysis, VATS meant absolute risk reductions between 2.25% and 2.96% and relative risk reductions between 65% and 70% [OR = 0.34 (95% confidence interval 0.15-0.79), all P-values <0.004). However, all the estimators turned out to be non-significant in the ITT analyses. A high sensitivity to unobservable confounders was proved (c-dependence 0.135, Gamma = 1.5). CONCLUSIONS: VATS can reduce the risk of 90-day mortality after anatomical lung resection. However, the implications of conversion to thoracotomy, comparing ITT versus treatment analysis, and the potential impact of hidden bias should deserve further attention in the future.

Reda, S., et al. (2020). "Pre-operative beta-blocker therapy does not affect short-term mortality after esophageal resection for cancer." BMC Surg **20**(1): 333.

BACKGROUND: It has been postulated that the hyperadrenergic state caused by surgical trauma is associated with worse outcomes and that beta-blockade may improve overall outcome by downregulation of adrenergic activity. Esophageal resection is a surgical procedure with substantial risk for postoperative mortality. There is insufficient data to extrapolate the existing association between preoperative beta-blockade and postoperative mortality to esophageal cancer surgery. This study assessed whether preoperative beta-blocker therapy affects short-term postoperative mortality for patients undergoing esophageal cancer surgery. METHODS: All patients

with an esophageal cancer diagnosis that underwent surgical resection with curative intent from 2007 to 2017 were retrospectively identified from the Swedish National Register for Esophagus and Gastric Cancers (NREV). Patients were subdivided into beta-blocker exposed and unexposed groups. Propensity score matching was carried out in a 1:1 ratio. The outcome of interest was 90-day postoperative mortality. RESULTS: A total of 1466 patients met inclusion criteria, of whom 35% (n = 513) were on regular preoperative beta-blocker therapy. Patients on beta-blockers were significantly older, more comorbid and less fit for surgery based on their ASA score. After propensity score matching, 513 matched pairs were available for analysis. No difference in 90-day mortality was detected between beta-blocker exposed and unexposed patients (6.0% vs. 6.6%, p = 0.798). CONCLUSION: Preoperative beta-blocker therapy is not associated with better short-term survival in patients subjected to curative esophageal tumor resection.

Reddy, S., et al. (2021). "Assessing Presenting Symptoms, Co-Morbidities, and Risk Factors for Mortality in Underserved Patients With Non-Hereditary Early-Onset Colorectal Cancer." Cureus **13**(7): e16117.

Background The presenting symptoms and co-morbidities contributing to mortality in young patients (age < 50 years old) with colorectal cancer (CRC) are poorly understood. We reviewed these features in our patient population with non-hereditary early-onset CRC (EO-CRC). Study aim This study aimed to assess characteristics of patients with a diagnosis of non-hereditary EO-CRC, including presenting symptoms and metabolic disorders contributing to mortality in underserved areas of southwest Virginia. Methods In this retrospective observational study, we selected patients aged 18-50 years with a diagnosis of non-hereditary EO-CRC from 2008 to 2016 at Carilion Roanoke Memorial Hospital. The electronic medical record was queried to identify demographic data, medical history, histopathology results, lab values, and mortality. The cumulative risks of symptoms and co-morbid metabolic disorders was estimated using Kaplan-Meier curves. Results We identified 139 patients with non-hereditary EO-CRC (mean age 41.6 +/- 6.9 years). Almost half of these patients were obese (BMI > 30), 30.9% had a diagnosis of hypertension, 29% had hyperlipidemia (HLD), and 17.35% had diabetes mellitus type 2 (DM2). Diagnosis was delayed by 4.5 months from initial presentation, and 17% had advanced disease (stage III/IV). Also, 68.5% of patients were symptomatic with one to three symptoms, most commonly with rectal bleeding (45.3%). The chronicity of HLD (>/=5 years) was associated with reduced survival in our patients with EO-CRC. The survival of females with multiple metabolic disorders was reduced compared to females with a single metabolic disorder. Conclusions Multiple symptoms, chronic HLD, and female gender with multiple metabolic disorders were factors associated with poor outcomes in non-hereditary EO-CRC patients.

Redondo-Sanchez, D., et al. (2021). "Cancer incidence estimation from mortality data: a validation study within a population-based cancer registry." Popul Health Metr **19**(1): 18.

BACKGROUND: Population-based cancer registries are required to calculate cancer incidence in a geographical area, and several methods have been developed to obtain estimations of cancer incidence in areas not covered by a cancer registry. However, an extended analysis of those methods in order to confirm their validity is still needed. METHODS: We assessed the validity of one of the most frequently used methods to estimate cancer incidence, on the basis of cancer mortality data and the incidence-to-mortality ratio (IMR), the IMR method. Using the previous 15-year cancer mortality time series, we derived the expected yearly number of cancer cases in the period 2004-2013 for six cancer sites for each sex. Generalized linear mixed models, including a polynomial function for the year of death and smoothing splines for age, were adjusted. Models were fitted under a Bayesian framework based on Markov chain Monte Carlo methods. The IMR method was applied to five scenarios reflecting different assumptions regarding the behavior of the IMR. We compared incident cases estimated with the IMR method to observed cases diagnosed in 2004-2013 in Granada. A goodness-of-fit (GOF) indicator was formulated to determine the best estimation scenario. RESULTS: A total of 39,848 cancer incidence cases and 43,884 deaths due to cancer were included. The relative differences between the observed and predicted numbers of cancer cases were less than 10% for most cancer sites. The constant assumption for the IMR trend provided the best GOF for colon, rectal, lung, bladder, and stomach cancers in men and colon, rectum, breast, and corpus uteri in women. The linear assumption was better for lung and ovarian cancers in women and prostate cancer in men. In the best scenario, the mean absolute percentage error was 6% in men and 4% in women for overall cancer. Female breast cancer and prostate cancer obtained the worst GOF results in all scenarios. CONCLUSION: A comparison with a historical time series of real data in a population-based cancer registry indicated that the IMR method is a valid tool for the estimation of cancer incidence. The goodness-of-fit indicator proposed can help select the best assumption for the IMR based on a statistical argument.

ReFaey, K., et al. (2021). "Cancer Mortality Rates Increasing vs Cardiovascular Disease Mortality Decreasing in the World: Future Implications." Mayo Clin Proc Innov Qual Outcomes **5**(3): 645-653.

OBJECTIVE: To highlight the current global trends in mortality for cardiovascular disease and cancer. METHODS: The World Health Organization and the World Bank DataBank databases were used to analyze mortality rates for cancer and cardiovascular disease by calculating age-standardized mortality rates (ASRs) from 2000 to 2015 for high-income, upper-middle-income, and lower-middle-income countries. Data for cancer mortality and population for 43 countries representing 5 of the 7 continents (except Australia and Antarctica) were analyzed. RESULTS: From 2000 to 2015, there was an increase in the ASR for cancer for both men and women irrespective of a country's income status, representing an overall 7% increase in cancer ASR (Pearson r, +0.99; P<.00001). We report a higher ASR for cancer in high-income countries than in upper-middle-income and lower-middle-income countries specifically; high-income countries saw a 3% increase in cancer ASR vs +31% for upper-middle-income and +19% for lower-middle-income countries (P<.01). There has been a decrease in the ASR for cardiovascular disease for the 15 years analyzed (P<.00001). In addition, high-income countries had a higher ASR for cardiovascular disease than upper-middle-income countries during the 15-year period (P<.05). CONCLUSION: We suspect that because of early detection and targeted interventions, cardiovascular disease mortality rates have decreased during the past decade. On the basis of our results, cancer mortality rates continue to rise, with the projection of surpassing cardiovascular disease mortality rates in the near future.

Reiter-Brennan, C., et al. (2021). "Fitness and prostate cancer screening, incidence, and mortality: Results from the Henry Ford Exercise Testing (FIT) Project." Cancer **127**(11): 1864-1870.

BACKGROUND: The relation between cardiorespiratory fitness (CRF) and prostate cancer is not well established. The objective of this study was to determine whether CRF is associated with prostate cancer screening, incidence, or mortality. METHODS: The Henry Ford Exercise Testing Project is a retrospective cohort study of men aged 40 to 70 years without cancer who underwent physician-referred exercise stress testing from 1995 to 2009. CRF was quantified in metabolic equivalents of task (METs) (<6 [reference], 6-9, 10-11, and >/=12 METs), estimated from the peak workload achieved during a symptom-limited, maximal exercise stress test. Prostate-specific antigen (PSA) testing, incident prostate cancer, and all-cause mortality were analyzed with multivariable adjusted Poisson regression and Cox proportional hazard models. RESULTS: In total, 22,827 men were included, of whom 739 developed prostate cancer, with a median follow-up of 7.5 years. Men who had high fitness (>/=12 METs) had an 28% higher risk of PSA screening (95% CI, 1.2-1.3) compared with those who had low fitness (<6 METs. After adjusting for PSA screening, fitness was associated with higher prostate cancer incidence (men aged <55 years, P = .02; men aged >55 years, P </= .01), but not with advanced prostate cancer. Among the men who were diagnosed with prostate cancer, high fitness was associated with a 60% lower risk of all-cause mortality (95% CI, 0.2-0.9). CONCLUSIONS: Although men with high fitness are more likely to undergo PSA screening, this does not fully account for the increased incidence of prostate cancer seen among these individuals. However, men with high fitness have a lower risk of death after a prostate cancer diagnosis, suggesting that the cancers identified may be low-risk with little impact on long-term outcomes.

Relation, T., et al. (2022). "Inflammatory breast cancer, trimodal treatment, and mortality: Does where you live matter?" Surgery **171**(3): 687-692.

BACKGROUND: The objective of this study is to examine the associations among neighborhood socioeconomic status, trimodal treatment, and disease-specific mortality among inflammatory breast cancer patients using data from the Surveillance, Epidemiology, and End Results program. METHODS: Patients diagnosed with inflammatory breast cancer (T4d) from 2010 to 2016 were identified in the Surveillance, Epidemiology, and End Results program. The cohort was stratified into neighborhood socioeconomic status groups (low, middle, high) based on National Cancer Institute census tract-level index. Trimodal treatment was defined as receipt of modified radical mastectomy, chemotherapy, and radiation therapy. Bivariable analysis, log-rank test, and a Cox proportional hazards model (hazard ratio, 95% confidence interval) were conducted to evaluate the relationship between neighborhood socioeconomic status, trimodal treatment, and disease-specific mortality. RESULTS: In total, 4,374 patients met study criteria. There was no difference between the neighborhood socioeconomic status groups in receipt of trimodal treatment (P = .19). On multivariable analysis, there was no association between low neighborhood socioeconomic status (hazard ratio 1.13, 0.98-1.30; ref high neighborhood socioeconomic status) or middle neighborhood socioeconomic status (hazard ratio 1.01, 0.88-1.64; ref high neighborhood socioeconomic status) and disease-specific mortality. Notably, triple negative subtype (hazard ratio 2.66,

2.21-3.20; ref luminal A) and Black race (hazard ratio 1.41, 1.16-1.72; ref White) were associated with a higher disease-specific mortality. CONCLUSION: For inflammatory breast cancer patients in the Surveillance, Epidemiology, and End Results program, disease-specific mortality appears to be driven by tumor biology and patient characteristics instead of treatment disparities or neighborhood socioeconomic status.

Ren, Q. W., et al. (2021). "Statin associated lower cancer risk and related mortality in patients with heart failure." Eur Heart J **42**(32): 3049-3059.

AIMS: Patients with heart failure (HF) have an increased risk of incident cancer. Data relating to the association of statin use with cancer risk and cancer-related mortality among patients with HF are sparse. METHODS AND RESULTS: Using a previously validated territory-wide clinical information registry, statin use was ascertained among all eligible patients with HF (n = 87 102) from 2003 to 2015. Inverse probability of treatment weighting was used to balance baseline covariates between statin nonusers (n = 50 926) with statin users (n = 36 176). Competing risk regression with Cox proportional-hazard models was performed to estimate the risk of cancer and cancer-related mortality associated with statin use. Of all eligible subjects, the mean age was 76.5 +/- 12.8 years, and 47.8% was male. Over a median follow-up of 4.1 years (interquartile range: 1.6-6.8), 11 052 (12.7%) were diagnosed with cancer. Statin use (vs. none) was associated with a 16% lower risk of cancer incidence [multivariable adjusted subdistribution hazard ratio (SHR) = 0.84; 95% confidence interval (CI), 0.80-0.89]. This inverse association with risk of cancer was duration dependent; as compared with short-term statin use (3 months to <2 years), the adjusted SHR was 0.99 (95% CI, 0.87-1.13) for 2 to <4 years of use, 0.82 (95% CI, 0.70-0.97) for 4 to <6 years of use, and 0.78 (95% CI, 0.65-0.93) for >/=6 years of use. Ten-year cancer-related mortality was 3.8% among statin users and 5.2% among nonusers (absolute risk difference, -1.4 percentage points [95% CI, -1.6% to -1.2%]; adjusted SHR = 0.74; 95% CI, 0.67-0.81). CONCLUSION: Our study suggests that statin use is associated with a significantly lower risk of incident cancer and cancer-related mortality in HF, an association that appears to be duration dependent.

Sehouli, J., et al. (2021). "Effects of sarcopenia and malnutrition on morbidity and mortality in gynecologic cancer surgery: results of a prospective study." J Cachexia Sarcopenia Muscle **12**(2): 393-402.

BACKGROUND: Malnutrition and sarcopenia often occur simultaneously in cancer patients and are thought to have harmful effects on both surgical and oncological outcomes. Therefore, we want to evaluate the effects of sarcopenia and malnutrition on severe postoperative complications and overall survival in gynecologic cancer patients. METHODS: We assessed nutritional parameters and run a bioelectrical impedance analysis in 226 women. Extracellular mass to body cell mass index, phase angle alpha, muscle mass, and fat mass were evaluated. To determine if patients suffer from sarcopenia, we ran the Timed 'Up and Go' test, performed hand grip strength, and calculated a skeletal muscle index. Postoperative complications were categorized using Clavien-Dindo Classification. Utilizing ROC analysis and logistic regression, we determined predictive clinical factors for severe postoperative complications. Kaplan-Meier method and log-rank test were used for overall survival analysis. RESULTS: Of the 226 female patients, 120 (53%) had a BMI >/= 25 kg/m(2) , 56 (26%) had a phase angle < 4.75 degrees , and 68 (32%) were sarcopenic according to skeletal muscle index < 27%. Within 30 days after surgery, 40 (18%) patients developed severe postoperative complications, and 4% had died. According to multivariable regression analysis, ECOG status > 1 (OR 4.56, 95% CI: 1.46-14.28, P = 0.009), BMI >/= 25 kg/m(2) (OR 8.22, 95% CI: 3.01-22.48, P < 0.001), phase angle < 4.75 degrees (OR 3.95, 95% CI: 1.71-9.10, P = 0.001), and tumour stage >/= III A (OR 3.65, 95% CI: 1.36-9.76, P = 0.01) were predictors of severe postoperative complications. During 59 months of follow-up, 108 (48%) patients had died. According to multivariable Cox regression ECOG status > 1 (HR 2.51, 95% CI: 1.25-5.03, P = 0.01), hypoalbuminemia (HR 2.15, 95% CI: 1.28-3.59, P = 0.004), phase angle < 4.5 degrees (HR 1.76, 95% CI 1.07-2.90, P = 0.03), tumour stage >/= III A (HR 2.61, 95% CI: 1.53-4.45, P < 0.001), and severe postoperative complications (HR 2.82, 95% CI: 1.80-4.41, P < 0.001) were predictors of overall mortality. CONCLUSIONS: We observed that preoperatively assessed ECOG status > 1, BMI > 25 kg, as well as phase angle alpha < 4.75 degrees and FIGO stage >/= III A are significantly associated with severe postoperative complications within the first month. Whereas ECOG status > 1, hypoalbuminemia, phase angle < 4.5 degrees as well as FIGO stage >/= III A and severe postoperative complications within 30 days correlate significantly with poor overall survival.

Seigneurin, A., et al. (2021). "Association of Mammography Screening With a Reduction in Breast Cancer Mortality: A Modeling Study Using Population-Based Data From 2 French Departments." Am J Epidemiol **190**(5): 827-835.

Meta-analyses of randomized controlled trials that started from 1963 to 1991 reported a decrease of breast cancer mortality, associated with mammography screening. However, the effectiveness of population-

based screening programs conducted currently might have changed due to the higher effectiveness of treatments for late-stage cancers and the better diagnostic performance of mammography. The main objective of this study was to predict the reduction of breast cancer mortality associated with mammography screening in the current French setting. We compared breast cancer mortality in 2 simulated cohorts of women, which differed from each other solely in a 70% biennial participation in screening from 50 to 74 years old. The microsimulation model used for predictions was calibrated with incidence rates of breast cancer according to stage that were observed in Isere and Loire-Atlantique departments, France, in 2007-2013. The model predicted a decrease of breast cancer mortality associated with mammography screening of 18% (95% CI: 5, 31) and 17% (95% CI: 3, 29) for models calibrated with data from Isere and Loire-Atlantique departments, respectively. Our results highlight the interest in biennial mammography screening from ages 50 to 74 years old to decrease breast cancer mortality in the current setting, despite improvements in treatment effectiveness.

Seikkula, H., et al. (2022). "Periodic trends in geographical variation of prostate cancer incidence and mortality in Finland between 1985 and 2019." Acta Oncol **61**(10): 1209-1215.

BACKGROUND: Evaluation of regional variation of prostate cancer (PCa) incidence and PCa-specific mortality is essential in the assessment of equity in a national healthcare system. We evaluated PCa incidence and PCa-specific mortality between different municipalities and hospital districts in Finland over 1985-2019. MATERIAL AND METHODS: Men diagnosed with PCa in Finland from 1985 through 2019 were retrieved from Finnish Cancer Registry. Age-standardized PCa incidence and mortality rates were estimated by municipality and hospital district as well as municipality urbanization, education, and income level using hierarchical Bayesian modeling. Standard deviations (SD) of the regional rates were compared between periods from 1985-1989 to 2015-2019. RESULTS: We identified 123,185 men diagnosed with any stage PCa between 1985 and 2019. SD of PCa incidence rate (per 100,000 person-years) showed that the total variation of PCa incidence between different municipalities was substantial and varied over time: from 22.2 (95% CI, 17.1-27.8) in 1985-1989 to 56.5 (95% CI, 49.8-64.5) in 2000-2004. The SD of PCa mortality rate between all municipalities was from 9.0 (95% CI, 6.6-11.8) in 2005-2009 to 2.4 (95% CI, 0.9-4.8) in 2015-2019. There was a trend toward a lower PCa-specific mortality rate in municipalities with higher education level. DISCUSSION: Regional variation in the incidence rate of PCa became more evident after initiation of PSA testing in Finland, which indicates that early diagnostic practice (PSA testing) of PCa has been different in different parts of the country. Variation in the national PCa mortality rate was indeed recognizable, however, this variation diminished at the same time as the mortality rate declined in Finland. It seems that after the initiation period of PSA testing, PSA has equalized PCa mortality outcomes in Finland.

Seiler, A., et al. (2021). "Delirium is associated with an increased morbidity and in-hospital mortality in cancer patients: Results from a prospective cohort study." Palliat Support Care **19**(3): 294-303.

OBJECTIVE: Delirium is a frequent complication in advanced cancer patients, among whom it is frequently underdiagnosed and inadequately treated. To date, evidence on risk factors and the prognostic impact of delirium on outcomes remains sparse in this patient population. METHOD: In this prospective observational cohort study at a single tertiary-care center, 1,350 cancer patients were enrolled. Simple and multiple logistic regression models were utilized to identify associations between predisposing and precipitating factors and delirium. Cox proportional-hazards models were used to estimate the effect of delirium on death rate. RESULTS: In our patient cohort, the prevalence of delirium was 34.3%. Delirium was associated inter alia with prolonged hospitalization, a doubling of care requirements, increased healthcare costs, increased need for institutionalization (OR 3.22), and increased mortality (OR 8.78). Predisposing factors for delirium were impaired activity (OR 10.82), frailty (OR 4.75); hearing (OR 2.23) and visual impairment (OR 1.89), chronic pneumonitis (OR 2.62), hypertension (OR 1.46), and renal insufficiency (OR 1.82). Precipitating factors were acute renal failure (OR 7.50), pressure sores (OR 3.78), pain (OR 2.86), and cystitis (OR 1.32). On multivariate Cox regression, delirium increased the mortality risk sixfold (HR 5.66). Age >/= 65 years and comorbidities further doubled the mortality risk of delirious patients (HR 1.77; HR 2.05). SIGNIFICANCE OF RESULTS: Delirium is common in cancer patients and associated with increased morbidity and mortality. Systematically categorizing predisposing and precipitating factors might yield new strategies for preventing and managing delirium in cancer patients.

Sng, C. C. T., et al. (2020). "Cancer History and Systemic Anti-Cancer Therapy Independently Predict COVID-19 Mortality: A UK Tertiary Hospital Experience." Front Oncol **10**: 595804.

BACKGROUND: The COVID-19 pandemic remains a pressing concern to patients with cancer as

countries enter the second peak of the pandemic and beyond. It remains unclear whether cancer and its treatment contribute an independent risk for mortality in COVID-19. METHODS: We included patients at a London tertiary hospital with laboratory confirmed SARS-CoV-2 infection. All patients with a history of solid cancer were included. Age- and sex-matched patients without cancer were randomly selected. Patients with hematological malignancies were excluded. RESULTS: We identified 94 patients with cancer, matched to 226 patients without cancer. After adjusting for age, ethnicity, and co-morbidities, patients with cancer had increased mortality following COVID-19 (HR 1.57, 95% CI:1.04-2.4, p = 0.03). Increasing age (HR 1.49 every 10 years, 95% CI:1.25-1.8, p < 0.001), South Asian ethnicity (HR 2.92, 95% CI:1.73-4.9, p < 0.001), and cerebrovascular disease (HR 1.93, 95% CI:1.18-3.2, p = 0.008) also predicted mortality. Within the cancer cohort, systemic anti-cancer therapy (SACT) within 60 days of COVID-19 diagnosis was an independent risk factor for mortality (HR 2.30, 95% CI: 1.16-4.6, p = 0.02). CONCLUSIONS: Along with known risk factors, cancer and SACT confer an independent risk for mortality following COVID-19. Further studies are needed to understand the socio-economic influences and pathophysiology of these associations.

So, R., et al. (2022). "Long-term exposure to air pollution and mortality in a Danish nationwide administrative cohort study: Beyond mortality from cardiopulmonary disease and lung cancer." Environ Int **164**: 107241.

BACKGROUND: The association between long-term exposure to air pollution and mortality from cardiorespiratory diseases is well established, yet the evidence for other diseases remains limited. OBJECTIVES: To examine the associations of long-term exposure to air pollution with mortality from diabetes, dementia, psychiatric disorders, chronic kidney disease (CKD), asthma, acute lower respiratory infection (ALRI), as well as mortality from all-natural and cardiorespiratory causes in the Danish nationwide administrative cohort. METHODS: We followed all residents aged >/= 30 years (3,083,227) in Denmark from 1 January 2000 until 31 December 2017. Annual mean concentrations of fine particulate matter (PM(2.5)), nitrogen dioxide (NO(2)), black carbon (BC), and ozone (warm season) were estimated using European-wide hybrid land-use regression models (100 m x 100 m) and assigned to baseline residential addresses. We used Cox proportional hazard models to evaluate the association between air pollution and mortality, accounting for demographic and socioeconomic factors. We additionally applied indirect adjustment for smoking and body mass index (BMI). RESULTS: During 47,023,454 person-years of follow-up, 803,881 people died from natural causes. Long-term exposure to PM(2.5) (mean: 12.4 microg/m(3)), NO(2) (20.3 microg/m(3)), and/or BC (1.0 x 10(-5)/m) was statistically significantly associated with all studied mortality outcomes except CKD. A 5 microg/m(3) increase in PM(2.5) was associated with higher mortality from all-natural causes (hazard ratio 1.11; 95% confidence interval 1.09-1.13), cardiovascular disease (1.09; 1.07-1.12), respiratory disease (1.11; 1.07-1.15), lung cancer (1.19; 1.15-1.24), diabetes (1.10; 1.04-1.16), dementia (1.05; 1.00-1.10), psychiatric disorders (1.38; 1.27-1.50), asthma (1.13; 0.94-1.36), and ALRI (1.14; 1.09-1.20). Associations with long-term exposure to ozone (mean: 80.2 microg/m(3)) were generally negative but became significantly positive for several endpoints in two-pollutant models. Generally, associations were attenuated but remained significant after indirect adjustment for smoking and BMI. CONCLUSION: Long-term exposure to PM(2.5), NO(2), and/or BC in Denmark were associated with mortality beyond cardiorespiratory diseases, including diabetes, dementia, psychiatric disorders, asthma, and ALRI.

Soderdahl, F., et al. (2022). "A Novel Risk Score (P-score) Based on a Three-Gene Signature, for Estimating the Risk of Prostate Cancer-Specific Mortality." Res Rep Urol **14**: 203-217.

PURPOSE: To develop and validate a risk score (P-score) algorithm which includes previously described three-gene signature and clinicopathological parameters to predict the risk of death from prostate cancer (PCa) in a retrospective cohort. PATIENTS AND METHODS: A total of 591 PCa patients diagnosed between 2003 and 2008 in Stockholm, Sweden, with a median clinical follow-up time of 7.6 years (1-11 years) were included in this study. Expression of a three-gene signature (IGFBP3, F3, VGLL3) was measured in formalin-fixed paraffin-embedded material from diagnostic core needle biopsies (CNB) of these patients. A point-based scoring system based on a Fine-Gray competing risk model was used to establish the P-score based on the three-gene signature combined with PSA value, Gleason score and tumor stage at diagnosis. The endpoint was PCa-specific mortality, while other causes of death were treated as a competing risk. Out of the 591 patients, 315 patients (estimation cohort) were selected to develop the P-score. The P-score was subsequently validated in an independent validation cohort of 276 patients. RESULTS: The P-score was established ranging from the integers 0 to 15. Each one-unit increase was associated with a hazard ratio of 1.39 (95% confidence interval: 1.27-1.51, p < 0.001). The P-score was validated and performed better in predicting

PCa-specific mortality than both D'Amico (0.76 vs 0.70) and NCCN (0.76 vs 0.71) by using the concordance index for competing risk. Similar improvement patterns are shown by time-dependent area under the curve. As demonstrated by cumulative incidence function, both P-score and gene signature stratified PCa patients into significantly different risk groups. CONCLUSION: We developed the P-score, a risk stratification system for newly diagnosed PCa patients by integrating a three-gene signature measured in CNB tissue. The P-score could provide valuable decision support to distinguish PCa patients with favorable and unfavorable outcomes and hence improve treatment decisions.

Soeroso, N. N., et al. (2021). "The correlation between hemostatic parameters and mortality rate in patients with non-small cell lung cancer." Hematol Rep **13**(3): 8361.

The increasing level of hemostatic parameters and tumor markers were associated with cancer progression and poor prognosis, particularly in NSCLC. The objective of this study is to determine whether there was a correlation between hemostatic parameters and mortality rate in patients with NSCLC. This was a prospective analytical study with a pretest-posttest design which included 41 patients with diagnosis of NSCLC. Plasma levels of PT, APTT, TT, D-dimer, and fibrinogen were measured before initiation of chemotherapy and remeasured after 4 cycles or 6 cycles of chemotherapy, based on the clinical condition of patients. Then, patients were followed up for 1 year to evaluate the mortality rate. The majority of subjects were male (85.4%) with adenocarcinoma (75.6%). There was no significant difference in mean between adenocarcinoma and squamous cell carcinoma (P>0.05). Most patients died after one month of follow up (61%). The parameters which could predict high mortality rate in NSCLC were prolonged PT and the increased of D-dimer with RR>1, although they had not significant in statistical analysis (P>0.05). There is no correlation between hemostatic parameters and mortality rate in patients with NSCLC.

Sogunro, O., et al. (2022). "Triple negative breast cancer and reconstruction: Predictors of recurrence, complications, and mortality." Breast Dis **41**(1): 343-350.

BACKGROUND: Only 42% of all breast cancer patients undergoing mastectomy elect for breast reconstruction. OBJECTIVE: We evaluate factors impacting complications, recurrence, and mortality in triple-negative breast cancer (TNBC) patients undergoing reconstruction. METHODS: Reconstructive TNBC patients at a single institution from 2010 to 2020 were retrospectively reviewed. Patient demographics, cancer characteristics, reconstruction choice, and complications were collected. Statistical significance was defined at $p < 0.05$. RESULTS: A total of 131 patients were identified. Average age was 47.8 years, 50.4% were Caucasian and 36.4% were African American. Most patients had invasive ductal carcinoma (90.8%), and most underwent nipple-sparing (41.2%) or skin-sparing (38.9%) mastectomies. Twenty-one patients (16.0%) experienced postoperative complications. Patients with complications tended to be older (52.1 versus 46.9 years, $p = 0.052$). At mean follow-up of 52.1 months, 14.5% experienced cancer recurrence and 5.3% died. Deceased patients were significantly younger at diagnosis (42.2 versus 48.5 years, $p = 0.008$) and had a lower BMI compared to surviving patients (21.2 versus 26.9 kg/m2; $p = 0.014$). Patients younger than age 45 years had higher Ki-67 than those older than 45 years (80.0% versus 60.0%, $p = 0.013$). Outcomes in autologous- versus implant-based reconstruction were not significantly different. CONCLUSIONS: In TNBC post-mastectomy reconstruction patients, age and BMI were predictors of mortality while race, smoking history, reconstruction choice, or type of implant-based reconstruction had no significant effect on these outcomes. SYNOPSIS: The purpose of this study is to evaluate factors that impact complications, recurrence, and mortality in triple negative breast cancer (TNBC) patients undergoing reconstruction. We identified BMI, neoadjuvant chemotherapy, and age as predictors of complications, recurrence, and mortality in TNBC.

Sogunro, O. A., et al. (2023). "Prognostic Predictors of Mortality in Male Breast Cancer: Outcomes in an Urban Population." J Surg Res **281**: 192-199.

INTRODUCTION: Male breast cancer (MBC) accounts for 0.5% to 1% of all breast cancers diagnosed annually. The purpose of this study is to evaluate prognostic factors in MBC. METHODS: We performed a retrospective chart review of patients with MBC between 2010 and 2021. Demographics, comorbidities, cancer characteristics, recurrence, and mortality were collected. Cox proportional hazards regression model was used to determine prognostic factors. A Kaplan-Meier curve was used to plot survival probabilities. RESULTS: A total of 47 male patients were identified. The mean age at presentation was 64.1 y. Twenty eight (59.6%) patients were African American and 14 patients (29.8%) were Caucasian. Most patients had invasive ductal carcinoma (89.4%) and presented with T1 or T2 tumors (40.4% and 38.3%, respectively). Three patients (6.4%) had a recurrence and eight patients (17%) died. Using mortality as an end point, age (>/= 76.1 y) indicated a hazard ratio (HR) of 1.13 ($P = 0.004$), diabetes mellitus (HR = 5.45, $P = 0.023$), atrial fibrillation (HR = 8.0, P

= 0.009), end-stage renal disease (HR 6.47, P = 0.023), Eastern Cooperative Oncology Group performance status of 3 (HR = 7.92, P = 0.024), poorly differentiated grade (HR = 7.21, P = 0.033), and metastatic disease (HR = 30.94, P = 0.015) had an increased risk of mortality. Overall survival at 3 y was 79.2%. CONCLUSIONS: Advanced age, diabetes mellitus, atrial fibrillation, end-stage renal disease, Eastern Cooperative Oncology Group score of 3, poorly differentiated tumors, and metastatic disease are unfavorable prognostic factors in MBC. Compared to female breast cancer, MBC showed poorer overall survival.

Song, I. A., et al. (2022). "Long-term opioid use and mortality in patients with chronic non-cancer pain: Ten-year follow-up study in South Korea from 2010 through 2019." EClinicalMedicine **51**: 101558.

BACKGROUND: We aimed to investigate the prevalence and factors associated with long-term opioid use among patients with chronic non-cancer pain (CNCP). METHODS: We extracted data from the National Health Insurance Service (NHIS) database in South Korea. As a nationwide database, the NHIS database contains information regarding all disease diagnoses and prescriptions for any drug and/or procedures. A total of 2.5% of adult patients (>/=20 years of age) who were diagnosed with musculoskeletal diseases and CNCP from 2010 to 2019 were selected using a stratified random sampling technique and included in the analysis. Patients who were prescribed opioids continuously for >/=90 days were classified as long-term opioid users. FINDINGS: A total of 19,645,161 patients with CNCP were included in the final analysis. The prevalence of long-term opioid use was 0.47% (95% confidence interval [CI]: 0.46%, 0.48%; 8421/1,808,043) in 2010, which gradually increased to 2.63% (95% CI: 2.61%, 2.66%; 49,846/1,892,913) in 2019. Among the 2010 cohort (n = 1,804,019), in multivariable logistic regression: old age, underlying disability, increased Charlson comorbidity index, use of benzodiazepine or Z-drug, rheumatoid arthritis, osteoarthritis, and low back pain were associated with an increased prevalence of long-term opioid use among patients with CNCP. In a multivariable Cox regression, the 10-year all-cause mortality in long-term opioid users was found to be 1.21-fold (hazard ratio: 1.21, 95% CI: 1.13, 1.31; P<0.001) higher than that in opioid-naive patients with CNCP. INTERPRETATION: Long-term opioid use increased in patients with CNCP in South Korea from 2010 to 2019. Certain factors were potential risk factors for long-term opioid use. Moreover, long-term opioid use was associated with increased 10-year all-cause mortality among patients with CNCP. FUNDING: None.

Song, M., et al. (2021). "Long-Term Incidence and Mortality of Colorectal Cancer After Endoscopic Biopsy With Normal Mucosa: A Swedish-Matched Cohort Study." Am J Gastroenterol **116**(2): 382-390.

INTRODUCTION: Endoscopic screening reduces colorectal cancer (CRC) incidence and mortality. Individuals with a negative result are recommended to undergo rescreening within a 10-year interval, but evidence supporting this advice is limited. METHODS: We performed a matched cohort study using prospectively collected data from 88,798 individuals in Sweden with normal mucosa at the first colorectal biopsy (aged >/=50 years) in the nationwide gastrointestinal epidemiology strengthened by histopathology reports (ESPRESSO) (1965-2016) and 424,150 matched reference individuals from the general population. Cox proportional hazards regression estimated multivariable hazard ratios and 95% confidence intervals (CIs) of CRC incidence and mortality of incident CRCs up to 44 years of follow-up. RESULTS: In the normal biopsy and reference groups, respectively, the 20-year incidences of CRC were 3.03% and 4.53% and the 20-year mortalities of incident CRC were 0.89% and 1.54%. The multivariable hazard ratio comparing the normal biopsy and reference groups was 0.62 for CRC incidence (95% CI = 0.58-0.66, P < 0.001) and 0.56 for mortality of incident CRC (95% CI = 0.49-0.64, P < 0.001). When assessed by time interval after biopsy, lower CRC incidence and mortality were observed throughout the follow-up. The association seemed weaker for proximal colon cancer than for rectal and distal colon cancer. DISCUSSION: A normal colorectal biopsy was associated with lower CRC incidence and mortality for at least 20 years after the examination. Our findings confirm previous data and suggest that the screening intervals after a normal colonoscopy could be longer than the commonly recommended 10 years. It may be time to open the discussion for a revision of the international guidelines.

Song, M., et al. (2021). "Associations of low hand grip strength with 1 year mortality of cancer cachexia: a multicentre observational study." J Cachexia Sarcopenia Muscle **12**(6): 1489-1500.

BACKGROUNDS: Hand grip strength (HGS) is one of diagnose criteria factors of sarcopenia and is associated with the survival of patients with cancer. However, few studies have addressed the association of HGS and 1 year mortality of patients with cancer cachexia. METHODS: This cohort study included 8466 patients with malignant solid tumour from 40 clinical centres throughout China. Cachexia was diagnosed using the 2011 International cancer cachexia consensus. The hazard ratio (HR) of all cancer

cachexia mortality was calculated using Cox proportional hazard regression models. Kaplan-Meier curves were generated to evaluate the association between HGS and the 1 year mortality of patients with cancer cachexia. The interaction analysis was used to explore the combined effect of low HGS and other factors on the overall survival of patients with cancer cachexia. RESULTS: Among all participants, 1434 (16.9%) patients with cancer were diagnosed with cachexia according to the 2011 International cancer cachexia consensus with a mean (SD) age of 57.75 (12.97) years, among which there were 871 (60.7%) male patients. The HGS optimal cut-off points of male and female patients were 19.87 and 14.3 kg, respectively. Patients with cancer cachexia had lower HGS than those patients without cachexia ($P < 0.05$). In the multivariable Cox analysis, low HGS was an independent risk factor of cachexia [HR: 1.491, 95% confidence interval (CI): 1.257-1.769] after adjusting other factors. In addition, all of cancer cachexia patients with lower HGS had unfavourable 1 year survival ($P < 0.001$). In a subset analysis, low HGS was an independent prognosis factor of male patients with cancer cachexia (HR: 1.623, 95% CI: 1.308-2.014, $P < 0.001$), but not in female patients (HR: 1.947, 95% CI: 0.956-3.963, $P = 0.0662$), and low HGS was associated with poor 1 year survival of digestive system, respiratory system, and other cancer cachexia patients (all $P < 0.05$). Low HGS has combined effects with high neutrophil-to-lymphocyte ratio or low albumin on unfavourable overall survival of patients with cancer cachexia. CONCLUSIONS: Low HGS was associated with poor 1 year survival of patients with cancer cachexia.

Song, M. J., et al. (2021). "A nationwide population-based study of incidence and mortality of lung cancer in idiopathic pulmonary fibrosis." Sci Rep **11**(1): 2596.

Idiopathic pulmonary fibrosis (IPF) is an independent risk factor for lung cancer (LC) development; however, there are currently no clinical guidelines for LC surveillance in IPF. This study aimed to investigate the cumulative incidence and survival outcomes of LC in IPF. Using the National Health Insurance Service database, including medical information on people aged >/= 40 years between 2011 and 2016, we identified IPF patients and confirmed the presence of comorbid LC. Patients diagnosed with IPF in 2011 were washed out, and mortality data were analyzed from 2012 to 2018. A total of 7277 newly diagnosed IPF patients were identified among Korean citizens aged >/= 40 years (about 50 million people) between 2011 and 2016. Their average age was 71.5 years and 72.8% of them were male. The prevalence of LC in the IPF cases was 6.4%. The cumulative incidence rates of LC in IPF patients who did not have LC at the time of IPF diagnosis were 1.7%, 4.7%, and 7.0%, at 1, 3, and 5 years, respectively. The median time from IPF diagnosis to LC development was 16.3 (Interquartile range, 8.2-28.8) months. The survival rate was significantly lower in the IPF with LC group than the IPF without LC group ($P < 0.001$). We concluded that IPF increases LC risk, and LC weakens survival outcomes in IPF. Close surveillance for LC development is mandatory for patients with IPF.

Song, S., et al. (2021). "Socioeconomic Inequalities in Premature Cancer Mortality Among U.S. Counties During 1999 to 2018." Cancer Epidemiol Biomarkers Prev **30**(7): 1375-1386.

BACKGROUND: This study investigated socioeconomic inequalities in premature cancer mortality by cancer types, and evaluated the associations between socioeconomic status (SES) and premature cancer mortality by cancer types. METHODS: Using multiple databases, cancer mortality was linked to SES and other county characteristics. The outcome measure was cancer mortality among adults ages 25-64 years in 3,028 U.S. counties, from 1999 to 2018. Socioeconomic inequalities in mortality were calculated as a concentration index (CI) by income (annual median household income), educational attainment (% with bachelor's degree or higher), and unemployment rate. A hierarchical linear mixed model and dominance analyses were used to investigate SES associated with county-level mortality. The analyses were also conducted by cancer types. RESULTS: CIs of SES factors varied by cancer types. Low-SES counties showed increasing trends in mortality, while high-SES counties showed decreasing trends. Socioeconomic inequalities in mortality among high-SES counties were larger than those among low-SES counties. SES explained 25.73% of the mortality. County-level cancer mortality was associated with income, educational attainment, and unemployment rate, at -0.24 [95% (CI): -0.36 to -0.12], -0.68 (95% CI: -0.87 to -0.50), and 1.50 (95% CI: 0.92-2.07) deaths per 100,000 population with one-unit SES factors increase, respectively, after controlling for health care environment and population health. CONCLUSIONS: SES acts as a key driver of premature cancer mortality, and socioeconomic inequalities differ by cancer types. IMPACT: Focused efforts that target socioeconomic drivers of mortalities and inequalities are warranted for designing cancer-prevention implementation strategies and control programs and policies for socioeconomically underprivileged groups.

Soni, K., et al. (2022). "Cancer surgery during COVID increased the patient mortality and the transmission risk to healthcare workers: results from a retrospective

cohort study (NCT05240378)." World J Surg Oncol **20**(1): 302.

BACKGROUND: India encountered two waves of COVID-19 pandemic with variability in its characteristics and severity. Concerns were raised over the safety of treatment, and higher morbidity was predicted for oncological surgery. The present study was conducted to evaluate and compare the rate of morbidity and mortality in patients undergoing curative surgery for cancer before and during the COVID-19 pandemic. METHOD: The prospectively obtained clinical data of 1576 patients treated between April 2019 and May 2021 was reviewed; of these, 959 patients were operated before COVID-19 and 617 during the pandemic. The data on complications, deaths, confirmed or suspected COVID-19 cases, and COVID-19 infection among health workers (HCW) was extracted. RESULTS: A 35% fall in number of surgeries was seen during the COVID period; significant fall was seen in genital and esophageal cancer. There was no difference in postoperative complication; however, the postoperative mortality was significantly higher. A total of 71 patients had COVID-19, of which 62 were preoperative and 9 postoperative, while 30/38 healthcare workers contracted COVID-19, of which 7 had the infection twice and 3 were infected after two doses of vaccination; there was no mortality in healthcare workers. CONCLUSION: The present study demonstrates higher mortality rates after surgery in cancer patients, with no significant change in morbidity rates. A substantial proportion of HCWs were also infected though there was no mortality among this group. The results suggest higher mortality in cancer patients despite following the guidelines and protocols.

Sopik, V. (2021). "International variation in breast cancer incidence and mortality in young women." Breast Cancer Res Treat **186**(2): 497-507.

PURPOSE: Breast cancer in young women (< 40 years) is rare and carries a poor prognosis relative to breast cancer in older women. Most studies examining global breast cancer patterns do not describe the trends in young women specifically. METHODS: Data from GLOBOCAN 2018 were used to compare breast cancer incidence and mortality rates among younger (ages 0-39) vs. older (ages 40+) women across 185 countries. The coefficient of variation (the ratio of the standard deviation to the mean) was used to quantify relative variability. RESULTS: The risk of developing breast cancer to age 39 ranged from 0.13% in Guinea to 0.95% in South Korea (coefficient of variation: 46%), and the risk of death from breast cancer to age 39 ranged from 0.02% in China to 0.72% in Cameroon (coefficient of variation: 81%). In contrast, the risk of developing breast cancer to age 74 ranged from 1.5% in Mozambique to 12.2% in Belgium (coefficient of variation: 50%), and the risk of death from breast cancer to age 74 ranged from 0.65% in South Korea to 3.0% in Somalia (coefficient of variation: 36%). CONCLUSIONS: Among young women, breast cancer mortality rates varied more worldwide than breast cancer incidence. In contrast, among older women/women of all ages, breast cancer incidence varied more than breast cancer mortality. Further research is required to examine the impact of stage at diagnosis, clinicopathologic features, and treatments received, on variations in the survival and mortality of breast cancer in young women around the world.

Sorce, G., et al. (2022). "Cancer-specific Mortality in T1a Renal Cell Carcinoma Treated with Local Tumor Destruction Versus Partial Nephrectomy." Eur Urol Focus.

BACKGROUND: Large-scale analyses addressing cancer-specific mortality (CSM) in T1a renal cell carcinoma (RCC) patients treated with local tumor destruction (LTD), relative to partial nephrectomy (PN), are scarce. OBJECTIVE: To compare CSM after LTD versus PN. DESIGN, SETTING, AND PARTICIPANTS: Within the Surveillance, Epidemiology, and End Results (SEER) database (2004-2018), we identified patients with clinical T1a stage RCC treated with LTD or PN. OUTCOME MEASUREMENTS AND STATISTICAL ANALYSES: After 1:1 ratio propensity score matching (PSM) between patients treated with LTD versus PN, competing risks regression (CRR) models addressed CSM, after adjustment for other-cause mortality (OCM) and other covariates (age, tumor size, tumor grade, and histological subtype). RESULTS AND LIMITATIONS: Relative to the 35 984 PN patients, 5936 LTD patients were older and more frequently harbored unknown RCC histological subtype or unknown grade. After 1:1 PSM that resulted in 5352 LTD versus 5352 PN patients, the 10-yr CSM rate was 8.7% versus 5.5%. In multivariable CRR models, LTD was associated with higher CSM, relative to PN (hazard ratio [HR]: 1.58, $p < 0.001$). Subgroup analyses revealed invariably higher CSM after LTD versus PN in patients with tumor size </=3 cm (10-yr CSM 7.2% vs 5.3%, multivariable HR: 1.47, $p < 0.001$) and in patients with tumor size 3.1-4 cm (10-yr CSM 11.4% vs 6.1%, multivariable HR: 1.72, $p < 0.001$). Lack of information regarding earlier cancer controls, retreatment, tumor location within the kidney, and type of surgery represented limitations. CONCLUSIONS: In T1a RCC patients, LTD is invariably associated with higher CSM relative to PN, even after adjustment for OCM and all available patient and tumor characteristics, and regardless of tumor size

considerations. However, the magnitude of CSM disadvantage was more pronounced in LTD patients with tumor size 3.1-4 cm than in those with tumor size </=3 cm. PATIENT SUMMARY: In patients with small renal masses, we observed higher cancer-specific death rates for local tumor destruction (LTD) than for partial nephrectomy. The LTD disadvantage was more pronounced for patients with tumor size 3.1-4 cm, but was also present in those with tumor size </=3 cm.

Sorce, G., et al. (2023). "Cancer-specific Mortality After Cryoablation vs Heat-based Thermal Ablation in T1a Renal Cell Carcinoma." J Urol **209**(1): 81-88.

PURPOSE: Guidelines suggest less favorable cancer control outcomes for local tumor destruction in T1a renal cell carcinoma patients with tumor size 3.1-4 cm. We compared cancer-specific mortality between cryoablation vs heat-based thermal ablation in patients with tumor size 3.1-4 cm, as well as in patients with tumor size </=3 cm. MATERIALS AND METHODS: Within the Surveillance, Epidemiology, and End Results database (2004-2018), we identified patients with clinical T1a stage renal cell carcinoma treated with cryoablation or heat-based thermal ablation. After up to 2:1 ratio propensity score matching between patients treated with cryoablation vs heat-based thermal ablation, we addressed cancer-specific mortality relying on competing risks regression models, adjusted for other-cause mortality and other covariates (age, tumor size, tumor grade, and histological subtype). RESULTS: Of 1,468 assessable patients with tumor size 3.1-4 cm, 1,080 vs 388 were treated with cryoablation vs heat-based thermal ablation, respectively. After up to 2:1 propensity score matching that resulted in 757 cryoablations vs 388 heat-based thermal ablations, in multivariable competing risks regression models, heat-based thermal ablation was associated with higher cancer-specific mortality (HR:2.02, P < .001), relative to cryoablation. Of 4,468 assessable patients with tumor size </=3 cm, 3,354 vs 1,114 were treated with cryoablation vs heat-based thermal ablation, respectively. After up to 2:1 propensity score matching that resulted in 2,217 cryoablations vs 1,114 heat-based thermal ablations, in multivariable competing risks regression models, heat-based thermal ablation was not associated with higher cancer-specific mortality (HR:1.13, P = .5) relative to cryoablation. CONCLUSIONS: Our findings corroborated that in cT1a patients with tumor size 3.1-4 cm, cancer-specific mortality is twofold higher after heat-based thermal ablation vs cryoablation. Conversely, in patients with tumor size </=3 cm either ablation technique is equally valid. These findings should be considered at clinical decision making and informed consent.

Soria-Utrilla, V., et al. (2022). "Prevalence of Anxiety and Depression Symptoms and Their Relationship with Nutritional Status and Mortality in Patients with Colorectal Cancer." Int J Environ Res Public Health **19**(20).

BACKGROUND: Anxiety and depression are common in patients with cancer. The aim of this study is to determine the prevalence of anxiety and depression symptoms in colorectal cancer (CRC) patients awaiting elective surgery and whether there is an association with their preoperative nutritional status and postoperative mortality. METHODS: A prospective study was conducted on 215 patients with CRC proposed for surgery. Data about nutritional status were collected using the Global Leadership Initiative on Malnutrition (GLIM) criteria, while anxiety and depression symptoms data were collected using Hospital Anxiety and Depression Scale (HADS). RESULTS: HADS detected possible anxiety in 41.9% of patients, probable anxiety in 25.6%, possible depression in 21.9%, and probable depression in 7.9%. GLIM criteria found 116 (53.9%) patients with malnutrition. The HADS score for depression subscale was significantly higher in malnourished patients than in well-nourished (5.61 +/- 3.65 vs. 3.95 +/- 2.68; p = 0.001). After controlling for potential confounders, malnourished patients were 10.19 times more likely to present probable depression (95% CI 1.13-92.24; p = 0.039). Mortality was 1.9%, 4,2%, and 5.6% during admission and after 6 and 12 months, respectively. Compared to patients without depressive symptomatology, in patients with probable depression, mortality risk was 14.67 times greater (95% CI 1.54-140.21; p = 0.02) during admission and 6.62 times greater (95% CI 1.34-32.61; p = 0.02) after 6 months. CONCLUSIONS: The presence of anxiety and depression symptoms in CRC patients awaiting elective surgery is high. There is an association between depression symptoms, preoperative nutritional status, and postoperative mortality.

Sorouri, M., et al. (2020). "Clinical characteristics, outcomes, and risk factors for mortality in hospitalized patients with COVID-19 and cancer history: a propensity score-matched study." Infect Agent Cancer **15**(1): 74.

BACKGROUND: COVID-19 has caused great concern for patients with underlying medical conditions. We aimed to determine the prognosis of patients with current or previous cancer with either a PCR-confirmed COVID-19 infection or a probable diagnosis according to chest CT scan. METHODS: We conducted a case control study in a referral hospital on confirmed COVID-19 adult patients with and without a history of cancer from February(25th) to April(21st), 2020. Patients were matched according to age, gender,

and underlying diseases including ischemic heart disease (IHD), diabetes mellitus (DM), and hypertension (HTN). Demographic features, clinical data, comorbidities, symptoms, vital signs, laboratory findings, and chest computed tomography (CT) images have been extracted from patients' medical records. Multivariable logistic regression was used to estimate odd ratios and 95% confidence intervals of each factor of interest with outcomes. RESULTS: Fifty-three confirmed COVID-19 patients with history of cancer were recruited and compared with 106 non-cancerous COVID-19 patients as controls. Male to female ratio was 1.33 and 45% were older than 65. Dyspnea and fever were the most common presenting symptoms in our population with 57.86 and 52.83% respectively. Moreover, dyspnea was significantly associated with an increased rate of mortality in the cancer subgroup (p = 0.013). Twenty-six patients (49%) survived among the cancer group while 89 patients (84%) survived in control (p = 0.000). in cancer group, patients with hematologic cancer had 63% mortality while patients with solid tumors had 37%. multivariate analysis model for survival prediction showed that history of cancer, impaired consciousness level, tachypnea, tachycardia, leukocytosis and thrombocytopenia were associated with an increased risk of death. CONCLUSION: In our study, cancer increased the mortality rate and hospital stay of COVID-19 patients and this effect remains significant after adjustment of confounders. Compared to solid tumors, hematologic malignancies have been associated with worse consequences and higher mortality rate. Clinical and para-clinical indicators were not appropriate to predict death in these patients.

Sorrentino, C., et al. (2022). "CRISPR/Cas9-mediated deletion of Interleukin-30 suppresses IGF1 and CXCL5 and boosts SOCS3 reducing prostate cancer growth and mortality." J Hematol Oncol **15**(1): 145.

BACKGROUND: Metastatic prostate cancer (PC) is a leading cause of cancer death in men worldwide. Targeting of the culprits of disease progression is an unmet need. Interleukin (IL)-30 promotes PC onset and development, but whether it can be a suitable therapeutic target remains to be investigated. Here, we shed light on the relationship between IL30 and canonical PC driver genes and explored the anti-tumor potential of CRISPR/Cas9-mediated deletion of IL30. METHODS: PC cell production of, and response to, IL30 was tested by flow cytometry, immunoelectron microscopy, invasion and migration assays and PCR arrays. Syngeneic and xenograft models were used to investigate the effects of IL30, and its deletion by CRISPR/Cas9 genome editing, on tumor growth. Bioinformatics of transcriptional data and immunopathology of PC samples were used to assess the translational value of the experimental findings. RESULTS: Human membrane-bound IL30 promoted PC cell proliferation, invasion and migration in association with STAT1/STAT3 phosphorylation, similarly to its murine, but secreted, counterpart. Both human and murine IL30 regulated PC driver and immunity genes and shared the upregulation of oncogenes, BCL2 and NFKB1, immunoregulatory mediators, IL1A, TNF, TLR4, PTGS2, PD-L1, STAT3, and chemokine receptors, CCR2, CCR4, CXCR5. In human PC cells, IL30 improved the release of IGF1 and CXCL5, which mediated, via autocrine loops, its potent proliferative effect. Deletion of IL30 dramatically downregulated BCL2, NFKB1, STAT3, IGF1 and CXCL5, whereas tumor suppressors, primarily SOCS3, were upregulated. Syngeneic and xenograft PC models demonstrated IL30's ability to boost cancer proliferation, vascularization and myeloid-derived cell infiltration, which were hindered, along with tumor growth and metastasis, by IL30 deletion, with improved host survival. RNA-Seq data from the PanCancer collection and immunohistochemistry of high-grade locally advanced PCs demonstrated an inverse association (chi-squared test, p = 0.0242) between IL30 and SOCS3 expression and a longer progression-free survival of patients with IL30(Neg)SOCS3(Pos)PC, when compared to patients with IL30(Pos)SOCS3(Neg)PC. CONCLUSIONS: Membrane-anchored IL30 expressed by human PC cells shares a tumor progression programs with its murine homolog and, via juxtacrine signals, steers a complex network of PC driver and immunity genes promoting prostate oncogenesis. The efficacy of CRISPR/Cas9-mediated targeting of IL30 in curbing PC progression paves the way for its clinical use.

Sousa, L. V. A., et al. (2021). "Inequalities in Mortality and Access to Hospital Care for Cervical Cancer-An Ecological Study." Int J Environ Res Public Health **18**(20).

Cervical cancer is the second most common form of cancer in the world among women, and it is estimated to be the third most frequent cancer in Brazil, as well as the fourth leading cause of death from cancer. There is a difference in cervical cancer mortality rates among different administrative regions in Brazil along with an inadequate distribution of cancer centers in certain Brazilian regions. Herein, we analyze the trends in hospital admission and mortality rates for CC between 2000 and 2012. This population-based ecological study evaluated the temporal trend in cervical cancer between the years 2000 and 2012, stratifying by Brazilian administrative regions. The North and Northeast regions had no reduction in mortality in all age groups studied (25 to 64 years); when analyzing hospitalization rates, only the age

group of 50 to 64 years from the North Region did not present a reduction. During the years studied, in the South Region, the age group ranging from 50 to 54 years had the greatest reduction in mortality rates (beta = -0.59, p = 0.001, r(2) = 0.63), and the group ranging from 45 to 49 years had the greatest reduction in hospital admission rates (beta = -8.87, p = 0.025, r(2) = 0.37). Between the years 2000 and 2012, the greatest reduction in the incidence of UCC was in the South Region (beta = -1.43, p = 0.236, r(2) = 0.12) followed by the Central-West (beta = -1, p < 0.001, r(2) = 0.84), the Southeast (beta = -0.95, p < 0.001, r(2) = 0.88), the Northeast (beta = -0.67, p = 0.080, r(2) = 0.25), and, finally, by the North (beta = -0.42, p = 0.157, r(2) = 0.17). There was a greater reduction in mortality rates and global hospitalization rates for CC in Brazil than in the United States during the same period with exceptions only in Brazil's North and Northeast regions.

Souza, B., et al. (2022). "Trend of incompleteness of cancer death records in the Mortality Information System database, state of Mato Grosso, Brazil, 2000 to 2016." Rev Bras Epidemiol **25**(Supl 1): e220003.

OBJECTIVE: To describe the trend of incompleteness of cancer death records in the Mortality Information System (SIM, in Portuguese) database, state of Mato Grosso, Brazil, 2000 to 2016. METHODS: This is a descriptive, ecological, time series study of records of death from cancer of people living in the state of Mato Grosso (codes C00 to C97 of the 10th revision of the International Statistical Classification of Diseases and Related Health Problems - ICD-10), collected from SIM. To asses incompleteness in the filling of the variables of race/skin color, education, marital status, occupation and underlying cause of death, the relative frequency was calculated in the percentage of null values. The time trend analyzes of the incomplete percentage of categories and variables of interest was performed using linear regression (p<0.05). RESULTS: From 2000 to 2016, there were 31,097 deaths from cancer among residents of the state of Mato Grosso. Race/skin color, marital status and occupation presented a stable trend of incompleteness; education and underlying cause of death were decreasing. An increasing trend was observed in the categories ignored (marital status) and retired (occupation); a decreasing trend was observed for blank (education), unidentified and housewife (occupation), and C76-other and ill-defined sites and C80-without specification of site (underlying cause of death). Incompleteness of occupation was classified as very poor, with emphasis on housewife and retired. For the remaining variables and categories, the classification was excellent or good. CONCLUSIONS: Although most of the indicators showed satisfactory trend and classification, the marital status and occupation variables stood out for indicating poorer quality in the records.

Sperling, C. D., et al. (2021). "Non-aspirin NSAID use and mortality of endometrial cancer. A nationwide cohort study." Cancer Causes Control **32**(5): 515-523.

PURPOSE: Laboratory studies have shown anti-neoplastic properties of non-aspirin NSAID; however, no studies have examined the influence of non-aspirin NSAIDs as potential adjuvant cancer therapy in women with endometrial cancer. We therefore examined the association between post-diagnostic use of non-aspirin NSAIDs and endometrial cancer mortality in Denmark. METHODS: We identified all women with a primary endometrial cancer diagnosis between 2000 and 2012, who were alive one year after the diagnosis. Information on drug use, cause-specific mortality and potential confounders was obtained from nationwide health- and demographic registries. Cox regression models were used to estimate adjusted hazard ratios (HRs) and 95% confidence intervals (CIs) for the association between post-diagnostic non-aspirin NSAID use and endometrial cancer mortality. RESULTS: Among 6 694 endometrial cancer patients with a maximum follow-up of 13 years, 753 women died from endometrial cancer. Post-diagnostic non-aspirin NSAID use (>/= 1 filled prescription) was associated with an overall HR of 1.15 (95% CI; 0.97-1.36) for endometrial cancer mortality, with higher HRs for the highest intensity of use (HR; 1.40, 95% CI; 1.11-1.77) and largest cumulative amount (HR; 1.56, 95% CI; 1.14-2.14). CONCLUSION: Our findings yielded no evidence that use of non-aspirin NSAIDs was associated with reduced endometrial cancer. Rather, we observed that high-intensity and large cumulative amount of non-aspirin NSAID use may be associated with increased endometrial cancer mortality.

Tao, Y., et al. (2021). "BRAF V600E Status Sharply Differentiates Lymph Node Metastasis-associated Mortality Risk in Papillary Thyroid Cancer." J Clin Endocrinol Metab **106**(11): 3228-3238.

CONTEXT: How lymph node metastasis (LNM)-associated mortality risk is affected by BRAF V600E in papillary thyroid cancer (PTC) remains undefined. OBJECTIVE: To study whether BRAF V600E affected LNM-associated mortality in PTC. DESIGN, SETTING, AND PARTICIPANTS: We retrospectively analyzed the effect of LNM on PTC-specific mortality with respect to BRAF status in 2638 patients (2015 females and 623 males) from 11 centers in 6 countries, with median age of 46 [interquartile range (IQR) 35-58] years and median follow-up time of 58 (IQR 26-107) months. RESULTS: Overall, LNM

showed a modest mortality risk in wild-type BRAF patients but a strong one in BRAF V600E patients. In conventional PTC (CPTC), LNM showed no increased mortality risk in wild-type BRAF patients but a robustly increased one in BRAF V600E patients; mortality rates were 2/659 (0.3%) vs 4/321 (1.2%) in non-LNM vs LNM patients (P = 0.094) with wild-type BRAF, corresponding to a hazard ratio (HR) (95% CI) of 4.37 (0.80-23.89), which remained insignificant at 3.32 (0.52-21.14) after multivariate adjustment. In BRAF V600E CPTC, morality rates were 7/515 (1.4%) vs 28/363 (7.7%) in non-LNM vs LNM patients (P < 0.001), corresponding to an HR of 4.90 (2.12-11.29) or, after multivariate adjustment, 5.76 (2.19-15.11). Adjusted mortality HR of coexisting LNM and BRAF V600E vs absence of both was 27.39 (5.15-145.80), with Kaplan-Meier analyses showing a similar synergism. CONCLUSIONS: LNM-associated mortality risk is sharply differentiated by the BRAF status in PTC; in CPTC, LNM showed no increased mortality risk with wild-type BRAF but a robust one with BRAF mutation. These results have strong clinical relevance.

Tashkandi, E., et al. (2020). "Thirty-Day Mortality After Curative and Palliative Anti-Cancer Treatment: Data Interpretation and Lessons for Clinical Implementation." Cancer Manag Res **12**: 12301-12308.

PURPOSE: Despite advancements in cancer therapeutics, mortality and morbidity due to anti-cancer treatments still occur but are not frequently reported. We aimed to report the 30-day mortality and morbidity of all curative and palliative anti-cancer treatments. PATIENTS AND METHODS: Adults with solid and hematological malignancies from two large cancer centers in Saudi Arabia, irrespective of the cancer stage and treatment type, were included in this retrospective observational study. RESULTS: Between December 1, 2019 and February 29, 2020, 1694 patients from King Abdullah Medical City in Makkah and King Fahad Medical City in Riyadh were included in the study. Among them, 77.5% were younger than 65 years of age; 72.8% were female; the prevalence of obesity, diabetes, and hypertension was 35%, 34%, and 28%, respectively; and 66.5% of patients had breast and gastrointestinal cancers. Fifty-nine (3.5%) patients died within 30 days of receiving anti-cancer treatment. Of them, 9 (0.3%) were treated with curative intent, and 50 (3%) were treated with palliative intent. CONCLUSION: Our results emphasize the need to address preventable metabolic changes and implement innovative, predictive, preventive, and personalized medicine (PPPM) approaches focusing on patient profiles. Reporting the 30-day outcomes of all anti-cancer treatments will also allow the identification of factors underlying mortality and morbidity and lead to an improvement in oncological outcomes via innovative programs designed to improve clinical decision-making.

Tatarinova, T. A. (2021). "[The morbidity and mortality of cervix cancer in The Russian Federation in 2007-2018]." Probl Sotsialnoi Gig Zdravookhranenniiai Istor Med **29**(4): 892-897.

All around the world, about 570 000 of new cases of cervical cancer are diagnosed annually and more than 300 000 of women die of this pathology. In the Russian Federation, in 2018, more than 17 500 of new cases of cervical cancer were diagnosed and more than 6 000 of women died of this pathology. The purpose of the study was to analyze incidence and mortality of cervical cancer in 2007-2018. The analysis of incidence rates of cervical cancer in the Russian Federation in 2007-2018 established steady trend of increasing of incidence rate from 12.8 (2007) to 15.8 (2018). The incidence rate increased up to 26.6%. The increasing is most pronounced in the age groups of 35-39, 40-44 and 45-49 years. The analysis of dynamics of mortality rates established relative stability indices in 2007-2018 (5.11 and 5.07 in standardized rates per 100 000). The decrease of 2018 as compared to 2007 made up to 0.78%. In most age groups mortality rates are decreasing. However, significant increase of mortality rate in age group of 40-44 years was established amounted up to 25%.

Tedesco, S., et al. (2021). "Investigation of the analysis of wearable data for cancer-specific mortality prediction in older adults." Annu Int Conf IEEE Eng Med Biol Soc **2021**: 1848-1851.

Cancer is an aggressive disease which imparts a tremendous socio-economic burden on the international community. Early detection is an important aspect in improving survival rates for cancer sufferers; however, very few studies have investigated the possibility of predicting which people have the highest risk to develop this disease, even years before the traditional symptoms first occur. In this paper, a dataset from a longitudinal study which was collected among 2291 70-year olds in Sweden has been analyzed to investigate the possibility for predicting 2-7 year cancer-specific mortality. A tailored ensemble model has been developed to tackle this highly imbalanced dataset. The performance with different feature subsets has been investigated to evaluate the impact that heterogeneous data sources may have on the overall model. While a full-features model shows an Area Under the ROC Curve (AUC-ROC) of 0.882, a feature subset which only includes demographics, self-report health and lifestyle data, and wearable dataset collected in free-living environments presents similar performance (AUC-ROC: 0.857). This analysis

confirms the importance of wearable technology for providing unbiased health markers and suggests its possible use in the accurate prediction of 2-7 year cancer-related mortality in older adults.

Teleka, S., et al. (2021). "Association between blood pressure and BMI with bladder cancer risk and mortality in 340,000 men in three Swedish cohorts." Cancer Med **10**(4): 1431-1438.

BACKGROUND: The relation between obesity, blood pressure (BP) and bladder cancer (BC) risk and mortality remains unclear, partially due to potential confounding by smoking, the strongest risk factor for BC, and not accounting for tumor stage and grade in such studies. We investigated body mass index (BMI) and BP in relation to BC risk by stage and grade, and BC-specific mortality, including separately among never-smokers aimed at minimizing confounding by smoking. METHODS: We analyzed 338,910 men from three Swedish cohorts, with 4895 incident BC's (940 among never-smokers) during follow-up. Cox regression was used to calculate hazard ratios (HR) and 95% confidence intervals adjusted for smoking status. HRs for BMI and BP were corrected for their regression dilution ratios, calculated from 280,456 individuals with 758,641 observations. RESULTS: Body mass index was positively associated with non-muscle invasive BC (NMIBC, HR per 5 kg/m(2) , 1.10 [1.02-1.19]) and NMIBC grade 3 (HR 1.17 [1.01-1.34]) in the full cohort, with similar effect sizes, albeit non-significant, among never-smokers. Systolic BP was positively associated with muscle-invasive BC (MIBC, HR per 10 mmHg, 1.25 [1.00-1.55]) and BC-specific mortality (HR 1.10 [1.01-1.20]) among never-smokers, with weaker and non-significant associations in the full cohort. CONCLUSIONS: In an analyses of BMI, BP and BC risk by stage and grade among men, we found modest positive associations between BMI and NMIBC and NMIBC grade 3. SBP was positively associated with MIBC and BC-specific mortality in an analysis of never-smokers, which may reflect the association, un-confounded by smoking, also in a broader population.

Tempo, J., et al. (2022). "Global changes in bladder cancer mortality in the elderly." Cancer Epidemiol **82**: 102294.

BACKGROUND: Bladder cancer is the 14th most common cause of cancer deaths worldwide and has a mean age of diagnosis of 73 years. Elderly people have fewer curative treatment options for muscle invasive bladder cancer. The aim of this study is to investigate how bladder cancer mortality has changed over the past forty years in different world regions to assess discrepancies between elderly and younger patients with bladder cancer. METHODS: Bladder cancer mortality data were extracted from the World Health Organisation's GLOBOCAN database. Age-standardised mortality rates (ASMR) for bladder cancer were computed by year, sex, region and Human Development Index (HDI) using the world standard population. RESULTS: Overall ASMR in all available countries with data between 1986 and 2014 for men aged >/= 75 has decreased from 101.2 to 89.9 per 100,000 (-11.2%). The decrease in ASMR for men < 75 has been 0.3-2.0 per 100,000 (-39.4%). In women aged >/= 75 ASMR has decreased from 26.9 to 22.5 per 100,000 (-16.4%) and in women < 75 the ASMR has decreased from 0.76 to 0.56 per 100,000 (-26.4%). Correlation analysis showed a positive linear relationship between Human Development Index (HDI) and improvement in age-standardised mortality rate in all ages. Pearson's coefficient showed that correlation was strongest in the 60-74 age group ($r = -0.61$, $p < 0.001$) and weakest in those aged >/= 75 ($r = -0.39$, $p = 0.01$). CONCLUSION: Bladder cancer mortality is not improving in the elderly at the same rate as the rest of the population. Particular focus should be applied in future research to enhance and expand treatment options for bladder cancer that are appropriate for elderly patients.

Teng, Y. H., et al. (2022). "Epidemiology and Mortality of Ovarian Cancer in Taiwan: A Population-Based Study." J Clin Med **11**(19).

Ovarian cancer is the second most common cause of death from gynecologic cancer. The aim of this study was to estimate the incidence of ovarian cancer and the trend of mortality in different histological subtypes of ovarian cancer in Taiwan. Patient information regarding ovarian cancer was provided by the Taiwan National Health Insurance database. The histological subtypes of ovarian cancer were retrieved from the Taiwan Cancer Registry database, while the survival rates were extracted from the National Death Registry database. In this population-based cohort study, the annual prevalence, incidence, and overall mortality of ovarian cancer during 2002-2015 were determined. The trend in the incidence and the mortality rate of different histologic subtypes were estimated using joinpoint regression analysis. It was found that age-standardized incidence of ovarian cancer increased from 9.46 in 2002 to 11.92 per 100,000 person-years in 2015, with an average annual percentage change of 2.0 (95% CI = 1.5-2.5). The 1-, 3-, and 5-year mortality rates of overall ovarian cancer declined progressively during the study period, especially the group of Charlson comorbidity index </= 1. Ovarian serous carcinoma was the most common histological subtype in Taiwan, comprising 30.9% of ovarian cancer patients in 2002-2015. This study

provides valuable information for use in developing healthcare policies for ovarian cancer.

Teoh, J. Y., et al. (2020). "Global Trends of Bladder Cancer Incidence and Mortality, and Their Associations with Tobacco Use and Gross Domestic Product Per Capita." Eur Urol **78**(6): 893-906.

BACKGROUND: Bladder cancer is a major urological disease, with approximately 550 000 new cases diagnosed in 2018. OBJECTIVE: We examined gender-specific incidence and mortality patterns, and trends of bladder cancer from a global perspective. We further investigated their associations with tobacco use and gross domestic product (GDP) per capita. DESIGN, SETTING, AND PARTICIPANTS: We retrieved data on the incidence and mortality of bladder cancer from the GLOBOCAN database, Cancer Incidence in Five Continents, and the WHO mortality database. Data on the rate of tobacco use were retrieved from the WHO Global Health Observatory. Data on GDP per capita was retrieved from the United Nations Human Development Report. OUTCOME MEASUREMENTS AND STATISTICAL ANALYSIS: We performed two sets of analyses. The first set of analysis is based on bladder cancer incidence and mortality data in 2018. The gender-specific age-standardised rates (ASRs) of incidence and mortality, and their correlations with the rate of tobacco use and GDP per capita were investigated. A multivariable linear regression analysis was also performed. In the second set of analysis, we examined the 10-yr temporal trends of bladder cancer incidence and mortality by average annual percent change using joinpoint regression analysis. A further exploratory analysis on GDP per capita in countries with decreasing trends of tobacco use was also performed. RESULTS AND LIMITATIONS: Wide variations in bladder cancer incidence and mortality were observed globally. There were positive correlations between the rate of tobacco use and the ASRs of bladder cancer incidence (r=0.20) and mortality (r=0.38) in men, and between the rate of tobacco use and the ASRs of bladder cancer incidence (r=0.67) and mortality (r=0.22) in women. There were positive correlations between GDP per capita, and the ASRs of bladder cancer incidence in men (r=0.48) and women (r=0.44). There was a weak positive correlation between GDP per capita and bladder cancer mortality in men (r=0.19), but no correlation with bladder cancer mortality in women (r=0.06). Upon multivariable linear regression analysis, tobacco use was significantly associated with bladder cancer incidence and mortality in men, and bladder cancer incidence in women. Regarding the 10-yr temporal trends of bladder cancer, Europe has an increasing incidence but decreasing mortality, and Asia has a decreasing incidence but increasing male mortality. Among countries with decreasing trends of tobacco use, the mean GDP per capita was higher in countries with decreasing trends of bladder cancer mortality than in those with increasing trends of bladder cancer mortality. A major limitation of the study is that cancer incidence might be underdetected and under-reported in less developed nations. CONCLUSIONS: There were observable trends of bladder cancer incidence and mortality globally. Tobacco use was significantly associated with both bladder cancer incidence and mortality. A certain level of economic capacity might be needed to further reduce bladder cancer mortality in countries with a decreasing trend of tobacco use. PATIENT SUMMARY: There are different trends of bladder cancer incidence and mortality globally. Smoking is significantly associated with the incidence and mortality of bladder cancer. A higher financial capacity may be needed to further improve the disease outcomes.

Teramoto, M., et al. (2022). "Secondhand Smoke Exposure in Childhood and Mortality from Coronary Heart Disease in Adulthood: the Japan Collaborative Cohort Study for Evaluation of Cancer Risk." J Atheroscler Thromb.

AIMS: We examined whether secondhand smoke exposure in childhood affects the risk of coronary heart disease (CHD) in adulthood. METHODS: In the Japan Collaborative Cohort Study, we analyzed data on 71,459 participants aged 40-79 years, with no history of CHD, stroke, or cancer at baseline (1988-1990) and who completed a lifestyle questionnaire including the number of smoking family members in childhood (0, 1, 2, and 3+ members) and followed them up until the end of 2009. The Cox proportional hazards model was used to calculate the multivariable hazard ratios (HRs) with 95% confidence intervals (CIs) of CHD mortality according to the number of smoking family members in childhood. RESULTS: During the median 18.9 years' follow-up, 955 CHD deaths were reported. There was a dose-response relationship between the number of smoking family members at home and CHD mortality among middle-aged individuals (40-59 years); the multivariable HRs (95% CIs) were 1.08 (0.76-1.54) for 1, 1.35 (0.87-2.08) for 2, and 2.49 (1.24-5.00) for 3+ smoking family members compared with 0 members (p for trend=0.03). The association for 3+ smoking family members among the middle-aged group was more evident in men than in women (the multivariable HRs [95% CIs] were 2.97 [1.34-6.58] and 1.65 [0.36-7.52], respectively) and more evident in non-current smokers than in current smokers (the multivariable HRs [95% CIs] were 4.24 [1.57-11.45]and 1.93 [0.72-5.15], respectively). CONCLUSIONS: Secondhand smoke

exposure in childhood was associated with an increased risk of CHD mortality in adulthood, primarily in middle-aged men and non-current smokers.

Teramoto, M., et al. (2022). "Secondhand Smoke Exposure During Childhood and Cancer Mortality in Adulthood Among Never Smokers: The Japan Collaborative Cohort Study for Evaluation of Cancer Risk." Am J Epidemiol **191**(5): 834-842.

We examined whether secondhand smoke exposure during childhood was associated with cancer mortality in adulthood among never smokers. In the Japan Collaborative Cohort Study for Evaluation of Cancer Risk, we analyzed data from 45,722 Japanese lifetime nonsmokers aged 40-79 years with no history of cancer at baseline (1988-1990) who had completed a lifestyle questionnaire, including information on the number of family members who had smoked at home during their childhood (0, 1, 2, or >/=3 family members). A Cox proportional hazards model and competing-risks regression were used to calculate multivariable hazard ratios and subdistribution hazard ratios with 95% confidence intervals for overall and site-specific cancer mortality according to the number of family members who smoked during the participant's childhood, after adjusting for potentially confounding factors. During a median follow-up period of 19.2 years, a total of 2,356 cancer deaths were documented. Secondhand smoke exposure was positively associated with the risk of mortality from pancreatic cancer in adulthood; the multivariable hazard ratio for having 3 or more family members who smoked (as compared with none) was 2.32 (95% confidence interval: 1.14, 4.72). Associations were not evident for total cancer risk or risk of other types of smoking-related cancer. In this study, secondhand smoke exposure during childhood was associated with an increased risk of pancreatic cancer mortality in adulthood.

Testa, R. S., et al. (2021). "Mortality and Life-Sustaining Therapy Decisions in Patients With Cancer and Acute Respiratory Failure Due to COVID-19 or Other Causes: An Observational Study." Front Med (Lausanne) **8**: 620818.

It is unknown if patients with cancer and acute respiratory failure due to COVID-19 have different clinical or cancer-related characteristics, decisions to forgo life-sustaining therapies (LST), and mortality compared to patients with cancer and acute respiratory failure due to other causes. In a cohort study, we tested the hypothesis that COVID-19 was associated with increased in-hospital mortality and decreased decisions to forgo LST in patients with cancer and acute respiratory failure. We employed two multivariate logistic regression models. Propensity score matching was employed as sensitivity analysis. We compared 382 patients without COVID-19 with 65 with COVID-19. Patients with COVID-19 had better performance status, less metastatic tumors, and progressive cancer. In-hospital mortality of patients with COVID-19 was lower compared with patients without COVID-19 (46.2 vs. 74.6%; $p < 0.01$). However, the cause of acute respiratory failure (COVID-19 or other causes) was not associated with increased in-hospital mortality [adjusted odds ratio (OR) 1.27 (0.55-2.93; 95% confidence interval, CI)] in the adjusted model. The percentage of patients with a decision to forgo LST was lower in patients with COVID-19 (15.4 vs. 36.1%; $p = 0.01$). However, COVID-19 was not associated with decisions to forgo LST [adjusted OR 1.21 (0.44-3.28; 95% CI)] in the adjusted model. The sensitivity analysis confirmed the primary analysis. In conclusion, COVID-19 was not associated with increased in-hospital mortality or decreased decisions to forgo LST in patients with cancer and acute respiratory failure. These patients had better performance status, less progressive cancer, less metastatic tumors, and less organ dysfunctions upon intensive care unit (ICU) admission than patients with acute respiratory failure due to other causes.

Teymoori, F., et al. (2022). "The association of dietary insulin load and index with the risk of cancer and cancer mortality: a systematic review and meta-analysis." J Diabetes Metab Disord **21**(1): 1105-1118.

PURPOSE: Insulin levels play an important role in cancer development. However, the link between an insulinogenic diet and cancer is still unclear. Therefore, we performed a systematic review with meta-analysis to investigate the association between dietary insulin index (II) and load (IL) with cancer risk and mortality. METHODS: A comprehensive search between electronic databases (Web of Science, PubMed/Medline, Scopus, and Google Scholar) was conducted to identify relevant studies up to January 2022. The relative risks (RR) and Odds ratios (OR) were extracted from eligible studies, and meta-analysis was performed to calculate the pooled effect size. RESULT: 12 papers including 14 studies (10 cohorts and 4 case-control) were included for the meta-analysis. Among them, 10 studies reported effect size for the risk of cancer, and 4 studies reported effect size for cancer mortality. We observed no significant association between II and IL with cancer overall (RR(II): 1.03, 95%CI: 0.91-1.17, RR(IL): 1.16, 95%CI: 0.94-1.42) and in cohort studies, however, in case-control studies was related with higher odds of cancer (OR(II): 2.30, 95%CI: 1.21-4.38, OR(IL): 2.57, 95%CI: 1.64-4.02). Higher II and IL scores were associated with the increased risk of total (RR(II): 1.29, 95%CI: 1.02-1.63) and (RR(IL): 1.39, 95%CI: 1.06-

1.83) and colorectal cancer mortality (RR(II): 1.29, 95%CI: 1.13-1.48) and (RR(IL): 1.37, 95%CI: 1.18-1.60). CONCLUSION: Higher dietary II and IL were not associated with cancer risk in overall and cohort studies, whereas related with a higher risk of cancer in case-control studies. We observed a significant positive relation of II and IL with cancer mortality, especially CRC mortality. SUPPLEMENTARY INFORMATION: The online version contains supplementary material available at 10.1007/s40200-022-01013-3.

Valencia, C. I., et al. (2021). "Renal Cell Carcinoma Health Disparities in Stage and Mortality among American Indians/Alaska Natives and Hispanic Americans: Comparison of National Cancer Database and Arizona Cancer Registry Data." Cancers (Basel) **13**(5).

Renal cell carcinoma (RCC) is one of the top 10 cancers in the United States. This study assessed RCC health disparities in American Indians/Alaska Natives (AIs/ANs) and Hispanic Americans (HAs) focusing on advanced-stage and mortality. RCC patients' data were obtained from the National Cancer Database (NCDB) and Arizona Cancer Registry (ACR). Logistic and Cox regression analyses were performed to ascertain the effect of race/ethnicity on stage and mortality, adjusting for neighborhood socioeconomic factors, rural/urban residence pattern, and other factors. In both data sets, AIs/ANs had significantly increased odds of advanced-stage RCC in the unadjusted model, but not in adjusted models. Mexican Americans had higher odds of advanced-stage compared to non-Hispanic Whites in NCDB (OR 1.22, 95% CI: 1.11-1.35) and ACR (OR 2.02, 95% CI: 1.58-2.58), even after adjusting for neighborhood characteristics. AIs/ANs did not show increased mortality risk in NCDB after adjusting for neighborhood characteristics, while the association remained significant in ACR (HR 1.33, 95% CI: 1.03-1.72). The great risk of all-cause and RCC-specific mortality was observed in U.S.-born Mexican Americans in Arizona (HR 3.21, 95% CI: 2.61-3.98 and sub-distribution HR 2.79, 95% CI: 2.05-3.81). RCC disparities in AIs/ANs is partially explained by neighborhood factors, but not in HAs.

Valenti, G., et al. (2022). "Parenchymal liver metastasis in advanced ovarian cancer: Can bowel involvement influence the frequency and the related mortality rate?" Eur J Obstet Gynecol Reprod Biol **280**: 48-53.

OBJECTIVE: This retrospective study estimates the frequency of parenchymal liver metastasis (PLM) and the overall survival (OS) rate of patients with FIGO Stage IIIC-IV Advanced Epithelial Ovarian Cancer (EOC) with bowel involvement. STUDY DESIGN: Between November 2008 and July 2020, all consecutive patients with FIGO Stage IIIC-IV EOC who underwent Visceral Peritoneal Debulking and bowel resection(s) at the Gynaecological Oncology Unit of "Centro di Riferimento Oncologico (CRO)", Aviano, Italy, without evidence of PLM at pre-operative imaging assessment, were included in the study. The presence and the time of the onset of PLM during the follow-up period were detected by diagnostic imaging (CT-scan, Ultrasound and PET). The OS of patients with and without PLM was compared. Considering the bowel's layers, the association between depth of bowel involvement, number of PLM, and the relative OS rate was evaluated. RESULTS: The median follow-up period was 47.3 (12-138) months. PLM occurred in 24/72 (33.0%) cases; the average onset time of PLM was 13 months. PLM was associated with increased significant mortality risk and an average OS of 33.2 versus 56.8 months ($p < 0.001$). The risk of developing PLM correlated directly with the depth of bowel involvement. However, there was no statistical difference between the layers in terms of OS at the end of the observational period. CONCLUSIONS: PLM occurred more frequently among patients with EOC and bowel involvement. The PLM arose within 15 months of follow-up and the frequency increased according to the depth of involvement. Particularly, the difference is remarkably higher starting from muscular layer where the total number of PLM arose significantly ($p = 0.02$). Although there was no significant difference among the infiltrated bowel layers in terms of OS, patients with bowel involvement up to muscular had a dramatic reduction in the OS rate during the first 30 months of follow-up.

Valerio, L., et al. (2022). "Decline in Overall Pulmonary Embolism-Related Mortality and Increasing Prevalence of Cancer-Associated Events in the Veneto Region (Italy), 2008-2019." Thromb Haemost **122**(5): 789-795.

BACKGROUND: Despite evidence of ongoing epidemiological changes in deaths from venous thromboembolism in high-income countries, little recent information is available on the time trends in mortality related to pulmonary embolism (PE) as underlying or concomitant cause of death in Europe. METHODS: We accessed the regional database of death certificates of Veneto Region (Northern Italy, population 4,900,000) from 2008 to 2019. We analyzed the trends in crude and age-adjusted annual rates of mortality related to PE (reported either as underlying cause or in any position in the death certificate) using Joinpoint regression; in the contribution of PE to mortality (proportionate mortality); and, using logistic

regression, in the association between PE and cancer at death. RESULTS: Between 2008 and 2019, the annual age-standardized mortality rate related to PE in Veneto decreased from 20.7 to 12.6 deaths per 100,000 population for PE in any position of the death certificate, and from 4.6 to 2.2 deaths per 100,000 population for PE as underlying cause of death. PE-related proportionate mortality remained up to twice as high in women. The age- and sex-adjusted odds ratio for cancer in deaths with versus without PE constantly increased from 1.01 (95% confidence interval [CI]: 0.88-1.16) in 2008 to 1.58 (95% CI: 1.35-1.83) in 2019. CONCLUSION: The descending trends in PE-related mortality reported for Europe up to 2015 for both sexes continued thereafter in this high-income region of Northern Italy. However, sex differences in proportionate mortality persist. The increasing strength in the association between cancer and PE may indicate a change in risk factor distribution, calling for tailored management practices in this patient group.

Van Blarigan, E. L., et al. (2023). "Dietary fat in relation to all-cause mortality and cancer progression and death among people with metastatic colorectal cancer: Data from CALGB 80405 (Alliance)/SWOG 80405." Int J Cancer **152**(2): 123-136.

Data on diet and survival among people with metastatic colorectal cancer are limited. We examined dietary fat in relation to all-cause mortality and cancer progression or death among 1149 people in the Cancer and Leukemia Group B (Alliance)/Southwest Oncology Group (SWOG) 80405 trial who completed a food frequency questionnaire at initiation of treatment for advanced or metastatic colorectal cancer. We examined saturated, monounsaturated, total and specific types (n-3, long-chain n-3 and n-6) of polyunsaturated fat, animal and vegetable fats. We hypothesized higher vegetable fat intake would be associated with lower risk of all-cause mortality and cancer progression. We used Cox proportional hazards regression to estimate adjusted hazard ratios (HR) and 95% confidence intervals (CI). Over median follow-up of 6.1 years (interquartile range [IQR]: 5.3, 7.2 y), we observed 974 deaths and 1077 events of progression or death. Participants had a median age of 59 y; 41% were female and 86% identified as White. Moderate or higher vegetable fat was associated with lower risk of mortality and cancer progression or death (HRs comparing second, third and fourth to first quartile for all-cause mortality: 0.74 [0.62, 0.90]; 0.75 [0.61, 0.91]; 0.79 [0.63, 1.00]; P trend: .12; for cancer progression or death: 0.74 [0.62, 0.89]; 0.78 [0.64, 0.95]; 0.71 [0.57, 0.88]; P trend: .01). No other fat type was associated with all-cause mortality and cancer progression or death. Moderate or higher vegetable fat intake may be associated with lower risk of cancer progression or death among people with metastatic colorectal cancer.

Van Blarigan, E. L., et al. (2022). "Associations Between Unprocessed Red Meat and Processed Meat With Risk of Recurrence and Mortality in Patients With Stage III Colon Cancer." JAMA Netw Open **5**(2): e220145.

IMPORTANCE: The American Cancer Society and American Institute for Cancer Research recommend that cancer survivors limit intake of red and processed meats. This recommendation is based on consistent associations between red and processed meat intake and cancer risk, particularly risk of colorectal cancer, but fewer data are available on red and processed meat intake after cancer diagnosis. OBJECTIVES: To examine whether intake of unprocessed red meat or processed meat is associated with risk of cancer recurrence or mortality in patients with colon cancer. DESIGN, SETTING, AND PARTICIPANTS: This prospective cohort study used data from participants with stage III colon cancer enrolled in the Cancer and Leukemia Group B (CALGB 89803/Alliance) trial between 1999 and 2001. The clinical database for this analysis was frozen on November 9, 2009; the current data analyses were finalized in December 2021. EXPOSURES: Quartiles of unprocessed red meat and processed meat intake assessed using a validated food frequency questionnaire during and 6 months after chemotherapy. MAIN OUTCOMES AND MEASURES: Hazard ratios (HRs) and 95% CIs for risk of cancer recurrence or death and all-cause mortality. RESULTS: This study was conducted among 1011 patients with stage III colon cancer. The median (IQR) age at enrollment was 60 (51-69) years, 442 patients (44%) were women, and 899 patients (89%) were White. Over a median (IQR) follow-up period of 6.6 (1.9-7.5) years, we observed 305 deaths and 81 recurrences without death during follow-up (386 events combined). Intake of unprocessed red meat or processed meat after colon cancer diagnosis was not associated with risk of recurrence or mortality. The multivariable HRs comparing the highest vs lowest quartiles for cancer recurrence or death were 0.84 (95% CI, 0.58-1.23) for unprocessed red meat and 1.05 (95% CI, 0.75-1.47) for processed meat. For all-cause mortality, the corresponding HRs were 0.71 (95% CI, 0.47-1.07) for unprocessed red meat and 1.04 (95% CI, 0.72-1.51) for processed meat. CONCLUSIONS AND RELEVANCE: In this cohort study, postdiagnosis intake of unprocessed red meat or processed meat was not associated with risk of recurrence or death among patients with stage III colon cancer.

Vukovic, M. M. N., et al. (2022). "Trend of breast cancer mortality in Montenegro, 1990-2018 - Joinpoint regression." Eur Rev Med Pharmacol Sci **26**(11): 3849-3857.

OBJECTIVE: In this study, we analyzed breast cancer mortality data overall and by age groups in women in Montenegro, to determine if there were any changes in trend for period 1990-2018. MATERIALS AND METHODS: The study gathered data on breast cancer mortality in Montenegro obtained from Vital Registration System. Annual data on breast cancer mortality were extracted for period 1990-2018 and analyzed using World Standard Population age-standardized and age-specific rates and Joinpoint regression. RESULTS: In 2018 in Montenegro, breast cancer accounted for 4.64% of all deaths in women and for 19.78% of all cancer deaths in women. In terms of total cancer mortality, it ranked first among women. Age-standardized rates ranged from 11.41/100,000 in 1990 to 20.46/100,000 in 2016. Joinpoint regression showed no one joinpoint for the entire population of all women and age groups. In the observed period, breast cancer mortality rates significantly increased in the women in Montenegro [average annual percentage change (AAPC) = 1.44%; 95% confidence interval (CI): 0.9-2.0]. The most affected age group was 55-64 years. CONCLUSIONS: There is a growing breast cancer mortality trend in Montenegro. It is necessary to create specific programs for urgent action, in order to reduce this undesirable trend. At the same time, support from the competent institutions is needed for increasing screening coverage and better prevention of breast cancer in the target population.

Wah, W., et al. (2021). "Influence of timeliness and receipt of first treatment on geographic variation in non-small cell lung cancer mortality." Int J Cancer **148**(8): 1828-1838.

Mortality from non-small cell lung cancer (NSCLC) exhibits substantial geographical disparities. However, there is little evidence on whether this variation could be attributed to patients' clinical characteristics and/or socioeconomic inequalities. This study evaluated the independent and relative contribution of the individual- and area-level risk factors on geographic variation in 2-year all-cause mortality among NSCLC patients. In the Hierarchical-related regression approach, we used the Bayesian spatial multilevel logistic regression model to combine individual- and area-level predictors with outcomes while accounting for geographically structured and unstructured correlation. Individual-level data included 3330 NSCLC cases reported to the Victoria Lung Cancer Registry between 2011 and 2016. Area-level data comprised socioeconomic disadvantage, remoteness and pollution data at the postal area level in Victoria, Australia. With the inclusion of significant individual- and area-level risk factors, timely (</=14 days) first definitive treatment (odds ratio [OR] = 0.73, 95% credible interval [Crl] = 0.56-0.94) and multidisciplinary meetings (MDM) (OR = 0.74, 95% Crl = 0.59-0.93) showed an independent association with a lower likelihood of NSCLC 2-year all-cause mortality. Timely and delayed (>14 days) first nondefinitive treatment, no treatment, advanced clinical stage, smoking, poor performance status, public hospital insurance and area-level deprivation were independently associated with a higher likelihood of 2- and 5-year all-cause mortality. NSCLC's 2-year all-cause mortality exhibited substantial geographic variation, mainly associated with timeliness and receipt of first definitive treatment, no treatment followed by patient prognostic factors with some contribution from area-level deprivation, MDM and public hospital insurance. This study highlights NSCLC patients should receive the first definitive treatment within the recommended 14-days from diagnosis.

Wakasugi, M., et al. (2021). "The Effect of CKD on Associations between Lifestyle Factors and All-cause, Cancer, and Cardiovascular Mortality: A Population-based Cohort Study." Intern Med **60**(14): 2189-2200.

Objective Results from previous studies on the dose-dependent effect of adhering to multiple lifestyle factors on all-cause mortality in patients with chronic kidney disease (CKD) are inconsistent, despite the reported dose-dependent effect in the general population. This study aimed to examine whether CKD modifies the dose-dependent effect of adhering to multiple lifestyle factors on mortality. Methods This population-based prospective cohort study targeted 262,011 men and women aged 40-74 years at baseline. Of these, 18.5% had CKD, which was defined as GFR <60 mL/min/1.73 m(2), >/=1+ proteinuria on urinalysis, or both. The following lifestyle behaviors were considered healthy: no smoking, body mass index <25 kg/m(2), moderate or lower alcohol consumption, regular exercise, and healthy eating habits. Healthy lifestyle scores were calculated by adding the total number of lifestyle factors for which each participant was at low risk. Cox proportional hazards models were used to examine associations between healthy lifestyle scores and all-cause, cancer, and cardiovascular mortality, and whether CKD modified these associations. Results During a median follow-up of 4.7 years, 3,471 participants died. The risks of all-cause and cancer mortality decreased as the number of five healthy lifestyle factors that were adhered to increased, irrespective of the CKD status. The risk of cardiovascular mortality, however, was modified by CKD (interaction p=0.07), and an unhealthy lifestyle and CKD synergistically increased cardiovascular

mortality. Conclusion A healthy lifestyle can reduce the risk of all-cause and cancer death in patients with or without CKD, while the prevention of CKD is essential for reducing the risk of cardiovascular death.

Wen, W., et al. (2021). "Racial disparities in mortality for patients with prostate cancer after radical prostatectomy." Cancer **127**(9): 1517-1528.

BACKGROUND: Although racial disparities in prostate cancer survival are well documented, the relative importance of contributing factors remains unclear. Few studies have examined the disparity between Whites and Hispanics or between Whites and Asian Americans and Pacific Islanders (AAPIs). METHODS: Using data from the National Cancer Database for 526,690 patients with prostate cancer who underwent radical prostatectomy between 2004 and 2014, this study systematically evaluated the impact of clinical characteristics and factors related to access to care on survival by race. Included in the analysis were 432,640 White patients (82.1%), 63,602 Black patients (12.1%), 8990 AAPI patients (1.7%), and 21,458 Hispanic patients (4.1%). Multivariable Cox proportional hazards models were used to estimate hazard ratios and 95% confidence intervals to measure racial survival disparities. Inverse probability weighting was used to adjust for imbalances of prognostic factors. RESULTS: When adjustments were made for age and year of diagnosis only, Blacks had 51% higher mortality, AAPIs had 22% lower mortality, and Hispanics had 6% lower mortality than Whites. Overall, with adjustments for all clinical factors and nonclinical factors, the Black-White survival disparity narrowed to 20%, whereas the AAPI-White disparity increased to 35%. Among the controlled-for factors, education, median household income, and insurance status contributed the most to the racial disparity. CONCLUSIONS: The overall survival disparity among men undergoing radical prostatectomy was significantly decreased, but not eliminated, for Blacks and significantly increased for AAPIs in comparison with Whites after adjustments for a number of clinical factors and factors related to access to care.

Wen, Y., et al. (2021). "Fibrinogen-to-Albumin Ratio is Associated with All-Cause Mortality in Cancer Patients." Int J Gen Med **14**: 4867-4875.

BACKGROUND: Past studies have identified fibrinogen-to-albumin ratio (FAR) as a novel prognostic immune biomarker in various diseases. Here, we investigated the prognostic value of FAR in all combined cancer mortality. METHODS: We extracted patient data from the Multiparameter Intelligent Monitoring in Intensive Care Database III. FAR was measured prior to hospital admission. Only first admission data from each patient were used. Baseline data were extracted within 24 h after admission. The clinical endpoints were 90- and 365-day all-cause cancer mortality. Cox proportional hazards models and subgroup analyses were used to determine the relationship between FAR and these clinical endpoints. RESULTS: A total of 652 eligible patients were enrolled. Upon adjusting for age and gender, multivariate analysis revealed correlation between higher FAR values and increased risk of all-cause mortality. After adjusting for more confounding factors, higher FAR values significantly correlated with 90- and 365-day all-cause mortality relative to low FAR values (tertile 3 vs tertile 1: HR, 95% CI: 1.65, 1.15-2.39; 1.52, 1.10-2.10). CONCLUSION: Our findings indicate that FAR may predict the risk of cancer mortality and is an independent prognostic indicator of all-cause mortality in cancer patients.

Wenzel, M., et al. (2022). "The impact of time to prostate specific antigen nadir on biochemical recurrence and mortality rates after radiation therapy for localized prostate cancer." Urol Oncol **40**(2): 57 e15-57 e23.

PURPOSE: To investigate the effect of time to prostate-specific antigen (PSA) nadir (TTN) after radiation therapy (RTx) for prostate cancer (PCa) on biochemical recurrence (BCR) and overall survival (OS) rates. PATIENTS AND METHODS: We analyzed 2,506 patients treated with RTx (external beam radiotherapy, brachytherapy or combinations) between years 2000 and 2021. Kaplan Meier and multivariable Cox regression models tested BCR-free survival and OS after stratification according to TTN (</=24 vs. 24.1-60 vs. >60 months). Similar analyses were performed after stratification according to absolute PSA values at nadir (<0.01 vs. 0.01-0.1 vs. 0.11-0.4 vs. >0.4 ng/ml). Finally, we repeated analyses after setting the time point of PSA nadir as the beginning of follow up in survival analyses. RESULTS: 10-year BCR-free survival rates were 55.5, 81.7 and 91.1% and OS rates were 71.5, 79.4 and 96.1% for TTN </=24 months, 24.1 month-60 month and >60 months, respectively. Longer TTN was an independent predictor for BCR-free survival and OS (all P<0.001). However, after accounting for lead-time bias, in multivariable analyses, this association remained only significant for BCR-free survival (P</=0.03), but not for OS (P>/=0.1). Finally, compared to a PSA nadir of <0.01 ng/ml, PSA nadir of 0.01-0.1 ng/ml, 0.11-0.4 ng/ml as well as >0.4 ng/ml were independent predictors for shorter BCR-free survival (P</=0.02), but not OS (P>/=0.08). CONCLUSION: Shorter time to TTN and high PSA values at nadir are indicative of early treatment failure (BCR) and OS. However, after accounting for lead-time bias, this effect only remained valid for BCR.

Wenzel, M., et al. (2021). "Non-cancer mortality in elderly prostate cancer patients treated with combination of radical prostatectomy and external beam radiation therapy." Prostate **81**(11): 728-735.

BACKGROUND: To test for rates of other cause mortality (OCM) and cancer-specific mortality (CSM) in elderly prostate cancer (PCa) patients treated with the combination of radical prostatectomy (RP) and external beam radiation therapy (EBRT) versus RP alone, since elderly PCa patients may be over-treated. METHODS: Within the Surveillance, Epidemiology and End Results database (2004-2016), cumulative incidence plots, after propensity score matching for cT-stage, cN-stage, prostate specific antigen, age and biopsy Gleason score, and multivariable competing risks regression models (socioeconomic status, pathological Gleason score) addressed OCM and CSM in patients (70-79, 70-74, and 75-79 years) treated with RP and EBRT versus RP alone. RESULTS: Of 18,126 eligible patients aged 70-79 years, 2520 (13.9%) underwent RP and EBRT versus 15,606 (86.1%) RP alone. After propensity score matching, 10-year OCM rates were respectively 27.9 versus 20.3% for RP and EBRT versus RP alone ($p < .001$), which resulted in a multivariable HR of 1.4 ($p < .001$). Moreover, 10-year CSM rates were respectively 13.4 versus 5.5% for RP and EBRT versus RP alone. In subgroup analyses separately addressing 70-74 year old and 75-79 years old PCa patients, 10-year OCM rates were 22.8 versus 16.2% and 39.5 versus 24.0% for respectively RP and EBRT versus RP alone patients (all $p < .001$). CONCLUSION: Elderly patients treated with RP and EBRT exhibited worrisome rates of OCM. These higher than expected OCM rates question the need for combination therapy (RP and EBRT) in elderly PCa patients and indicate the need for better patient selection, when combination therapy is contemplated.

Wenzel, M., et al. (2021). "Assessment of the optimal number of positive biopsy cores to discriminate between cancer-specific mortality in high-risk versus very high-risk prostate cancer patients." Prostate **81**(14): 1055-1063.

BACKGROUND: Number of positive prostate biopsy cores represents a key determinant between high versus very high-risk prostate cancer (PCa). We performed a critical appraisal of the association between the number of positive prostate biopsy cores and CSM in high versus very high-risk PCa. METHODS: Within Surveillance, Epidemiology, and End Results database (2010-2016), 13,836 high versus 20,359 very high-risk PCa patients were identified. Discrimination according to 11 different positive prostate biopsy core cut-offs (>/=2->/=12) were tested in Kaplan-Meier, cumulative incidence, and multivariable Cox and competing risks regression models. RESULTS: Among 11 tested positive prostate biopsy core cut-offs, more than or equal to 8 (high-risk vs. very high-risk: n = 18,986 vs. n = 15,209, median prostate-specific antigen [PSA]: 10.6 vs. 16.8 ng/ml, <.001) yielded optimal discrimination and was closely followed by the established more than or equal to 5 cut-off (high-risk vs. very high-risk: n = 13,836 vs. n = 20,359, median PSA: 16.5 vs. 11.1 ng/ml, $p < .001$). Stratification according to more than or equal to 8 positive prostate biopsy cores resulted in CSM rates of 4.1 versus 14.2% (delta: 10.1%, multivariable hazard ratio: 2.2, $p < .001$) and stratification according to more than or equal to 5 positive prostate biopsy cores with CSM rates of 3.7 versus 11.9% (delta: 8.2%, multivariable hazard ratio: 2.0, $p < .001$) in respectively high versus very high-risk PCa. CONCLUSIONS: The more than or equal to 8 positive prostate biopsy cores cutoff yielded optimal results. It was very closely followed by more than or equal to 5 positive prostate biopsy cores. In consequence, virtually the same endorsement may be made for either cutoff. However, more than or equal to 5 positive prostate biopsy cores cutoff, based on its existing wide implementation, might represent the optimal choice.

Wenzel, M., et al. (2022). "The effect of race/ethnicity on cancer-specific mortality after salvage radical prostatectomy." Front Oncol **12**: 874945.

BACKGROUND: To test the effect of race/ethnicity on cancer-specific mortality (CSM) after salvage radical prostatectomy (SRP). MATERIAL AND METHODS: We relied on the Surveillance, Epidemiology and End Results database (SEER, 2004-2016) to identify SRP patients of all race/ethnicity background. Univariate and multivariate Cox regression models addressed CSM according to race/ethnicity. RESULTS: Of 426 assessable SRP patients, Caucasians accounted for 299 (69.9%) vs. 68 (15.9%) African-Americans vs. 39 (9.1%) Hispanics vs. 20 (4.7%) Asians. At diagnosis, African-Americans (64 years) were younger than Caucasians (66 years), but not younger than Hispanics (66 years) and Asians (67 years). PSA at diagnosis was significantly higher in African-Americans (13.2 ng/ml), Hispanics (13.0 ng/ml), and Asians (12.2 ng/ml) than in Caucasians (7.8 ng/ml, $p = 0.01$). Moreover, the distribution of African-Americans (10.3%-36.6%) and Hispanics (0%-15.8%) varied according to SEER region. The 10-year CSM was 46.5% in African-Americans vs. 22.4% in Caucasians vs. 15.4% in Hispanics vs. 15.0% in Asians. After multivariate adjustment (for age, clinical T stage, lymph node dissection status), African-American race/ethnicity was an independent predictor of higher CSM (HR: 2.2, $p < 0.01$), but not Hispanic or Asian race/ethnicity. The independent effect of

African-American race/ethnicity did not persist after further adjustment for PSA. CONCLUSION: African-Americans treated with SRP are at higher risk of CSM than other racial/ethnic groups and also exhibited the highest baseline PSA. The independent effect of African-American race/ethnicity on higher CSM no longer applies after PSA adjustment since higher PSA represents a distinguishing feature in African-American patients.

Wu, F. Z., et al. (2022). "Impact of Smoking Status on Lung Cancer Characteristics and Mortality Rates between Screened and Non-Screened Lung Cancer Cohorts: Real-World Knowledge Translation and Education." J Pers Med **12**(1).

This was a retrospective hospital-based cohort study of participants diagnosed with lung cancer in the lung cancer register database, and our goal was to evaluate the impact of smoking and screening status on lung cancer characteristics and clinical outcomes. According to the hospital-based lung cancer register database, a total of 2883 lung cancers were diagnosed in 2883 patients between January 2007 and September 2017, which were divided into four groups according to smoking and screening status. A comparison was performed in terms of clinical characteristics and outcomes of lung cancer between the four groups. For non-smokers, age, gender, screened status, tumor size, targeted therapy, and curative surgery were independent prognostic factors of overall survival for lung cancer subjects. However, screened status and gender were not significant prognostic factors for lung cancer survival in smokers with lung cancer. For the non-smoker group, about 4.9% of lung cancer subjects (N = 81) were detected by screening. However, only 0.97% of lung cancer subjects (N = 12) were detected by screening in smokers. This could be attributed to smokers' negative attitudes and low socioeconomic status preventing LDCT lung cancer screening. In summary, our real-world data suggest that effectively encouraging smokers to be more willing to participate in lung cancer screening programs with screening allowance and educational training in the future is an important issue.

Wu, H. L., et al. (2022). "Dose-response relationship between epidural bupivacaine dose and mortality risk after surgical resection of nonsmall-cell lung cancer." J Chin Med Assoc **85**(9): 952-957.

BACKGROUND: Preclinical studies have shown that local anesthetics may modify the growth and invasion of cancer cells. However, few clinical studies have evaluated their impact on cancer outcomes after tumor resection. METHODS: In this single-center cohort study, patients who underwent surgical resection of stage IA through IIIB nonsmall-cell lung cancer and used patient-controlled epidural analgesia from 2005 to 2015 were recruited and followed until May 2017. Data of the epidural bupivacaine dose for each patient were obtained from infusion pump machines. Proportional hazards regression models were used to analyze the associations between bupivacaine dose with postoperative cancer recurrence and all-cause mortality. RESULTS: A total of 464 patients were analyzed. Among these patients, the mean bupivacaine dose was 352 mg (+/- standard deviation 74 mg). After adjusting for important clinical and pathological covariates, a significant dose-response relationship was observed between epidural bupivacaine dose and all-cause mortality (adjusted hazard ratio: 1.008, 95% confidence interval: 1.001-1.016, p = 0.029). The association between bupivacaine dose and cancer recurrence were not significant (adjusted hazard ratio: 1.000, 95% confidence interval: 0.997-1.002, p = 0.771). Age, sex, body mass index, mean daily maximum pain score, and pathological perineural infiltration were independently associated with bupivacaine dose. CONCLUSION: A dose-dependent association was found between epidural bupivacaine dose and long-term mortality among patients following surgical resection of nonsmall-cell lung cancer. Our findings do not support the hypothetical anticancer benefits of local anesthetics. More studies are needed to elucidate the role of local anesthetics in cancer treatment.

Wu, H. L., et al. (2021). "Epidural analgesia does not impact recurrence or mortality in patients after rectal cancer resection." Sci Rep **11**(1): 913.

The relationship between epidural analgesia and rectal cancer outcome is not fully clarified. We aimed to investigate the putative effect of epidural analgesia on the risks of recurrence and mortality after rectal tumour resection. In this monocentric cohort study, we consecutively enrolled patients with stage I-III rectal cancer who underwent tumour resection from 2005 to 2014. Patients received epidural analgesia or intravenous opioid-based analgesia for postoperative pain control. Primary endpoint was first cancer recurrence. Secondary endpoints were all-cause mortality and cancer-specific mortality. We collected 1282 patients in the inverse probability of treatment weighting analyses, and 237 (18.5%) used epidurals. Follow-up interval was median 46.1 months. Weighted Cox regression analysis showed the association between epidural analgesia and recurrence-free survival was non-significant (adjusted hazard ratio [HR] 0.941, 95% CI 0.791-1.119, p = 0.491). Similarly, the association between epidural analgesia and overall survival (HR 0.997, 95% CI 0.775-1.283, p = 0.984) or cancer-specific survival (HR 1.113, 95% CI 0.826-1.501, p = 0.482) was non-significant either. For

sensitivity tests, quintile stratification and stepwise forward model selection analyses showed similar results. We did not find a significant association between epidural analgesia and risk of recurrence, all-cause mortality, or cancer-specific mortality in patients with rectal cancer undergoing tumour resection.

Wu, M., et al. (2021). "Longitudinal changes in fasting plasma glucose are associated with risk of cancer mortality: A Chinese cohort study." Cancer Med **10**(15): 5321-5328.

BACKGROUND: Numerous studies have suggested that fasting plasma glucose (FPG) was associated with the risk of mortality. However, relationship on longitudinal changes of FPG with the risk of mortality remained inconsistent. METHODS: We examined the association of FPG at baseline and its longitudinal changes with risk of mortality based on a cohort study in Yinzhou, China, during 2010-2018. Cox regression models and competing risk models were separately used to examine the association of FPG levels and long-term fluctuation with risk of total and cause-specific mortality. RESULTS: Subjects who had an impaired fasting glucose or diabetes suffered a higher risk of total mortality than subjects who had a normal fasting glucose (HRs and 95% CIs: 1.17 [1.01-1.35], 1.30 [1.10-1.53], respectively). The HR for total mortality was 1.54 (95% CI: 1.29-1.84) and for cancer mortality was 1.41 (95% CI: 1.04-1.92) in the highest quartile of coefficient of variation of FPG. Trajectory analysis indicated that subjects with a significantly changed FPG suffered a higher risk of total mortality. CONCLUSION: According to this cohort study, we found that long-term fluctuation of FPG was significantly associated with the risk of total and cancer mortality. Our findings suggest that long-term fluctuation of FPG could be used as an efficient indicator for predicting the subsequent risk of mortality.

Wu, S. L., et al. (2022). "Gastric cancer incidence, mortality and burden in adolescents and young adults: a time-trend analysis and comparison among China, South Korea, Japan and the USA." BMJ Open **12**(7): e061038.

OBJECTIVES: To evaluate and compare the burden of gastric cancer in adolescents and young adults (GCAYA) among China, South Korea, Japan and the USA, four countries with similar or different rates of gastric cancer (GC) incidence, development levels and cancer control strategies. DESIGN: This population-based observational study collected the epidemiological data of GCAYA from the Global Burden of Diseases Study 2019. The trend magnitude and directions over time for incidence and mortality of GCAYA were analysed and compared among four countries. MAIN OUTCOMES AND MEASURES: Outcomes included new cases, deaths, mortality-to-incidence ratios (MIRs), disability-adjusted life years, and their age-standardised rates and estimated annual percentage changes (AAPCs). RESULTS: There were 49 008 new cases and 27 895 deaths from GCAYA in 2019, nearly half of which occurred in China. The AAPCs for the age-standardised incidence and mortality rate were 0.3 (-0.1 to 0.7), -3.6 (-3.7 to -3.4), -3.2 (-3.8 to -2.6), -0.1 (-0.6 to 0.5) and -2.0 (-2.3 to -1.6), -5.6 (-6.2 to -5.0), -4.4 (-4.7 to -4.1), -0.7 (-1.0 to -0.3) in China, South Korea, Japan and the USA, respectively. The incidence rate for females in the USA rose by 0.4% annually. GC ranks fifth, first, fourth and ninth in China, South Korea, Japan and the USA regarding burdens caused by cancer in adolescents and young adults. The MIRs declined constantly in South Korea and China, and the MIR in the USA became the highest in 2019. CONCLUSIONS: Although not covered by prevention and screening programmes, variations in disease burden and time trends may reflect variations in risk factors, cancer control strategies and treatment accessibility of GC among the four countries. Investigating the reasons behind the varying disease burden and changing trends of GCAYA across countries will inform recommendations for prevention measures and timely diagnosis specific to this underserved population to further decrease the GC burden.

Wu, X., et al. (2022). "Determining Association between Lung Cancer Mortality Worldwide and Risk Factors Using Fuzzy Inference Modeling and Random Forest Modeling." Int J Environ Res Public Health **19**(21).

Lung cancer remains the leading cause for cancer mortality worldwide. While it is well-known that smoking is an avoidable high-risk factor for lung cancer, it is necessary to identify the extent to which other modified risk factors might further affect the cell's genetic predisposition for lung cancer susceptibility, and the spreading of carcinogens in various geographical zones. This study aims to examine the association between lung cancer mortality (LCM) and major risk factors. We used Fuzzy Inference Modeling (FIM) and Random Forest Modeling (RFM) approaches to analyze LCM and its possible links to 30 risk factors in 100 countries over the period from 2006 to 2016. Analysis results suggest that in addition to smoking, low physical activity, child wasting, low birth weight due to short gestation, iron deficiency, diet low in nuts and seeds, vitamin A deficiency, low bone mineral density, air pollution, and a diet high in sodium are potential risk factors associated with LCM. This study demonstrates the usefulness of two approaches for multi-factor analysis

of determining risk factors associated with cancer mortality.

Wu, X., et al. (2021). "Cause-specific mortality of low and selective intermediate-risk prostate cancer patients with active surveillance or watchful waiting." Transl Androl Urol **10**(1): 154-163.

BACKGROUND: Active surveillance or watchful waiting (AS/WW) is increasingly being used as an alternative strategy to radical prostatectomy or radiation therapy for appropriately selected patients with prostate cancer (PCa). However, the prognosis of low-risk and selective intermediate-risk PCa patients after AS/WW is poorly defined. In this study we reviewed the patients registered in the Surveillance, Epidemiology, and End Results (SEER) Program to establish a competing risk nomogram for the prediction of prostate cancer-specific mortality (PCSM). METHODS: The information of patients undergoing AS/WW in the SEER program from 2004 to 2015 was obtained. All patients were ISUP (International Society of Urological Pathology) grade 1 or 2 PCa and also fulfilled the National Comprehensive Cancer Network's definition of low-risk PCa [prostate specific antigen (PSA) <10 ng/mL and cT2aN0M0 or less)]. A competing risk nomogram was used to analyze the association of tumor characteristics with PCSM and non-PCSM among the PCa patients with AS/WW. All cases were randomly divided into a training cohort and a validation cohort (1:1). A competing risk nomogram was constructed to predict PCSM in PCa patients with AS/WW. The performance of the PCSM nomogram was evaluated using the concordance index (C-index) and calibration curve. RESULTS: A total of 30,538 PCa patients were identified as low risk or selective intermediate risk with AS/WW. The 10-year cumulative incidence of death from prostate cancer and death from other cause were 2.8% (95% CI: 2.4-3.1%) and 19.3% (95% CI: 17.8-20.5%), respectively. Variables associated with PCSM included age, marital status, PSA, and ISUP grade. The PCSM nomogram had a good performance in both the training and validation cohorts, with a C-index of 0.744 (95% CI: 0.700-0.781, P<0.001) and 0.738 (95% CI: 0.700-0.777, P<0.001), respectively. CONCLUSIONS: Overall, the prognosis was favorable for the low- and selective intermediate-risk PCa patients with AS/WW. The competing risk nomogram yielded a good performance in identifying subgroups of patients with a higher risk of PCSM and potential candidates for AS/WW.

Wu, X., et al. (2022). "Nutritional status, lifestyle habits and cancer mortality: a population-based prospective cohort study." Eur J Nutr **61**(3): 1343-1352.

PURPOSE: We aimed to investigate the relationship between overall nutritional status and cancer mortality. METHODS: A total of 12 262 US adults from six consecutive surveys of the National Health and Nutrition Examination Survey (NHANES 2003-2014) were analyzed. The overall health nutritional biomarkers index (HNBI) score, capturing characteristics of 17 biomarkers was developed to assess the overall nutritional status. The lower the HNBI score, the healthier nutritional status would be. Hazard ratio (HR) and 95% confidence intervals (95% CIs) were calculated by Cox proportional hazards regression models to evaluate the association between the HNBI score and cancer mortality. RESULTS: The lower overall HNBI score was associated with decreased risk of cancer mortality, compared with participants in the 4th quartile of overall HNBI score, the HR (95% CIs) for participants in the 1st quartiles was 0.54 (0.33-0.89) (P-trend = 0.019). Healthier lifestyle habits and not obesity interacted with HNBI score, compared with participants with higher HNBI score and smoking currently/not exercising regularly/obesity, participants with lower HNBI score and not smoking currently/exercising regularly/not obesity were associated with lower risk of cancer mortality, the HR (95% CIs) were 0.43 (0.26-0.73), 0.57 (0.33-0.97), and 0.62 (0.47-0.97), respectively. These significant associations remained among participants who were followed-up more than 2 years. CONCLUSION: Our findings suggested that healthier overall nutritional status was associated with lower risk of cancer mortality among US adults. Not smoking, exercise regularly and not obesity interacted with overall nutritional status. Adherence to better overall nutritional status, lifestyle habits and optimal weight would prevent premature death from cancer.

Wu, Y., et al. (2022). "Using machine learning for mortality prediction and risk stratification in atezolizumab-treated cancer patients: Integrative analysis of eight clinical trials." Cancer Med.

BACKGROUND: Few models exist to predict mortality in cancer patients receiving immunotherapy. Our aim was to build a machine learning-based risk stratification model for predicting mortality in atezolizumab-treated cancer patients. METHODS: Data from 2538 patients in eight atezolizumab-treated cancer clinical trials across three cancer types (non-small-cell lung cancer, bladder transitional cell carcinoma, and renal cell carcinoma) were included. The whole cohort was randomly split into development and validation cohorts in a 7:3 ratio. Machine-learning algorithms (extreme gradient boosting, random forest, logistic regression with lasso regularization, support vector machine, and K-nearest neighbor) were applied to develop prediction models. Model performance was

mainly assessed by area under the receiver operating characteristic curve (AUC) value, calibration plot, and decision curve analysis. The probability of death risk was then stratified. RESULTS: One thousand and three hundred and seventy-nine (54.33%) patients died. The random forest (RF) model was overall the best in terms of predictive performance, with the AUC of 0.844 (95% confidence interval [CI]: 0.826-0.862) in the development cohort and 0.786 (95% CI: 0.754-0.818) in the validation cohort for predicting mortality. Twelve baseline variables contributing to mortality prediction in the RF model were C-reactive protein, PD-L1 level, cancer type, prior liver metastasis, derived neutrophil-to-lymphocyte ratio, alkaline phosphatase, albumin, hemoglobin, white blood cell count, number of metastatic sites, pulse rate, and Eastern Cooperative Oncology Group (ECOG) performance status. A total of 1782 (70.2%) patients were separated into the high-risk and 756 (29.8%) low-risk groups. Patients in the high-risk group were significantly more likely to die, experience disease progression, discontinue study, and discontinue treatment than patients in the low-risk group (all p values < 0.001). Risk groups were not associated with immune-related adverse events and grades 3-5 treatment-related adverse events (all p values > 0.05). CONCLUSION: RF model has good performance in mortality prediction and risk stratification for cancer patients receiving atezolizumab monotherapy.

Wulczyn, E., et al. (2021). "Predicting prostate cancer specific-mortality with artificial intelligence-based Gleason grading." Commun Med (Lond) **1**: 10.

BACKGROUND: Gleason grading of prostate cancer is an important prognostic factor, but suffers from poor reproducibility, particularly among non-subspecialist pathologists. Although artificial intelligence (A.I.) tools have demonstrated Gleason grading on-par with expert pathologists, it remains an open question whether and to what extent A.I. grading translates to better prognostication. METHODS: In this study, we developed a system to predict prostate cancer-specific mortality via A.I.-based Gleason grading and subsequently evaluated its ability to risk-stratify patients on an independent retrospective cohort of 2807 prostatectomy cases from a single European center with 5-25 years of follow-up (median: 13, interquartile range 9-17). RESULTS: Here, we show that the A.I.'s risk scores produced a C-index of 0.84 (95% CI 0.80-0.87) for prostate cancer-specific mortality. Upon discretizing these risk scores into risk groups analogous to pathologist Grade Groups (GG), the A.I. has a C-index of 0.82 (95% CI 0.78-0.85). On the subset of cases with a GG provided in the original pathology report (n = 1517), the A.I.'s C-indices are 0.87 and 0.85 for continuous and discrete grading, respectively, compared to 0.79 (95% CI 0.71-0.86) for GG obtained from the reports. These represent improvements of 0.08 (95% CI 0.01-0.15) and 0.07 (95% CI 0.00-0.14), respectively. CONCLUSIONS: Our results suggest that A.I.-based Gleason grading can lead to effective risk stratification, and warrants further evaluation for improving disease management.

Wurnschimmel, C., et al. (2021). "Validation of the STAR-CAP Clinical Prognostic System for Predicting Biochemical Recurrence, Metastasis, and Cancer-specific Mortality After Radical Prostatectomy in a European Cohort." Eur Urol **80**(4): 400-404.

The proposed international staging collaboration for cancer of the prostate (STAR-CAP) clinical prognostic system for prostate cancer predicts cancer-specific mortality (CSM) for patients for whom active treatment, such as radical prostatectomy (RP), is planned. Until now, no validation of STAR-CAP has been performed. We retrospectively analyzed data from our institutional database for 19 552 patients treated with RP between 1992 and 2015. We applied the STAR-CAP point assignment criteria to calculate total individual scores and then classified patients according to the STAR-CAP stage groups ranging from IA (lowest risk) to IIIC (highest risk). We evaluated biochemical recurrence (BCR)-free survival, metastasis-free survival (MFS), and cancer-specific survival (CSS) stratified by STAR-CAP stage groups over 10 yr, calculated the area under the receiver operating characteristics curve (AUC), and performed decision curve analyses to assess the ability of STAR-CAP to predict these outcomes after fitting the data from our single-institution data set. STAR-CAP performed well in stratifying individual survival outcomes for BCR-free survival, MFS, and CSS for each stage group in Kaplan-Meier analyses (p < 0.001 between groups). The AUC for prediction of BCR, metastasis, and CSM at 10 yr was 0.73, 0.84, and 0.75, respectively. Our findings validate the performance of STAR-CAP for European patients treated with RP. PATIENT SUMMARY: We validated the STAR-CAP system for predicting cancer outcomes after removal of the prostate. Our results show that the system performs well and could help in counseling patients with prostate cancer.

Xia, Q., et al. (2022). "shinyOPTIK, a User-Friendly R Shiny Application for Visualizing Cancer Risk Factors and Mortality Across the University of Kansas Cancer Center Catchment Area." JCO Clin Cancer Inform **6**: e2100118.

PURPOSE: The University of Kansas Cancer Center (KU Cancer Center) recently developed a data warehouse to Organize and Prioritize Trends to Inform KU Cancer Center (OPTIK). The OPTIK database

aggregates and standardizes data collected across the bistate catchment area served by the KU Cancer Center. To improve the usability of the OPTIK database, we developed shinyOPTIK, a user-friendly, interactive web application for visualizing cancer risk factor and mortality rate data across the KU Cancer Center Catchment area. METHODS: Data in the OPTIK database were first consolidated at the county level across the KU Cancer Center catchment area. Next, the shinyOPTIK development team met with the KU Cancer Center leadership to discuss the needs and priorities of the shinyOPTIK web application. shinyOPTIK was developed under the R Shiny framework and consists of a user interface (ui.R) and a web server (server.R). At present, shinyOPTIK can be used to generate county-level geographical heatmaps; bar plots of demographic, screening, and risk factors; and line plots to visualize temporal trends at different Rural-Urban Continuum Codes (RUCCs), rural-urban status, metropolitan, or county levels across the KU Cancer Center catchment area. RESULTS: Two examples, adult obesity prevalence and lung cancer mortality, are presented to illustrate how researchers can use shinyOPTIK. Each example is accompanied by post hoc visualizations to help explain key observations in terms of rural-urban disparities. CONCLUSION: Although shinyOPTIK was developed to improve understanding of spatial and temporal trends across the population served by the KU Cancer Center, our hope is that the description of the steps involved in the creation of this tool along with open-source code for our application provided herein will serve as a guide for other research centers in the development of similar tools.

Xiu, W., et al. (2022). "Comorbidities and mortality risk among extensive-stage small-cell lung cancer patients in mainland China: impacts of hypertension, type 2 diabetes mellitus, and chronic hepatitis B virus infection." Anticancer Drugs **33**(1): 80-90.

The present study investigated the impact of major comorbidities, including hypertension, type 2 diabetes mellitus (T2DM), and chronic hepatitis B virus (HBV) infection, on the progression-free survival (PFS) and overall survival (OS) of extensive-stage small-cell lung cancer (ES-SCLC) patients in China. Patients having a pathologic diagnosis of ES-SCLC between 2009 and 2017 were enrolled and grouped according to their specific comorbidities. The PFS and OS for each group were evaluated using the Kaplan-Meier method and Cox proportional hazard models. In total, 632 patients were analyzed. The median PFS (mPFS) of these patients was 9 months [95% confidence interval (CI), 6-12 months]. The mPFS of patients without hypertension or T2DM was 9 months; conversely, it was significantly reduced for patients with hypertension [7 months ($P < 0.0001$)] or T2DM [5 months ($P < 0.0001$)]. However, mPFS was not significantly different between patients with and without HBV infection ($P = 0.2936$). A similar trend was observed for OS as well. Further multivariate analyses showed that the OS of patients with hypertension [hazard ratio (HR), 1.344; 95% CI, 1.073-1.683; $P = 0.010$] or T2DM (HR, 1.455; 95% CI, 1.134-1.868; $P = 0.003$) was significantly shorter than that of patients without these comorbidities. Accordingly, mortality risk was the highest in patients with concurrent hypertension and T2DM (HR, 1.665; 95% CI, 1.037-2.672; $P = 0.00058$). Our study found that hypertension and T2DM may be associated with a worse prognosis in ES-SCLC patients. Considerable attention should be paid to the accompanying anti-comorbidity therapies available for patients with ES-SCLC.

Xu, B., et al. (2021). "Association of dietary intake of branched-chain amino acids with long-term risks of CVD, cancer and all-cause mortality." Public Health Nutr: 1-11.

OBJECTIVES: We aimed to investigate the associations between dietary branched-chain amino acids (BCAA) intake and long-term risks of CVD, cancer and all-cause mortality in nationwide survey participants aged >/= 18. DESIGN: This was a prospective cohort study. Dietary intakes of BCAA (leucine, isoleucine and valine) were determined from the total nutrient intake document. The main outcomes were CVD, cancer and all-cause mortality. SETTING: A nationally representative sample of US adults were recruited by the National Center for Health Statistics (NCHS) from 1988 to 1994. PARTICIPANTS: A total of 14 397 adults aged >/= 18 who participated in the United States National Health and Nutrition Examination Survey III (NHANES III) were included. RESULTS: During 289 406 person-years of follow-up, we identified 4219 deaths, including 1133 from CVD and 926 from cancer. After multivariate adjustment, the hazard ratios (95 % confidence intervals) of all-cause mortality in the highest dietary BCAA and isoleucine intake quintile (reference: lowest quintiles) were 0.68 (0.48, 0.97) and 0.68 (0.48, 0.97), respectively. Each one-standard-deviation increase in total dietary BCAA or isoleucine intake was associated with an 18 % or 21 % decrease in the risk of all-cause mortality, respectively. The serum triglyceride (TAG) concentration was found to modify the association between the dietary BCAA intake and all-cause mortality (Pfor interaction = 0.008). CONCLUSIONS: In a nationally representative cohort, higher dietary intakes of BCAA and isoleucine were independently associated with a lower risk of all-cause mortality, and

these associations were stronger in participants with higher serum TAG concentrations.

Xu, C., et al. (2022). "Machine learning models for 180-day mortality prediction of patients with advanced cancer using patient-reported symptom data." Qual Life Res.

PURPOSE: The objective of the current study was to develop and test the performances of different ML algorithms which were trained using patient-reported symptom severity data to predict mortality within 180 days for patients with advanced cancer. METHODS: We randomly selected 630 of 689 patients with advanced cancer at our institution who completed symptom PRO measures as part of routine care between 2009 and 2020. Using clinical, demographic, and PRO data, we trained and tested four ML algorithms: generalized regression with elastic net regularization (GLM), extreme gradient boosting (XGBoost) trees, support vector machines (SVM), and a single hidden layer neural network (NNET). We assessed the performance of algorithms individually as well as part of an unweighted voting ensemble on the hold-out testing sample. Performance was assessed using area under the receiver-operating characteristic curve (AUROC), sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV). RESULTS: The starting cohort of 630 patients was randomly partitioned into training (n = 504) and testing (n = 126) samples. Of the four ML models, the XGBoost algorithm demonstrated the best performance for 180-day mortality prediction in testing data (AUROC = 0.69, sensitivity = 0.68, specificity = 0.62, PPV = 0.66, NPV = 0.64). Ensemble of all algorithms performed worst (AUROC = 0.65, sensitivity = 0.65, specificity = 0.62, PPV = 0.65, NPV = 0.62). Of individual PRO symptoms, shortness of breath emerged as the variable of highest impact on the XGBoost 180-mortality prediction (1-AUROC = 0.30). CONCLUSION: Our findings support ML models driven by patient-reported symptom severity as accurate predictors of short-term mortality in patients with advanced cancer, highlighting the opportunity to integrate these models prospectively into future studies of goal-concordant care.

Xu, H. F., et al. (2022). "[Changing trend of incidence and mortality of stomach cancer during 2010-2016 in Henan Province, China]." Zhonghua Zhong Liu Za Zhi **44**(1): 93-98.

Objective: To estimate stomach cancer incidence and mortality in Henan, 2016 and analyze the trend of stomach cancer incidence and mortality from 2010 to 2016. Methods: Stomach cancer related data in 2016 was extracted from Henan cancer registration and follow-up system. All data were qualified in validity, reliability and completeness according to the Guideline on Cancer Registration in China and International Agency for Research on Cancer (IARC/IACR). The incidence and mortality of stomach cancer were estimated by areas, gender and age based on the quality data and the registered population data of Henan province in 2016. The epidemic trend of stomach cancer was also been evaluated based on the age-standardized incidence and mortality by Chinese population (ASR China) from 2010 to 2016. Results: In 2016, the estimated incident cases of stomach cancer were 44 311. The incidence was 41.07/100 000, ASR China was 30.17/100 000, ASR by world population (ASR world) was 30.36/100 000, and the cumulative incidence rate was 3.84%. The incidences of male and female were 55.65/100 000 and 25.35/100 000, respectively. Meanwhile, 32 927 people died of stomach cancer in Henan. The mortality was 30.52/100 000, ASR China was 21.45/100 000, ASR world was 21.54/100 000, and the cumulative mortality was 2.53%. From 2010 to 2016, both the ASR China for incidence and mortality of stomach cancer in Henan showed a steady downward trend. In rural, the ASR China for incidence and mortality decreased rapidly, while the stable trend was observed in urban. Nevertheless, the incidence and mortality of stomach cancer in rural were still higher than those in urban. Conclusions: The incidence and mortality of stomach cancer in Henan province showed steadily declining trend from 2010 to 2016, and the geographical distribution difference between rural and urban areas was gradually narrowing. However, the disease burden was still high in 2016.

Yang, L., et al. (2021). "Trends in Cardiometabolic and Cancer Multimorbidity Prevalence and Its Risk With All-Cause and Cause-Specific Mortality in U.S. Adults: Prospective Cohort Study." Front Cardiovasc Med **8**: 731240.

Several prospective cohort studies have assessed the association between multimorbidity and all-cause mortality, but the findings have been inconsistent. In addition, limited studies have assessed the association between multimorbidity and cause-specific mortality. In this study, we used the population based cohort study of National Health Interview Survey (1997-2014) with linkage to the National Death Index records to 31 December 2015 to examine the trends in prevalence of multimorbidity from 1997 to 2014, and its association with the risk of all-cause and cause-specific mortality in the U.S. population. A total of 372,566 adults aged 30-84 years were included in this study. From 1997 to 2014, the age-standardized prevalence of specific chronic condition and multimorbidity increased significantly ($P < 0.0001$). During a median follow-up of 9.0 years, 50,309 of

372,566 participants died from all causes, of which 11,132 (22.1%) died from CVD and 13,170 (26.2%) died from cancer. Compared with participants without the above-mentioned chronic conditions, those with 1, 2, 3, and >/=4 of chronic conditions had 1.41 (1.37-1.45), 1.94 (1.88-2.00), 2.64 (2.54-2.75), and 3.68 (3.46-3.91) higher risk of all-cause mortality after adjustment for important covariates. Similarly, a higher risk of CVD-specific and cancer-specific mortality was observed as the number of chronic conditions increased, with the observed risk stronger for CVD-mortality compared with cancer-specific mortality. Given the prevalence of multimorbidity tended to increase from 1997 to 2014, our data suggest effective prevention and intervention programs are necessary to limit the increased mortality risk associated with multimorbidity.

Yang, M., et al. (2022). "Global trends and age-specific incidence and mortality of cervical cancer from 1990 to 2019: an international comparative study based on the Global Burden of Disease." BMJ Open **12**(7): e055470.

OBJECTIVE: To describe the trends of incidence and mortality of cervical cancer in different age groups and regions from 1990 to 2019. DESIGN: An international comparative study based on the Global Burden of Disease (GBD) study estimates. PARTICIPANTS: Data were publicly available and individuals were not involved. METHODS: We collected detailed information on cervical cancer from the GBD study between 1990 and 2019. Average annual percentage changes (AAPCs) of age-standardised incidence and mortality rate (ASIR and ASMR) in cervical cancer, by age group and region, were calculated to quantify the temporal trends. RESULTS: Globally, the absolute numbers of incident cases and deaths were increasing, with the most cervical cancer cases and deaths being reported in China, India and Brazil. Although the ASIR and ASMR have declined overall from 1990 to 2019, an increasing or stable trend was also observed in East Asia and Southern sub-Saharan Africa. Particularly, we found that the age-specific AAPC of incidence showed an increasing trend in the age group of 15-49 years globally, and the high Sociodemographic Index region increased the most. CONCLUSIONS: Cervical cancer remains a concerning disease that affects women all over the world, although the ASIR and ASMR are decreasing. Efforts to control the younger trend and to reduce the disparity between regions are imminent.

Yang, R., et al. (2020). "Trends in cancer incidence and mortality rates in the United States from 1975 to 2016." Ann Transl Med **8**(24): 1671.

BACKGROUND: Cancer is the second leading cause of death in the United States (US). The goal of this study was to characterize the trends in cancer incidence and mortality in the US from 1975 to 2016. METHODS: In this study, we analyzed 4,711,958 cancer cases and 21,489,462 cancer death cases from the Surveillance, Epidemiology and End Results (SEER) database. Cancer incidence and mortality were assessed according to sex, race, and age group. Cancer survival rates between 2010 and 2016 were also examined. RESULTS: The continuous decline in the overall cancer mortality rate from the early 1990s has resulted in overall decreases of 33.6% and 23.6% in the cancer mortality rates of males and females, respectively. In males, the top three leading cancers and causes of cancer death from 1975 to 2016 were prostate, lung and bronchial, and colon and rectal cancers, while in females, the top three leading cancers and causes of cancer death from 1979 to 2016 were breast, lung and bronchial, and colon and rectal cancers. The 5-year relative survival rates of males and females for all cancers combined, diagnosed from 2010-2016, were 68.5% and 70.1%, respectively. The overall cancer incidence and mortality were higher in males than females from 1975-2016. Also, black people had higher mortality and shorter survival rates for all cancers combined compared with white people (in both sexes). CONCLUSIONS: This study presents a comprehensive overview of cancer incidence and mortality in the US over the past 42 years. Such information can provide a scientific basis for cancer prevention and control.

Yang, S. X., et al. (2022). "Locoregional tumor burden and risk of mortality in metastatic breast cancer." NPJ Precis Oncol **6**(1): 22.

The role of lymph node involvement and tumor size in metastatic disease including breast cancer is unclear. Here, nodal metastasis and T stage on the risk of mortality were investigated in de novo metastatic breast cancer population (35812 patients) in the Surveillance, Epidemiology, and End Results (SEER) Program database in the United States. We found an association between all-cause mortality and regional node involvement (adjusted hazard ratio [HR] = 1.45, 95% confidence interval [CI] 1.36-1.55, $p < 0.0001$) or T stage (HR = 1.20, 95% CI 1.14-1.25, $p < 0.0001$), independent of known clinicopathologic measurements. Number of positive nodes, and size and chest wall involvement of the breast tumors exhibited similar significance for breast cancer-specific mortality in the population ($p < 0.0001$ each), and all-cause mortality in hormone receptor (HR)-positive/HER2-negative (HR(+)/HER2(-)), HR(+)/HER2(+), HR(-)/HER2(+) and triple-negative metastatic breast cancer subtypes. Thus, nodal involvement and T stage are independent risk factors for mortality in the population of de novo metastatic breast cancer.

Yang, T. W., et al. (2021). "Improvement in the Mortality-to-Incidence Ratios for Gastric Cancer in Developed Countries With High Health Expenditures." Front Public Health **9**: 713895.

The mortality-to-incidence ratio (MIR) is widely used to evaluate the efficacy of cancer management outcomes for individual countries. However, the association among health care expenditure, human development index (HDI), and changes in MIR over time (deltaMIR) remains unknown. We aimed to elucidate the significance between these indicators and gastric cancer outcomes in different countries. Among the regions, Asia had the highest number of new gastric cancer cases, gastric cancer-related deaths, age-standardized ratio of incidence, and mortality. Chile had the highest age-standardized ratio (ASR) for gastric cancer incidence and the highest ASR for mortality. Moreover, MIR was highest in Africa (0.91) and lowest in North America (0.43). Of note, MIR was negatively associated with HDI, current health expenditure (CHE) per capita, and CHE/GDP % and deltaMIR was positively associated with CHE/GDP % in countries with very high HDI. However, deltaMIR showed no significant associations with these indicators in the countries analyzed. In conclusion, increased HDI, CHE per capita, and CHE/GDP are associated with improved gastric cancer outcomes. In addition, the deltaMIR could be an indicator that can be used to evaluate the improvement in cancer management outcomes over time.

Yang, X., et al. (2021). "Temporal trends of the lung cancer mortality attributable to smoking from 1990 to 2017: A global, regional and national analysis." Lung Cancer **152**: 49-57.

OBJECTIVES: Understanding the global trend of lung cancer deaths attributable to smoking is crucial for prioritizing global lung cancer prevention, as well as tobacco control. We assessed patterns of smoking-induced lung cancer deaths at global, regional, and national levels from 1990 to 2017. MATERIALS AND METHODS: We extracted detailed data on lung cancer deaths attributable to smoking from the Global Burden of Disease 2017 Study. The estimated annual percentage change (EAPC) was used to quantify temporal trends in the age-standardized mortality rate (ASMR) of smoking-induced lung cancer. RESULTS: In 2017, estimated 1.19 million lung cancer deaths were attributable to smoking, accounting for 63.17 % of all lung cancer deaths. The corresponding ASMR decreased by 13.36 % from 17.29/100,000 in 1990 to 14.98/100,000 in 2017, with an EAPC of -0.59 (95 % confidence interval: -0.66, -0.53). The ASMR of lung cancer in most geographic regions has significantly decreased since 1990; however, the EAPC of ASMR in 20 countries exceeded 1 during the same period. The reductions in the ASMR were pronounced in areas with high Socio-demographic Index and high disease burden, and kept pace with the decrease of smoking prevalence at least 10 years ago. CONCLUSION: Despite the decline in lung cancer ASMR attributable to smoking over the past 28 years, the corresponding number of lung cancer deaths increased steadily due to population aging and growth. Tobacco prevention needs to be strengthened, especially in countries with high smoking prevalence and countries where the ASMR of smoking-induced lung cancer is increasing.

Yang, X., et al. (2022). "Incidence and mortality of post-polypectomy colorectal cancer in patients with low-risk adenomas: A systematic review and meta-analysis of observational studies." Dig Dis.

INTRODUCTION: The long-term risks of post-polypectomy colorectal cancer (CRC) incidence and mortality among patients with low-risk adenomas (LRAs) are unclear. This study aimed to perform a systematic review and meta-analysis of the risk of CRC incidence and mortality following LRAs removal. METHODS: We searched the PubMed, Embase, and Cochrane library for studies that reported the risk of metachronous CRC incidence and mortality after colonoscopy. The primary outcome was the risk of CRC incidence and mortality in patients with LRAs. Random-effects models were used to calculate pooled risk ratio (RR) with 95% CI. RESULTS: Thirteen observational studies with 1,750,305 patients (45.4% male; follow-up: 4.5-16.5 years) were included. A meta-analysis of seven studies showed a higher CRC incidence in patients with LRAs than those without adenomas [per 10,000 person-years: 5.2 vs 3.9; RR 1.25 (95% CI 1.05-1.49), I2=0%]. However, the CRC-related death was not significantly different between the two groups [RR 1.13 (95% CI 0.75-1.69), I2=0%]. When compared with the general population, the meta-analysis showed a significantly lower risk of CRC incidence in patients with LRAs [RR 0.59 (95%CI 0.45-0.77), I2=0%], and another three studies, which could not be pooled, showed a reduction in the risk of CRC-related death in the LRAs group. CONCLUSIONS: Patients with LRAs have a small but higher risk of post-polypectomy CRC incidence than patients without adenomas. The marginally higher absolute incidence seemed insufficient for more intensive surveillance colonoscopy, but the significant difference suggested different follow-up strategies between patients with LRAs and those without adenomas.

Yang, Y., et al. (2021). "Correlation between early brain natriuretic peptide level and mortality in cancer

patients with septic shock." Ann Palliat Med **10**(4): 4214-4219.

BACKGROUND: This study aimed to examine the correlation between early brain natriuretic peptide (BNP) levels and mortality in cancer patients with septic shock. METHODS: A retrospective analysis of 159 cancer patients with septic shock admitted to the intensive care unit (ICU) from Dec. 2012 to Dec. 2019 was performed. BNP levels and other variables, including blood lactate (Lac), procalcitonin (PCT), white blood cell (WBC) counts, acute physiology and chronic health status system II scores (APACHE-II scores) were collected within 24 hours after ICU admission. According to 28-day mortality, patients were divided into a death group (60 cases) and a survival group (99 cases). All variables were compared by univariate analysis, and then a multiple logistic regression analysis was performed on the variables that showed significant differences. Receiver operating characteristic curve (ROC curve) analysis was used to evaluate the predictive value of BNP on mortality in cancer patients with septic shock. RESULTS: BNP, APACHE-II score, Lac, and PCT in the death group were significantly higher than those in the survival group (P<0.05). Multiple logistic regression analysis of these four variables indicated that BNP, APACHE-II score and Lac were independent risk predictors of mortality in these patients (P<0.05). The BNP level at 899.6 pg/mL predicted mortality with a sensitivity of 76.7% and a speci fi city of 84.7%. The area under the ROC curve was 0.86+/-0.03 (P<0.05) for BNP, which was significantly larger than that of the APACHE-II score (P<0.05) and Lac (P<0.05). CONCLUSIONS: BNP was an independent risk factor for mortality in cancer patients with septic shock, and had a higher predictive value than the APACHE-II score and Lac.

Yang, Y., et al. (2022). "Based on the Development and Verification of a Risk Stratification Nomogram: Predicting the Risk of Lung Cancer-Specific Mortality in Stage IIIA-N2 Unresectable Large Cell Lung Neuroendocrine Cancer Compared With Lung Squamous Cell Cancer and Lung Adenocarcinoma." Front Oncol **12**: 825598.

BACKGROUND: The purpose of this study is to predict overall survival (OS) and lung cancer-specific survival (LCSS) in patients with stage IIIA-N2 unresectable lung squamous cell cancer (LUSC), lung adenocarcinoma (LUAD), and large cell neuroendocrine cancer (LCNEC) by constructing nomograms and to compare risk and prognostic factors affecting survival outcomes in different histological subtypes. METHODS: We included 11,505 unresectable NSCLC patients at stage IIIA-N2 between 2010 and 2015 from the Surveillance, Epidemiology, and End Results (SEER) database. Moreover, competition models and nomograms were developed to predict prognostic factors for OS and LCSS. RESULTS: Analysis of the SEER database identified 11,505 NSCLC patients, of whom 5,559 (48.3%) have LUAD, 5,842 (50.8%) have LUSC, and 104 (0.9%) have LCNEC. Overall, both OS and LCSS were significantly better in stage IIIA-N2 unresectable LUAD than in LCNEC, while there was no statistically significant difference between LUSC and LCNEC. Age, gender, T stage, chemotherapy, and radiotherapy were significantly associated with OS rates in LUAD and LUSC. However, chemotherapy was the only independent factor for LCNEC ($p < 0.01$).From competitive risk models, we found that older age, larger tumors, non-chemotherapy and non-radiotherapy were associated with a increased risk of death from LUAD and LUSC. Unlike prognostic factors for OS, our study showed that both chemotherapy and radiotherapy were all LCNEC-specific survival factors for both LCSS and non-LCSS LCNEC. CONCLUSION: Our study reports that unresectable patients with stage IIIA-N2 LCNEC and LUSC have worse LCSS than LUAD. The study's first prognostic nomogram constructed for patients with unresectable stage IIIA-N2 NSCLC can accurately predict the survival of different histological types, which may provide a practical tool to help clinicians assess prognosis and stratify these prognostic risks to determine which patients should be given an optimized individual treatment strategy based on histology.

Yang, Y. S., et al. (2022). "Prediction of cancer survivors' mortality risk in Korea: a 25-year nationwide prospective cohort study." Epidemiol Health: e2022075.

OBJECTIVES: To investigate the factors affecting cancer survivors and develop a Korean mortality prediction model for cancer survivors. Our study identified lifestyle and mortality risk factors and attempted to determine if health-promoting lifestyles affect mortality. METHODS: Among the 1,637,287 participants, 200,834 cancer survivors who were alive after cancer diagnosis were analyzed in the Korean Cancer Prevention Study (KCPS) cohort. Discrimination and calibration for predicting the 10-year mortality risk were evaluated. The prediction model was derived using the Cox model coefficients, mean risk factor values, and mean mortality from the cancer survivors in KCPS cohort. RESULTS: During the 21.6-year follow-up, the all-cause mortality rates of cancer survivors were 57.2% and 39.4% in men and women, respectively. Men, older age, current smoking, and history of diabetes were high-risk factors for mortality. In contrast, exercise habits and a family history of cancer showed a reduced risk. The prediction

model discriminations in the validation dataset for both KCPS all-cause mortality (KAR) and KCPS cancer mortality (KCR) were C-statistics, 0.69 and 0.68, respectively. Based on the constructed prediction models, when we modified exercise status and smoking status, which are modifiable factors, the risk of mortality of cancer survivors decreased linearly (30% to 9%). Moreover, there was an equally linear reduction in the risk of cancer-related mortality, decreasing from 24% to 3%. CONCLUSION: A mortality prediction model for cancer survivors was developed and may be helpful in supporting a healthy life. Lifestyle modifications in cancer survivors may affect the risk of mortality in the future.

Yang, Z. Y., et al. (2022). "Return to Work and Mortality in Breast Cancer Survivors: A 11-Year Longitudinal Study." Int J Environ Res Public Health **19**(21).

Breast cancer is the most commonly occurring cancer in women, and it is a major cause of cancer death around the world. With the development of diagnostic methods and improvements in treatment methods, the incidence rate of breast cancer and the number of breast cancer survivors continue to simultaneously increase. We used national registry database to analyze the features that affect employment and return to work among breast cancer survivors. A total of 23,220 employees, who were newly diagnosed with breast cancer were recruited based on the Labor Insurance Database (LID), the Taiwan Cancer Registry (TCR), and National Health Insurance Research Database (NHIRD) during the period 2004-2015. The correlations between return to work (RTW) and independent confounding factors were examined using Cox proportional hazards model. Survival probability was analyzed using the Kaplan-Meir method. After adjusting for confounding variables, cancer stage, chemotherapy and higher income were significantly negatively correlated with RTW. Among breast cancer survivors, RTW was found to be related to a lower risk of all-cause mortality in both the unadjusted and fully adjusted model. Patients who had RTW exhibited better survival in all stages. Work-, disease- and treatment-related factors influenced RTW among employees with breast cancer. RTW was associated with better breast cancer survival. Our study demonstrates the impact of RTW and the associated factors on breast cancer survivorship.

Yang, Z. Y., et al. (2021). "Epidemiological Study of Return to Work and Mortality in Lung Cancer Survivors." Int J Environ Res Public Health **19**(1).

Lung cancer is the second most common cancer and the leading cause of cancer-related deaths worldwide. Return to work (RTW) plays an important role for lung cancer survivors. Few studies focus solely on the relationship among possible variables and the RTW of lung cancer patients. The aim of our study was to examine sociodemographic, disease-related and work-related factors associated with RTW among lung cancer survivors in Taiwan. A total of 2206 employees who had been diagnosed with lung cancer at the Labor Insurance Database (LID), Taiwan Cancer Registry (TCR) and the National Health Insurance Research Database (NHIRD) during the period 2004-2015, were included in the study. We used the Cox proportional hazards model to investigate the associations between sociodemographic, disease-related and work-related factors on one hand and RTW on the other hand. The Kaplan-Meier method was used for analyzing the survival probability. Patients with an early cancer stage and those who underwent surgery had a higher likelihood of RTW. Factors including older age, male, higher monthly income and receipt of radiotherapy were inversely correlated with RTW. For lung cancer patients, RTW was a predictor of a lower risk of all-cause mortality in both the unadjusted and fully adjusted model. A better survival rate was found in stage III and IV lung cancer patients who had RTW. Sociodemographic and clinical-related variables had an impact on RTW among employees with lung cancer. RTW was correlated with a lower risk of all-cause mortality and better lung cancer survival. Our study showed the influence of RTW and independent confounding factors in lung cancer survivorship.

Yao, X., et al. (2021). "Associations of Dietary Fat Intake With Mortality From All Causes, Cardiovascular Disease, and Cancer: A Prospective Study." Front Nutr **8**: 701430.

The impact of fat intake on health has become a growing public concern. The existing evidence linking specific dietary fat intake with mortality is controversial. We aimed to investigate the association between fat intake and total and cause-specific mortality in the Prostate, Lung, Colorectal, and Ovarian (PLCO) cancer screening trial. Intakes of saturated fatty acids (SFAs), trans-fatty acids (TFAs), monounsaturated fatty acids (MUFAs), and polyunsaturated fatty acids (PUFAs) were assessed via food frequency questionnaires. The primary outcomes were total, cardiovascular disease (CVD), and cancer mortality. Multivariable hazard ratios (HRs) and 95% confidence intervals (CIs) were estimated using Cox regression model adjusting for confounders. Overall, 24,141 deaths were recorded over a total 1,672,715 person-years of follow-up. There was a significant positive association between SFA consumption and total mortality (HR (Q5 vs. Q1) = 1.13, 95% CI 1.05-1.22; P (for trend) < 0.001). PUFA intake was strongly inversely associated with total mortality (HR (Q5 vs.

Q1) = 0.79, 95% CI 0.73-0.85; P (for trend) < 0.001) and CVD mortality (HR (Q5 vs. Q1) = 0.66, 95% CI 0.58-0.75; P (for trend) < 0.001). There was a similar, but to a lesser extent, association between MUFA intake and total and CVD mortality [HR (Q5 vs. Q1) 0.91 (95% CI: 0.84-0.99), P (for trend) = 0.044 and 0.85 (0.73-0.98), P (for trend) = 0.020, respectively]. None of these types of dietary fat were associated with cancer mortality (all P (for trend) > 0.05). In conclusion, this study observed a detrimental effect of SFA intake on total mortality; in contrast, greater consumption of PUFAs and MUFAs were associated with lower risks of all-cause death and CVD mortality.

Yap, D. W. T., et al. (2022). "The Association of Obstructive Sleep Apnea With Breast Cancer Incidence and Mortality: A Systematic Review and Meta-analysis." J Breast Cancer **25**(3): 149-163.

PURPOSE: Emerging evidence from animal models suggests that intermittent hypoxia due to obstructive sleep apnea (OSA) is a risk factor for breast cancer. Despite their biological plausibility, human epidemiological studies have reported conflicting results. Therefore, we conducted a meta-analysis to delineate this relationship. METHODS: We searched the PubMed, Embase, Scopus, and Cochrane Library databases for eligible studies from inception until June 6, 2021. Two reviewers selected randomized trials or observational studies reporting the association between OSA and breast cancer incidence compared with those without OSA. Two reviewers extracted relevant data and assessed the quality of evidence using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) framework and Newcastle-Ottawa Scale (NOS). We pooled the maximally covariate-adjusted hazard ratios (HRs) using a random-effects inverse variance-weighted meta-analysis and performed pre-specified subgroup analyses. RESULTS: We included six studies out of 1,707 records, comprising a combined cohort of 5,165,200 patients. All studies used the International Classification of Diseases codes to classify OSA and breast cancer. OSA patients had a 36% increased breast cancer risk (HR, 1.36; 95% confidence interval [CI], 1.03-1.80; N = 6, I(2) = 96%) compared to those without OSA. Most studies adjusted for confounders, such as age, sex, obesity, diabetes mellitus, alcohol use, and hypertension. Subgroup analyses for studies with (1) multivariate adjustment and (2) at least five years of follow-up yielded HRs of 1.35 (95% CI, 0.98-1.87; N = 5, I(2) = 96%) and 1.57 (95% CI, 1.14-2.18; N = 4; I(2) = 90%), respectively. One Mendelian randomization study suggested a causal relationship, with a two-fold increase in the odds of breast cancer in patients with OSA. CONCLUSION: This meta-analysis suggested that OSA is a risk factor for breast cancer. Future studies should explore the dose-response relationship between OSA and breast cancer, and whether treatment may mitigate breast cancer risk or progression.

Zengin, A., et al. (2022). "Is Prognostic Nutritional Index an Indicator for Postoperative 90-Day Mortality in Laparoscopic Gastric Cancer Surgery?" Nutr Cancer **74**(6): 2088-2094.

Gastic cancer is a life-threatening malignancy in the world. The aim of this study was to investigate the clinical significance of the prognostic nutritional index (PNI) as a guiding marker for gastric cancer patients with laparoscopic gastrectomy. We retrospectively examined the medical records of 138 gastric cancer patients who had adenocarcinoma pathological diagnosis and operated laparoscopically. Patients were divided into two groups (survived and death) and these groups were compared with clinical and laboratory parameters results. The PNI was calculated as 10 x serum albumin (g/dL) + 0.005 x total lymphocyte count (per mm(3)). Logistic regression analyses were performed to identify the risk factors of 90-day mortality. The median age of the study cohort was 62.5 (19-91) years, 98 (71%) were males, and 9 (6.5%) patients died during the 90-day after laparoscopic gastrectomy. The PNI levels were significantly lower in death group compared with survived group 37.5 (25-47.1) to 46.9 (22.8-64.9). The PNI (Odds Ratio = 0.81, 95% Confidence Interval 0.70-0.92, p = 0.003) was found as an independent factor for 90-day mortality in multivariate analysis. Receiver operating characteristic (ROC) curve analysis showed that 45.15 is the best-cutoff value for 90-day mortality after laparoscopic gastrectomy. 90-day mortality rate of PNI > 45.15 was 2.2% and PNI </= 45.15 was 13.6% found. Lower PNI is associated with increased 90-day mortality in laparoscopic gastrectomy for gastric cancer. The PNI may be a useful marker for predicting the 90-day mortality of gastric cancer patients after laparoscopic gastrectomy.

Zessner-Spitzenberg, J., et al. (2022). "Comparison of adenoma detection rate and proximal serrated polyp detection rate and their effect on post-colonoscopy colorectal cancer mortality in screening patients." Endoscopy.

BACKGROUND: Patients with serrated polyps are at increased risk for post-colonoscopy colorectal cancer (PCCRC); however, evidence for a dedicated serrated polyp detection rate is lacking. The aim of this study was to investigate the association of the proximal serrated polyp detection rate (PSDR) and adenoma detection rate (ADR) with PCCRC death. METHODS: This was a retrospective analysis within the Austrian quality assurance program for screening colonoscopy. Spearman's rank coefficient was

calculated for the assessment of association between ADR and PSDR. Whether ADR or PSDR were associated with colorectal cancer mortality was assessed by Cox proportional hazards model. RESULTS: 229 /729 screening colonoscopies performed by 308 endoscopists were analyzed. The ADR (hazard ratio [HR] per 1 percentage point increase 0.98, 95 %CI 0.96-0.99) as well as the PSDR (HR per 1 percentage point increase 0.97, 95 %CI 0.94-0.99) were significantly associated with PCCRC death. The correlation coefficient of the ADR and PSDR calculated at every colonoscopy was 0.70 (95 %CI 0.70-0.71), and the corresponding PSDR value for an ADR performance standard of 25 % was 11.1 %. At the end of the study period, 86 endoscopists (27.9 %) reached an ADR of > 25 % and a PSDR of > 11.1 %. CONCLUSIONS: The ADR as well as the PSDR were associated with PCCRC death. Striving for a high PSDR in addition to a high ADR might reduce the risk for PCCRC mortality in patients undergoing screening colonoscopy.

Zewde, M. G., et al. (2022). "Methodological Considerations on COVID-19 Mortality in Cancer Patients: A Systematic Review and Meta-Analysis." JNCI Cancer Spectr **6**(5).

BACKGROUND: Patients with cancer are at risk for severe COVID-19. Previous studies examining mortality in cancer patients with COVID-19 have produced inconclusive results. Several published meta-analyses have aimed to estimate this association; however, because of methodological limitations in study selection and data aggregation, these studies do not reliably estimate the independent association between cancer and COVID-19 mortality. We conducted this systematic review and meta-analysis to determine whether cancer is an independent risk factor for COVID-19 mortality. METHODS: A literature search was performed in PubMed to identify studies that compared COVID-19 mortality in adult patients with and without cancer. Selection criteria included polymerase chain reaction-confirmed COVID-19, multivariate adjustment and/or matching for mortality risk estimates, and inclusion of hospitalized noncancer controls. Adjusted odds ratios and/or hazard ratios for mortality based on cancer status were extracted. Odds ratio and hazard ratio estimates were pooled using a random effects model. RESULTS: The analysis included 42 studies comprising 129 840 patients: 8612 cancer patients and 121 228 noncancer patients. Of these studies, 18 showed a null difference in survival between cancer and noncancer patients with COVID-19, and 24 studies showed statistically significantly worse survival in cancer patients with COVID-19. Meta-analysis revealed an increased risk of mortality in patients with cancer compared with noncancer patients with COVID-19 (odds ratio = 1.93, 95% confidence interval = 1.55 to 2.41; hazard ratio = 1.54, 95% confidence interval = 1.29 to 1.84). CONCLUSION: We conclude that cancer is an independent risk factor for mortality in unvaccinated patients admitted for or diagnosed with COVID-19 during hospitalization.

Zha, Z., et al. (2022). "The effects of air pollution on the lung cancer mortality in rural areas of eastern China: a multi-region study." Environ Sci Pollut Res Int **29**(30): 45716-45729.

Recently, the burden of lung cancer (LC) has attracted global attention. Meanwhile, LC has become the leading cause of death in China. Many studies found a strong link between air pollutants and the risk of LC mortality in some large cities, but the results have been inconsistent, and most studies have only focused on the daily effects of six pollutants in large cities, ignoring their potential cumulative effects. This study was to investigate the weekly effects of six air pollutants (CO, NO(2), O(3), PM(2.5), PM(10), and SO(2)) on LC mortality in rural areas of eastern China and to further clarify which population groups were susceptible to air pollution and seasonal trends. First, a generalized additive model was combined with a distributed lag nonlinear model to evaluate the individual impact of air pollution on LC deaths in each area. The random-effect model was then used to pool the associations between air pollutants and LC mortality risk in ten counties or districts. The results showed that six air pollutants had a statistically significant effect on the risk of LC mortality at different lag weeks. The effects of NO(2), PM(10), and CO on weekly LC mortality were strongest at a cumulative lag of 1, 0, and 1 week, respectively, the maximum cumulative risk ratio (RR) of 1.37 (95%CI: 1.23 to 1.52), 1.30 (95%CI: 1.15 to 1.46), and 1.30 (95%CI: 1.17 to 1.43), with interquartile concentrations increasing. In summary, air pollution was an important factor in LC mortality, and the effect was stronger on males, the elderly, and during cold season. It was suggested that relevant departments should formulate air pollution management measures for the elderly, males, and in different seasons in rural areas and reduce the burden of lung cancer caused by air pollution.

Zhai, M., et al. (2020). "Short-term mortality risks among patients with non-metastatic bladder cancer." BMC Cancer **20**(1): 1148.

BACKGROUND: Population-based analysis for the short-term non-bladder cancer related mortality among patients with non-metastatic bladder cancer is currently lacking. The objective of the current study was to assess and quantify cause of death after bladder cancer diagnosis. METHODS: The custom

Surveillance, Epidemiology, and End Results (SEER) dataset for standardized mortality ratios (SMRs) was utilized to identify 24,074 patients who were diagnosed with nonmetastatic (M0) bladder cancer from 2014 to 2015. SMRs for causes of death were calculated. Risk factors for bladder cancer-specific mortality, competing mortality, second-cancer mortality, and noncancer mortality were determined using either multivariable Cox or competing risk regression models. RESULTS: Among all the 4179 (17.4%) deaths occurred during the follow-up period, almost half of them (44.2%) were attributed to non-bladder cancer cause, including second non-bladder cancer (10%) and other non-cancer causes (34.2%). The most common noncancer causes of death were heart diseases followed by chronic obstructive pulmonary disease. Patients had a higher risk of death from second malignancies (SMR, 1.59; 95% CI, 1.47-1.74) compared with death from first malignancies in the US general population, and also had higher risks of death from heart diseases (SMR, 1.29; 95% CI, 1.18-1.40) and chronic obstructive pulmonary disease (SMR, 1.52; 95% CI, 1.29-1.79) compared with the US general population. Additionally, some risk factors for competing second malignancies or noncancer mortality were determined, such as age, gender, marital status and treatment modalities. CONCLUSIONS: Death from non-bladder cancer cause contributed to almost half of all deaths in bladder cancer survivors during the short-term follow-up period. These findings can inform medical management and assist clinicians in counseling those survivors regarding their short-term health risks.

Zhang, A. C., et al. (2021). "Incidence and mortality trends of metastatic prostate cancer: Surveillance, Epidemiology, and End Results database analysis." Can Urol Assoc J **15**(12): E637-E643.

INTRODUCTION: In the past decade, prostate cancer screening decreased, raising the concern of delays in diagnosis and leading to an increase in new cases of metastatic prostate cancer. This study evaluated whether these changes may have impacted trends in metastatic prostate cancer incidence and survival. METHODS: Metastatic prostate cancer diagnoses from 2008-2016 were identified from the Surveillance, Epidemiology, and End Results (SEER) 18 registries. Age-adjusted incidence rates per 100 000 were calculated by time periods and demographic variables. Two-year all-cause and prostate cancer-specific mortality were calculated for patients diagnosed from 2008-2014, and multivariable Cox proportional hazards models were used to evaluate the impact of demographic and clinical variables. RESULTS: Incidence rates of metastatic prostate cancer increased by 18% from 2008-2009 to 2014-2016 (incidence rate ratio [IRR]=1.18, 95% confidence interval [CI] 1.14-1.21). This trend was observed across multiple subgroups but was greatest in non-Hispanic Whites and patients living in counties 0-10% below poverty level. There was an overall decreased risk of all-cause and prostate cancer-specific mortality, but unmarried men and men living in counties >20% below poverty level showed statistically significant increased risk of prostate cancer-specific mortality. CONCLUSIONS: Non-Hispanic Whites and the wealthiest subgroups had the largest increase in incidence of metastatic prostate cancer since 2008. Despite trends of decreased risk of prostate cancer-specific mortality, we found certain populations experienced increases in mortality risk. Studies exploring the role of socioeconomic factors on screening and access to newer treatments are needed.

Zhang, D., et al. (2022). "Frailty and risk of mortality in older cancer survivors and adults without a cancer history: Evidence from the National Health and Nutrition Examination Survey, 1999-2014." Cancer **128**(15): 2978-2987.

BACKGROUND: Epidemiologic evidence reporting the role of frailty in survival among older adults with a prior cancer diagnosis is limited. METHODS: A total of 2050 older adults (>/=60 years old) surviving for at least 1 year after a cancer diagnosis and 9474 older adults without a cancer history from the National Health and Nutrition Examination Survey (1999-2014) were included for analysis. The exposure variable, a 45-item frailty index (FI), was categorized on the basis of validated cutoffs (FI </= 0.10 [fit], 0.10 < FI </= 0.21 [prefrail], and FI > 0.21 [frail]). All-cause mortality was ascertained via the National Death Index. Multivariable Cox proportional hazards models were used to estimate adjusted hazard ratios (aHRs) and 95% confidence interval (CIs) for the FI, and this was followed by restricted cubic splines depicting dose-response curves. RESULTS: For older cancer survivors, the mean age at the baseline was 72.6 years (SD, 7.1 years); 5.9% were fit, 38.2% were prefrail, and 55.9% were frail. Older adults without a cancer history were slightly younger (mean age, 70.0 years) and less frail (47.9% were frail). At each level of the FI, cancer survivors (1.9 per 100 person-years for FI </= 0.10, 3.4 per 100 person-years for 0.10 < FI </= 0.21, and 7.5 per 100 person-years for FI > 0.21) had higher mortality than their cancer-free counterparts (1.4 per 100 person-years for FI </= 0.10, 2.4 per 100 person-years for 0.10 < FI </= 0.21, and 5.4 per 100 person-years for FI > 0.21). The multivariable model suggested a positive association between the FI and all-cause mortality for survivors (aHR for FI > 0.21 vs FI </= 0.10, 2.80; 95% CI, 1.73-4.53) and participants without a cancer history (aHR for FI > 0.21 vs FI </= 0.10, 2.75; 95% CI, 2.29-3.32).

Restricted cubic splines indicated that all-cause mortality risk increased with the FI in a monotonic pattern. CONCLUSIONS: Frailty is associated with a higher risk of death in older cancer survivors and the elderly without a cancer history.

Zhang, D., et al. (2020). "Association of vitamin C intake with breast cancer risk and mortality: a meta-analysis of observational studies." Aging (Albany NY) **12**(18): 18415-18435.

The association between vitamin C intake and breast cancer is unclear. This meta-analysis aimed to precisely assess the association of vitamin C intake with breast cancer risk and mortality. We searched the PubMed, Embase, and Web of Science databases up to June 2020 and found 69 studies relevant to breast cancer risk (54 studies) and survival (15 studies). Relative risks and 95% confidence intervals were calculated using the random-effects models. Pooled results suggested that the highest versus lowest vitamin C intake was significantly associated with a lower risk of breast cancer incidence (Relative Risk = 0.86; 95% confidence interval, 0.81-0.92). Dietary vitamin C but not supplements was found to reduce breast cancer risk (Relative Risk = 0.89; 95% confidence interval, 0.82-0.96). For the highest versus lowest vitamin C intake, the pooled hazard risk for breast cancer-specific mortality was 0.78 (95% confidence interval, 0.69-0.88), totality mortality was 0.82 (95% confidence interval, 0.74-0.91), and recurrence was 0.81 (95% confidence interval, 0.67-0.99). Our analysis suggests that higher vitamin C intake is significantly associated with reduced breast cancer incidence and mortality. However, the intake of vitamin C supplements has no significant effect on breast cancer prevention.

Zhao, J., et al. (2022). "Association between Dietary Fiber Intake and Mortality among Colorectal Cancer Survivors: Results from the Newfoundland Familial Colorectal Cancer Cohort Study and a Meta-Analysis of Prospective Studies." Cancers (Basel) **14**(15).

We examined dietary fiber intake for its relevance to Colorectal cancer (CRC) survival in a cohort of CRC patients and a meta-analysis including results from four prospective cohort studies. We analyzed 504 CRC patients enrolled in the Newfoundland Familial Colorectal Cancer Study (NFCCS) who were newly diagnosed with CRC between 1999 and 2003. Follow-up for deaths was through April 2010. All participants completed a self-administered food frequency questionnaire to evaluate their dietary intakes one year before diagnosis. Multivariable Cox proportional hazard models were used to explore the associations of dietary fiber intake with all-cause mortality and CRC-specific mortality. In the meta-analysis, we identified prospective cohort studies published between January 1991 and December 2021 by searching PubMed, EMBASE, and Cochrane Library. Fixed-effects or random-effects models were used to combine the study-specific hazard ratio (HR) from our original analysis and three other cohorts. In the NFCCS, we found that CRC patients with the second quartile of dietary fiber intake had a 42% lower risk of all-cause mortality (HR: 0.58, 95% CI: 0.35-0.98) and 58% lower risk of CRC-specific mortality (HR: 0.42, 95% CI: 0.21-0.87) compared with those with the lowest quartile. In the meta-analysis, a similar inverse association between dietary fiber and total mortality was detected among CRC patients; each 10 g/day increase in dietary fiber intake was associated with a 16% decreased risk of total mortality. The dose-response meta-analysis showed a linear relationship between dietary fiber intake and all-cause mortality, with no sign of a plateau. For CRC-specific mortality, intriguingly, the benefit associated with increasing dietary fiber intake achieved its maximum at approximately 22 g/day, and no further reduction in CRC-specific mortality was observed beyond this intake level. Our results suggest that high dietary fiber intake may be associated with prolonged survival among CRC patients. Our findings add to the sparse literature on the role of dietary fiber in CRC survival.

Zhao, S., et al. (2021). "Digoxin reduces the incidence of prostate cancer but increases the cancer-specific mortality: A systematic review and pooled analysis." Andrologia **53**(11): e14217.

Digoxin, a commonly used drug for congestive heart failure and cardiac arrhythmias, has been reported to exert cytotoxic and apoptosis-inducing effects on prostate cancer (PCa) cells. In this study, we aimed to perform a pooled analysis to summarise all the evidence related to the effects of digoxin on PCa development. Four electronic databases were systematically searched to filter the eligible studies. The hazard ratio (HR) with its 95% confidence interval (CI) was calculated. This study was registered on PROSPERO (ID: CRD42021226885). Ten clinical studies with a total of 108,444 participants (15,835 individuals were digoxin users) were included. The pooled result from 6 included studies demonstrated that digoxin usage was correlated with a significant decrease in PCa risk (adjusted RR = 0.892, 95% CI: 0.799-0.997, p = .044) when compared with the nonusers. Synthetic result of 4 eligible studies revealed that digoxin significantly correlated with higher prostate cancer-specific mortality than the controls (adjusted HR = 1.142, 95% CI: 1.005-1.297). No statistical heterogeneity was detected during this analysis (all $I(2) < 50\%$, $p > .1$). Our study confirmed a preventive effect of digoxin usage for the risk of PCa in men. However, digoxin use was associated with a

significantly elevated risk of prostate cancer-specific mortality. This finding needs more well-designed studies to better interpret the causality.

Zhao, Y., et al. (2022). "Primary site as a novel prognostic factor for cardiovascular mortality post-radiotherapy in limited-stage small cell lung cancer: A large population-based study." Front Cardiovasc Med **9**: 922811.

BACKGROUND: The effect of primary site on cardiovascular mortality (CVM) post-radiotherapy (RT) in patients with limited-stage small cell lung cancer (LS-SCLC) remains unclear. METHODS: We screened the Surveillance, Epidemiology, and End Results (SEER) database between 1988 and 2013. We used cumulative incidence function (CIF) curves to compare CVM incidences, and performed Cox proportional hazards and Fine-Gray competing risk analyses to identify independent risk factors of CVM. Propensity score matching (PSM) analysis was conducted. RESULTS: Among enrolled 4,824 patients (median age 57 years old, 49.2% were male), CVM accounts for 10.0% of all deaths after 5 years since cancer diagnosis. Hazard ratios (HRs) for CVM were 1.97 (95% CI: 1.23-3.16, P = 0.005) for main bronchus (MB) patients, 1.65 (95% CI: 1.04-2.63, P = 0.034) for lower lobe (LL) patients and 1.01 (95% CI: 0.40-2.59, P = 0.977) for middle lobe (ML) patients compared to upper lobe (UL) patients. CIF curves showed that the cumulative CVM incidence was greater in the re-categorized MB/LL group compared to UL/ML group both before PSM (P = 0.005) and after PSM (P = 0.012). Multivariate regression models indicated that MB/LL was independently associated with an increased CVM risk, before PSM (HR(Cox): 1.79, 95% CI: 1.23-2.61, P = 0.002; HR(Fine-Gray): 1.71, 95% CI: 1.18-2.48, P = 0.005) and after PSM (HR(Cox): 1.88, 95% CI: 1.20-2.95, P = 0.006; HR(Fine-Gray): 1.79, 95% CI: 1.15-2.79, P = 0.010). CONCLUSIONS: MB/LL as the primary site is independently associated with an increased CVM risk post-RT in patients with LS-SCLC.

Zheng, J., et al. (2022). "Association between dietary inflammatory potential and mortality after cancer diagnosis in the Women's Health Initiative." Br J Cancer.

BACKGROUND: Chronic inflammation is implicated in cancer prognosis and can be modulated by diet. We examined associations between post-diagnosis dietary inflammatory potential and mortality outcomes among post-menopausal women diagnosed with cancer in the Women's Health Initiative (WHI). METHODS: Energy-adjusted dietary inflammatory index scores (E-DII) were calculated from dietary and supplemental intake data collected on the first food frequency questionnaire following the diagnosis of primary invasive cancer for 3434 women in the WHI. Cox proportional hazards models were used to estimate hazard ratios (HR) and 95% confidence intervals (CIs) for risk of death from any cause, cancer, cardiovascular disease (CVD) and other causes by post-diagnosis quartiles of E-DII. Subgroup analyses by cancer stage and grade were performed. RESULTS: There were 1156 deaths after a median 13 years of follow-up from the date of a cancer diagnosis. In the multivariable-adjusted analyses, a more anti-inflammatory diet plus supplements after cancer diagnosis was associated with lower all-cause mortality, cancer mortality, CVD mortality and mortality from other causes with HRs(Q1vs.Q4) ranging from 0.47 to 0.68 (all P-trends < 0.05). Associations were stronger for cancers diagnosed at more distant stages or moderately differentiated grades. CONCLUSION: A more anti-inflammatory diet plus supplements after a cancer diagnosis may improve survival for post-menopausal cancer survivors.

Zheng, L., et al. (2022). "Stratified analysis of multiple management of gastric cancer: A population-based study of incidence, mortality and DALY." Medicine (Baltimore) **101**(43): e31341.

The aim was to illuminate the difference in incidence, mortality, and disability-adjusted life-years (DALYs) of gastric cancer (GC) between the United States of America (US) and China. The multiple management was analyzed with stratification to explore an effective survival improvement strategy. The Global Burden of Disease Study data was analyzed to assess GC morbidity, mortality and DALYs from 1990 to 2019 in the US and China. The age-period-cohort model was established to generate estimation of metrics. Verification was completed and stratified analysis of the multiple management was performed by accessing data of Surveillance, Epidemiology, and End Results database in 1992 to 2019. Continuous downtrends in GC incidence, mortality and DALYs from 1990 to 2019 and persistent uptrends in 1-, 3-year survival from 1992 to 2019 were observed in the US population. In the Chinese population, the overall trends of incidence, mortality and DALYs decreased with a fluctuating manner. The lower overall survival rates were observed in elderly, unmarried patients, distant disease and poor grade, as well as patients lacking of medical treatment (P < .05). In stratified analyses, single local therapy decreased and the other modalities increased over time across different stages. Moreover, combined treatment and single systemic therapy decreased, but single local and conservative therapy increased with age. The study quantified the incidence, GC-specific mortality and DALYs in the US and China and estimated stage profiles, 1- and 3-year

survival in the US. The heavy burden on later-onset GC (>70) and potential increase on early-onset GC (<40) needed to be addressed. Combined modalities and single chemotherapy were becoming more widely used over time, however, their uses decreased with age because of poor physical fitness. Our findings provide new insights into management tailoring appropriately to specific subgroups contributes to the increasing survival rate.

Zheng, R., et al. (2021). "Impact of cancer on short-term in-hospital mortality after primary acute myocardial infarction." Open Heart **8**(2).

BACKGROUND: Cardiovascular diseases are the second most common cause of mortality among cancer survivors, after death from cancer. We sought to assess the impact of cancer on the short-term outcomes of acute myocardial infarction (AMI), by analysing data obtained from a large-scale database. METHODS: This study was based on the Diagnosis Procedure Combination database in the Japanese Registry of All Cardiac and Vascular Diseases and the Diagnosis Procedure Combination. We identified patients who were hospitalised for primary AMI between April 2012 and March 2017. Propensity Score (PS) was estimated with logistic regression model, with cancer as the dependent variable and 21 clinically relevant covariates. The main outcome was in-hospital mortality. RESULTS: We split 1 52 208 patients into two groups with or without cancer. Patients with cancer tended to be older (cancer group 73+/-11 years vs non-cancer group 68+/-13 years) and had smaller body mass index (cancer group 22.8+/-3.6 vs non-cancer 23.9+/-4.3). More patients in the non-cancer group had hypertension or dyslipidaemia than their cancer group counterparts. The non-cancer group also had a higher rate of percutaneous coronary intervention (cancer 92.6% vs non-cancer 95.2%). Patients with cancer had a higher 30-day mortality (cancer 6.0% vs non-cancer 5.3%) and total mortality (cancer 8.1% vs non-cancer 6.1%) rate, but this was statistically insignificant after PS matching. CONCLUSION: Cancer did not significantly impact short-term in-hospital mortality rates after hospitalisation for primary AMI.

Zheng, W., et al. (2021). "Urban-rural disparity in cancer mortality and changing trend in Tianjin, China, during 1999 and 2016." BMC Cancer **21**(1): 1208.

OBJECTIVE: Compare the urban-rural disparity in cancer mortality and changing trend during the past 18 years in Tianjin, China. METHODS: Cancer death data were obtained from Tianjin All Cause of Death Registration System (CDRS), which covers the whole population of Tianjin. We calculated and compared the constituent ratio of cancer deaths, age-standardized mortality rate(ASR)and changing trends between urban and rural areas. RESULTS: From 1999 to 2016, a total of 245,744 cancer deaths were reported, accounting 21.7% of all deaths in Tianjin. The ASR of total cancer mortality was higher in urban areas than in rural areas. A total of 33,739 persons were avoided dying of cancers in rural area compared to the urban death level from 1999 to 2016, which was 40.1% compare to the current level of rural areas. But the gap between urban and rural areas became narrowed gradually. The urban-rural ratios (urban/rural) of total cancer mortality changed from 1.76 (125.7/71.5)[95%CI,1.67,1.84] in 1999 to 1.11 (99.6/90.0)[95%CI,1.06,1.15] in 2016. The ASR of lung, liver and esophagus cancer became higher in rural areas than in urban areas in 2016. CONCLUSION: Cancer transition was obviously occurred in Tianjin and showed different speeds and big gap between urban and rural areas. Much more attention was needed to pay in rural areas which still have increasing trends in most cancers mortality recently.

Zheng, W. L., et al. (2020). "[Analysis on long-term trend of mortality and years of life lost of breast cancer in women in Tianjin, 1999-2017]." Zhonghua Liu Xing Bing Xue Za Zhi **41**(9): 1477-1481.

Objective: To analyze the trends of mortality and years of life lost (YLL) of breast cancer in women in Tianjin and provide references for the development of intervention strategies. Methods: The crude mortality rate, standard mortality rate, cumulative rate (0-74 years old) and truncated rate (35-64 years old) of breast cancer in women in Tianjin from 1999 to 2017 were calculated. The annual percentage change of the mortality rate and YLL rate were analyzed by Joinpoint regression. Results: From 1999 to 2017, a total of 8 356 deaths of breast cancer were reported in Tianjin, resulting in a YLL of 262 835.53 person-years. The average crude mortality rate was 9.15/100 000. The average age standardized rate(ASR) (World) was 6.14/100 000. The ratio of ASR (World) between urban and rural areas was 1.73ratio1. The peak mortality ratio of age groups between urban area and rural area was 3.13ratio1. From 1999 to 2017, both the crude mortality rate and ASR of breast cancer in Tianjin had rising trends. In 2017, the crude mortality rate and the ASR of breast cancer increased by 113.7% and 44.4% respectively compared with 1999. The increase of urban mortality mainly came from elderly group aged >/=75 years, and the mortality of young age groups in rural area showed an fast increases, which was most obvious in age group 45-59 years (average annual percentage change=3.6%, P<0.01). Conclusions: The mortality rate of breast cancer and disease burden in women in Tianjin are still in rapid increase. We should continue to implement the prevention and control

strategies such as lifestyle intervention and screening of key groups. More attention need to be paid to the increase of breast cancer incidence in rural area.

Zheng, Y. Z., et al. (2021). "Breast Cancer-Specific Mortality in Small-Sized Tumor with Stage IV Breast Cancer: A Population-Based Study." Oncologist **26**(2): e241-e250.

BACKGROUND: Small-sized primary tumor does not always indicate a better prognosis. We hypothesized that very small primary breast tumors with extensive lymph node (LN) metastases represented an aggressive biologic behavior in stage IV disease. MATERIALS AND METHODS: Data between 2010 and 2015 were retrieved retrospectively from the Surveillance, Epidemiology, and End Results database with inclusion criteria of female sex, unilateral, metastatic, and T1/2 invasive ductal carcinoma. Primary study variables included T stage, N stage, grade, metastatic sites, number of involved sites, estrogen receptor status, progesterone receptor status, and human epidermal growth factor receptor 2 status. Kaplan-Meier and adjusted Cox proportional hazards models with interaction terms were used. One-, 2- and 3-year breast cancer-specific mortality (BCSM) was examined according to tumor size. RESULTS: We identified 5,340 eligible patients with breast cancer. In multivariate analysis, race, age, grade, molecular subtype, surgery, brain metastases, and liver metastases were found to be independently associated with BCSM. For T1 tumors, the N0, N1, and N2+ groups had the same BCSM. In tumors smaller than 50 mm, the 1-, 2-, and 3-year BCSM did not decline with the decrease of tumor size. For triple-negative breast cancers (TNBCs), the T1a/T1bN2+ group had significantly worse BCSM than any other group did. CONCLUSION: Patients with stage IV cancer with small-sized tumors may have BCSM as high as those with larger tumors. In TNBCs, very small tumors with severe LN involvement are associated with the worst BCSM. Continued efforts are needed to further investigate Ta1/T1bN2 + M1 TNBCs and individualize the treatment for affected patients. IMPLICATIONS FOR PRACTICE: This study revealed that for stage IV breast cancer, smaller primary tumors were not always associated with better breast cancer-specific mortality. This study illustrated that very small triple-negative breast cancers (TNBCs) with extensive regional lymph node involvement may be a surrogate for biologically aggressive disease. Because of poor prognosis of T1a/T1bN2+ TNBCs, there might be an urgent need of more individualized treatment for affected patients. Future correlative studies ought to focus on the genetic and molecular differences in Ta1/T1bN2+ TNBCs that contribute to the biological behavior. Clarification of the regulation mechanism of very small-sized primary TNBCs with metastatic outgrowth in nodes and distant sites will play an integral role in developing targeted therapies.

Zhong, G. C., et al. (2021). "Chocolate consumption and all-cause and cause-specific mortality in a US population: a post hoc analysis of the PLCO cancer screening trial." Aging (Albany NY) **13**(14): 18564-18585.

Few studies with mixed results have examined the association between chocolate consumption and mortality. We aimed to examine this association in a US population. A population-based cohort of 91891 participants aged 55 to 74 years was identified. Chocolate consumption was assessed via a food frequency questionnaire. Cox regression was used to estimate risk estimates. After an average follow-up of 13.5 years, 19586 all-cause deaths were documented. Compared with no regular chocolate consumption, the maximally adjusted hazard ratios of all-cause mortality were 0.89 [95% confidence interval (CI) 0.84-0.94], 0.84 (95% CI 0.79-0.90), 0.86 (95% CI 0.81-0.93), and 0.87 (95% CI 0.82-0.93) for >0-0.5 servings/week, >0.5-1 serving/week, >1-2 servings/week, and >2 servings/week, respectively (P(trend) = 0.009). A somewhat stronger inverse association was observed for mortality from cardiovascular disease and Alzheimer's disease. A nonlinear dose-response pattern was found for all-cause and cardiovascular mortality (all P(nonlinearity) < 0.01), with the lowest risk observed at chocolate consumption of 0.7 servings/week and 0.6 servings/week, respectively. The favorable associations with all-cause and cardiovascular mortality were found to be more pronounced in never smokers than in current or former smokers (all P(interaction) < 0.05). In conclusion, chocolate consumption confers reduced risks of mortality from all causes, cardiovascular disease, and Alzheimer's disease in this US population.

Zhou, B., et al. (2022). "Global burden and temporal trends in incidence and mortality of oesophageal cancer." J Adv Res.

INTRODUCTION: Oesophageal cancer is a prevalent and deadly cancer around the world. OBJECTIVES: We aimed to present a comprehensive analysis of the global geographic patterns and temporal trends in the mortality and incidence of oesophageal cancer. METHODS: The mortality and incidence data of oesophageal cancer in 2020 were obtained from the GLOBOCAN database. Based on World Health Organization (WHO) mortality database and the Cancer Incidence in Five Continents (CI5), we also retrieved the mortality and incidence age-standardized rates (ASRs) of oesophageal cancer. The average annual percentage changes (AAPCs) of mortality and incidence were calculated using the joinpoint

regression analysis. RESULTS: Globally, 0.54 million deaths and 0.6 million new cases were identified in 2020. In the majority of countries of South America and Asia, the mortality and incidence trends have substantially decreased, but trends in European countries have varied. The prevalence in European nations varied, but the incidence in most other continents decreased dramatically. In terms of mortality, the global average rate was 5.6 per 100000, ranging from 16.7 (Malawi) to 0.28 (Belize). European countries varied in mortality, such as Norway (AAPC, male: 0.68; female: 0.89) and Ireland (AAPC, male: -0.96; female: -1.52). Most non-European countries saw large decreases in mortality, such as Singapore (AAPC, male: -4.78; female: -6.89). The elderly had more noticeable trends in mortality and incidence in most countries. CONCLUSIONS: We have identified different trends in mortality and incidence among European countries, whereas declining trends were identified in most non-European countries. However, increasing trends were identified in specific subgroups of some countries, such as men in Thailand. For populations with rising mortality and incidence trends, more preventative efforts are required.

Zhou, C. M., et al. (2021). "Machine learning to predict the cancer-specific mortality of patients with primary non-metastatic invasive breast cancer." Surg Today **51**(5): 756-763.

PURPOSE: We used five machine-learning algorithms to predict cancer-specific mortality after surgical resection of primary non-metastatic invasive breast cancer. METHODS: This study was a secondary analysis of data for 1661 women with primary non-metastatic invasive breast cancer. The overall patient population was divided into a training group and a test group at a ratio of 8:2 and python was used for machine learning to establish the prognosis model. RESULTS: The machine-learning Gbdt algorithm for cancer-specific death caused by various factors showed the five most important factors, ranked from high to low as follows: the number of regional lymph node metastases, LDH, triglyceride, plasma fibrinogen, and cholesterol. Among the five algorithm models in the test group, the highest accuracy rate was by DecisionTree (0.841), followed by the gbm algorithm (0.838). Among the five algorithms, the AUC values from high to low were GradientBoosting (0.755), gbm (0.755), Logistic (0.733), Forest (0.715), and DecisionTree (0.677). CONCLUSION: Machine learning can predict cancer-specific mortality after surgery for patients with primary non-metastatic invasive breast.

Zhou, J., et al. (2022). "High red blood cell distribution width is associated with the mortality of critically ill cancer patients: A propensity-matching study." Adv Clin Exp Med.

BACKGROUND: The red blood cell distribution width (RDW) is related to the mortality of patients with malignant tumors, but the relationship between RDW and the prognosis of cancer patients in the intensive care unit (ICU) has not been fully clarified. OBJECTIVES: To investigate the role of RDW in predicting the prognosis of critically ill cancer patients. MATERIAL AND METHODS: A propensity score matching (PSM) study was conducted using data from adult patients with cancer, admitted to the ICU from the Intensive Care Medical Information Market IV (MIMIC-IV, v. 1.4) database. The correlation between RDW and ICU all-cause mortality was evaluated using a logistic regression model; stratification factors were considered. Additionally, a receiver operating characteristic (ROC) curve analysis was performed to compare the prognostic values of various blood biomarkers. RESULTS: Overall, 4836 cancer patients were included. The optimal critical RDW value was 15%. The RDW levels were independently correlated with ICU mortality in critically ill cancer patients, with odds ratios (ORs) of 1.56 (1.12-2.18) in the original cohort, 1.64 (1.27-2.12) in the imputation cohort, 1.65 (1.22-2.24) in the matched cohort, and 1.55 (1.19-2.03) in the weighted cohort. The forecasted performance of RDW is better than other blood biomarkers with an area under the ROC curve (AUC) of 0.637 (0.591-0.683). CONCLUSIONS: The RDW has a prognostic value in critically ill cancer patients and a high RDW is independently associated with high mortality.

Zhou, J., et al. (2022). "Association between glucosamine use and cancer mortality: A large prospective cohort study." Front Nutr **9**: 947818.

OBJECTIVE: Previous studies have shown anti-cancer and anti-inflammatory benefits of glucosamine. This study was performed to prospectively evaluate the association between glucosamine supplementation and the mortality of multiple cancers based on the UK Biobank cohort study. MATERIALS AND METHODS: A total of 453,645 participants aged 38-73 who had no cancer at baseline were recruited between 2006 and 2010 and followed until March 2021. We used cox and poission proportional hazards models to explore the association between habitual use of glucosamine and cancer mortality. Subgroup analyses were conducted to understand the potential effect modifications of demographics, lifestyle factors, and health outcomes. Sensitivity analyses were performed to determine the robustness of the results. RESULTS: Of the participants, 88,224 (19.4%) reported habitual glucosamine use at baseline. There were 9,366 cancer

deaths during a median follow-up of 12.1 years, and we observed a significant association between the use of glucosamine and lower overall cancer mortality (HR = 0.95, 95% CI = 0.90-1.00, p < 0.05), kidney cancer (IRR = 0.68, 95% CI = 0.49-0.95, p < 0.05), lung cancer mortality (IRR = 0.84, 95% CI = 0.74-0.95, p < 0.05), and rectum cancer (IRR = 0.76, 95% CI = 0.59-0.98, p < 0.05). Subgroup analysis showed that habitual glucosamine supplementation was correlated with lower overall cancer mortality among participants who were aged >/= 60 years, male, current smoker, without high cholesterol and not obese. Sensitivity analysis showed that the results were stable. CONCLUSION: Habitual glucosamine use was significantly related to decreased overall cancer, kidney cancer, lung cancer, and rectum cancer mortality, based on data from the large-scale, nationwide, prospective UK Biobank cohort study.

Zhou, M. J., et al. (2021). "Low Subcutaneous Adiposity and Mortality in Esophageal Cancer." Cancer Epidemiol Biomarkers Prev **30**(1): 114-122.

BACKGROUND: Recent data suggest that subcutaneous adiposity represents an independent prognostic marker in cancer. We aimed to determine whether subcutaneous adiposity estimated by the subcutaneous adiposity tissue index (SATI) was associated with mortality in esophageal cancer. METHODS: We conducted a retrospective analysis of a prospectively enrolled cohort from 2009 to 2015 with esophageal cancer at two major cancer centers. CT scans for initial staging were used to quantify adiposity and skeletal muscle areas. Subjects were categorized as above or below median SATI using sex-specific values. Sarcopenia was defined using previously established skeletal muscle area cutoffs. Cox proportional hazards modeling was performed to determine associations between SATI and all-cause mortality. RESULTS: Of the original 167 patients, 78 met inclusion criteria and had CT images available. Mean age was 67 years, 81.8% had adenocarcinoma, and 58.9% had stage 3 or 4 disease. Median follow-up time was 29.5 months. Overall 5-year survival was 38.9% [95% confidence interval (CI), 26.8-50.7]. Lower body mass index, higher Charlson comorbidity score, and more advanced stage were independently associated with low SATI. Patients with low SATI had increased mortality (unadjusted HR 2.23; 95% CI, 1.20-4.12), even when adjusted for sarcopenia or for percent weight loss. In a multivariable model including age, histology, stage, and receipt of curative surgery, the association between low SATI and mortality was attenuated (adjusted HR 1.64; 95% CI, 0.81-3.34). CONCLUSIONS: Low subcutaneous adiposity as estimated by SATI may be associated with increased mortality in esophageal cancer. IMPACT: Interventions to reduce loss of subcutaneous fat may improve survival in esophageal cancer.

Zhou, T., et al. (2022). "Adherence to a healthy sleep pattern is associated with lower risks of all-cause, cardiovascular and cancer-specific mortality." J Intern Med **291**(1): 64-71.

BACKGROUND: Individual unhealthy sleep behaviours have been associated with increased risks of all-cause mortality and deaths due to cardiovascular disease (CVD) or cancer. The evidence regarding the association of sleep patterns with these risks is limited. OBJECTIVE: To examine the associations of sleep patterns with all-cause, CVD and cancer mortality in a large prospective cohort. METHODS: This prospective cohort study included 283,443 adults from UK Biobank without CVD and cancer at baseline. We created a healthy sleep score and sleep patterns combining five individual sleep behaviours. RESULTS: During a mean (standard deviation) of 8.9 (1.1) years (2.5 million person-years) of follow up, a total of 7936 all-cause deaths, 762 CVD-caused deaths, and 4540 cancer-caused deaths occurred during follow up. One point increase of the healthy sleep score was associated with a 4-11% lower risk of all-cause mortality (Hazard Ratio [HR], 0.94; 95% CI, 0.92-0.96), CVD mortality (HR, 0.89; 95% CI, 0.83-0.95) and cancer mortality (HR, 0.96; 95% CI, 0.93-0.99), with adjustment for age, sex, assessment centres, smoking status, alcohol intake status, socioeconomic status and physical activity. Compared with participants with an unfavourable sleep pattern, those with a favourable sleep pattern had 24-42% lower risks of all-cause and CVD mortality. The association with all-cause mortality tended to be stronger among underweight participants and those with insufficient physical activity. CONCLUSIONS: A healthy sleep pattern was associated with lower risks of all-cause mortality and mortality from CVD and cancer. Our findings highlight the importance of improving overall sleep behaviours in lowering mortality.

Zhu, J., et al. (2020). "[An analysis of mortality trends for lung cancer during 1972-2016 in Qidong city of Jiangsu Province]." Zhonghua Yu Fang Yi Xue Za Zhi **54**(12): 1457-1460.

Crude mortality rate (CR) for lung cancer in Qidong increased from 11.50/10(5) in 1972-1976 to 76.61/10(5) in 2012-2016, China age-standardized rate (CASR) from 13.11/10(5) in 1972-1976 to 34.27/10(5) in 2012-2016, and World age-standardized rate (WASR) from 13.40/10(5) in 1972-1976 to 34.30/10(5) in 2012-2016. The average annual percentage change (AAPCs) of CR, CASR, WASR were 4.87% (95%CI: 4.63%-5.12%), 2.17% (95%CI: 1.96%-2.38%), 2.12% (95%CI: 1.92%-2.33%) (all P values<0.001),

respectively. AAPCs for 45-54, 55-64, 65-74 and over 75 age groups were 0.74% (95%CI: 0.36%-1.11%), 1.23% (95%CI: 0.92%-1.53%), 2.55% (95%CI: 2.20%-2.90%), 4.26% (95%CI: 3.56%-4.96%) (all P values<0.001), respectively.

Zhu, J., et al. (2020). "[Analysis on incidence and mortality of ovarian cancer in Jiangsu province, 2006-2015]." Zhonghua Liu Xing Bing Xue Za Zhi **41**(11): 1859-1864.

Objective: To estimate the incidence/mortality of ovarian cancer in 2015 and the incidence/mortality trend of ovarian cancer from 2006 to 2015 in Jiangsu province, and provide evidence for prevention and treatment of ovarian cancer in Jiangsu. Methods: The incidence and death data of cancer in Jiangsu from 2006 to 2015 collected from 35 cancer registries and verified by Jiangsu provincial CDC in 2018 were used for the extraction of ovarian cancer data. The data were stratified by urban and rural, gender and age groups. The crude rates of incidence and mortality, age-standardized incidence/mortality rates (ASIR/ASMR), cumulative incidence/mortality rates (0-74 years) and truncated incidence/mortality rates (35-64 years) of ovarian cancer were calculated. Chinese population census in 2000 and world Segi's standard population were used for the calculations of age-standardized incidence/mortality rates. Software Joinpoint 4.7.0.0 was used to analyze the annual percentage changes (APCs) of two rates from 2006 to 2015. Results: It was estimated that 2 229 ovarian cancer cases occurred in Jiangsu in 2015, accounting for 2.23% of all cancer cases and ranking 12(th) of cancer incidence in women. The crude incidence rate was 5.91/100 000, the age-standardized incidence rates by Chinese standard population (ASIRC) and by world standard population (ASIRW) were 4.01/100 000 and 3.81/100 000, respectively. The cumulative incidence rate (0-74 years) was 0.42%. It was estimated that 1 239 deaths of ovarian cancer occurred in Jiangsu in 2015, accounting for 2.18% of all cancer deaths and ranking 13(th) of cancer mortality in women. The crude mortality rate was 3.29/100 000, the ASMRC and ASMRW were 1.99/100 000 and 1.96/100 000, respectively. The cumulative mortality rate (0-74 years) was 0.24%. The APCs of crude incidence rate and crude mortality rate were 4.66% (95%CI: 2.11%-7.29%) and 7.45% (95%CI: 5.46%-9.47%) (all P<0.05). The APCs of ASIRC and ASIRW were 2.30% (95%CI: -0.32%-4.99%) and 2.41% (95%CI: -0.29%-5.20%) (all P>0.05), and the APCs of ASMRC and ASMRW were 4.43% (95%CI: 2.54%-6.36%) and 4.55% (95%CI: 2.58%-6.57%) (all P<0.05). Conclusions: The incidence and mortality of ovarian cancer in Jiangsu were at low levels, and were higher in urban areas than in rural areas. The crude incidence and mortality rates increased, and age-standardized incidence rate was stable, but age-standardized mortality rate increased obviously.

Zhu, Y., et al. (2020). "Associations Between Circulating Insulin-Like Growth Factor 1 and Mortality in Women With Invasive Breast Cancer." Front Oncol **10**: 1384.

Background: Studies on the association between circulating insulin-like growth factor 1 (IGF1) and prognosis of breast cancer are limited. Whether this association is modified by insulin levels and clinical characteristics is unclear. Methods: Serum concentrations of IGF1 as well as IGF binding protein 3 (IGFBP3), IGF1/IGFBP3 ratio, insulin, and C-peptide were prospectively examined in 2,682 invasive breast cancer patients who received surgery in Ruijin Hospital, Shanghai, between 2012 and 2017. Cox proportional hazards models were used to calculate hazard ratios (HRs) and 95% confidence intervals (CIs) for all-cause mortality, breast cancer-specific mortality, and breast cancer recurrence associated with different levels of IGF1 and other biomarkers with multivariable adjustment. Results: Compared with patients with low IGF1, patients with high IGF1 had a significantly lower risk of all-cause mortality (HR, 0.53; 95% CI, 0.29-0.96) and a borderline lower risk of breast cancer-specific mortality (HR, 0.53; 95% CI, 0.27-1.02). The inverse association between IGF1 and all-cause mortality was consistent across stratification subgroups but was more pronounced among patients with high insulin (HR, 0.40; 95% CI, 0.18-0.89), were premenopausal (HR, 0.34; 95% CI, 0.12-0.97), with a tumor size >2 cm (HR, 0.35; 95% CI, 0.17-0.73), with positive lymph node (HR, 0.49; 95% CI, 0.25-0.98), and with a high Ki-67 level (HR, 0.49; 95% CI, 0.26-0.95) (all P for interaction >0.05). No significant associations were found for IGFBP3, IGF1/IGFBP3 ratio, insulin, and C-peptide levels with all-cause mortality, breast cancer-specific mortality, and breast cancer recurrence. Conclusion: Circulating IGF1 was inversely and independently associated with all-cause mortality in invasive breast cancer patients, and this association was consistent across clinical risk factors.

Zhu, Z., et al. (2021). "Association between serum ferritin, incident primary liver cancer, and chronic liver disease mortality in the Linxian Nutrition Intervention Trials: A nested case-control study." J Gastroenterol Hepatol **36**(12): 3410-3417.

BACKGROUND AND AIM: Previous studies suggest that serum ferritin may be associated with higher risk of liver cancer. However, additional studies of the association are needed. It is also not clear whether serum ferritin is associated with mortality from chronic liver disease (CLD). METHODS: We

performed a nested case-control study in the Linxian Nutrition Intervention Trials. Baseline serum ferritin was measured for 226 incident primary liver cancer cases, 281 CLD mortalities diagnosed, and 1061 age-matched, gender-matched, and trial-matched controls. We used multivariable logistic regression models to calculate odds ratios and 95% confidence intervals. Subgroup analysis and interaction tests were performed by age, gender, alcohol drinking, hepatitis B virus seropositivity (HBV+)/hepatitis C virus seropositivity (HCV+), and trial. RESULTS: Participants with serum ferritin in the highest quartile, as compared with those in the lowest quartile, had an increased risk of CLD mortality (odds ratio = 1.72, 95% confidence interval = 1.12, 2.64, P-trend < 0.01). Moreover, the association with higher serum ferritin was stronger among alcohol drinkers and those who were HCV+ (P-interaction < 0.05). For incident liver cancer, risk estimates were above one but were not statistically significant. CONCLUSION: In this study, higher levels of serum ferritin at baseline were associated with subsequent mortality from CLD, particularly if combined with alcohol drinking or viral hepatitis. Further work is warranted to confirm our findings.

Zhuang, C. L., et al. (2020). "Associations of low handgrip strength with cancer mortality: a multicentre observational study." J Cachexia Sarcopenia Muscle **11**(6): 1476-1486.

BACKGROUND: Handgrip strength (HGS) is associated with poor clinical outcomes, including all-cause, non-cardiovascular, and cardiovascular mortalities. The published cut-off points for HGS are mostly based on community populations from Western countries, lacking information on cancer patients from China. The objective of this study was to establish sex-specific cut-off points for Chinese cancer patients and investigate the effect of low HGS on cancer mortality. METHODS: We did a retrospective cohort study of patients who were diagnosed with malignant cancer from June 2012 to December 2018. HGS was measured using a hand dynamometer in 8257 cancer patients. Optimal stratification was used to solve threshold points. The hazard ratio (HR) of all cancer mortality and cancer-specific mortality was calculated using Cox proportional hazard regression models. RESULTS: Among all participants, there were 3902 (47.3%) women and 4355 (52.7%) men. The median age was 58 years old. The cut-off points of HGS to best classify patients with respect to time to mortality were <16.1 kg for women and <22 kg for men. Low HGS was associated with overall cancer mortality in both women and men [HR = 1.339, 95% confidence interval (CI) = 1.170-1.531, P < 0.001; HR = 1.346, 95% CI = 1.176-1.540, P < 0.001, respectively]. For specific cancer types, low HGS was associated with breast cancer (HR = 1.593, 95% CI = 1.230-2.063, P < 0.001) in women, and lung cancer (HR = 1.369, 95% CI = 1.005-1.866, P = 0.047) and colorectal cancer (HR = 1.399, 95% CI = 1.007-1.944, P = 0.045) in men. CONCLUSIONS: On the basis of our sex-specific cut-off points, low HGS was strongly associated with cancer mortalities. These results indicate the usefulness of HGS measurement in routine clinical practice for improving patient assessments, cancer prognosis, and intervention.

Zimbwa, B., et al. (2021). "Retrospective analysis of mortality within 30 days of systemic anticancer therapy and comparison with a previous audit at an Australian Regional Cancer Centre." J Oncol Pharm Pract: 10781552211016086.

PURPOSE: To retrospectively determine the rate of death occurring within 14 and 30 days of systemic anticancer therapy (SACT), compare this against a previous audit and benchmark results against other cancer centres. Secondly, to determine if the introduction of immune checkpoint inhibitors (ICI), not available at the time of the initial audit, impacted mortality rates. METHOD: All adult solid tumour and haematology patients receiving SACT at an Australian Regional Cancer Centre (RCC) between January 2016 and July 2020 were included. RESULTS: Over a 55-month period, 1709 patients received SACT. Patients dying within 14 and 30 days of SACT were 3.3% and 7.0% respectively and is slightly higher than our previous study which was 1.89% and 5.6%. Mean time to death was 15.5 days. Males accounted for 63.9% of patients and the mean age was 66.8 years. 46.2% of the 119 patients dying in the 30 days post SACT started a new line of treatment during that time. Of 98 patients receiving ICI, 22.5% died within 30 days of commencement. Disease progression was the most common cause of death (79%). The most common place of death was the RCC (38.7%). CONCLUSION: The rate of death observed in our re-audit compares favourably with our previous audit and is still at the lower end of that seen in published studies in Australia and internationally. Cases of patients dying within 30 days of SACT should be regularly reviewed to maintain awareness of this benchmark of quality assurance and provide a feedback process for clinicians.

Znaor, A., et al. (2022). "Progress in reducing premature mortality from cancer and cardiovascular disease in the former Soviet Union, 2000-19." Eur J Public Health **32**(4): 624-629.

BACKGROUND: A reduction in non-communicable diseases premature mortality by one-third by 2030 is one of the targets of the UN Sustainable Development Goals (SDG3.4). We examined the mortality profiles in the Newly

Independent States of the former Soviet Union (NIS) and the European Union (EU) and assessed progress in reductions of premature mortality from cancer, as compared to cardiovascular disease (CVD). METHODS: We used WHO's Global Health Estimates and GLOBOCAN 2020 to examine current mortality profiles and computed the unconditional probabilities of dying at ages 30-70 from CVD and cancer for the years 2000-19 in both sexes, using a linear extrapolation of this trend to predict whether the target of a one-third reduction, as set in 2015, would be met in 2030. RESULTS: CVD was the main cause of premature death in the NIS (43%), followed by cancer (23%), inversely from the EU with 42% cancer and 24% CVD deaths. The NIS achieved major reductions in premature CVD mortality, although the probabilities of death in 2019 remained about five times higher in the NIS compared to the EU. For cancer, mortality reductions in most NIS were quite modest, other than large declines seen in Kazakhstan (44%) and Kyrgyzstan (30%), with both on course to meet the 2030 target. CONCLUSIONS: Limited progress in cancer control in the NIS calls for policy action both in terms of structural changes towards universal health coverage, and scaling up of national cancer control plans, including a shift from opportunistic to evidence-based early detection practices.

Znaor, A., et al. (2022). "Global patterns in testicular cancer incidence and mortality in 2020." Int J Cancer **151**(5): 692-698.

With 74 500 new cases worldwide in 2020, testicular cancer ranks as the 20th leading cancer type, but is the most common cancer in young men of European ancestry. While testicular cancer incidence has been rising in many populations, mortality trends, at least those in high-income settings, have been in decline since the 1970s following the introduction of platinum-based chemotherapy. To examine current incidence and mortality patterns, we extracted the new cases of, and deaths from cancers of the testis from the GLOBOCAN 2020 database. In 2020, testicular cancer was the most common cancer in men aged 15 to 44 in 62 countries worldwide. Incidence rates were highest in West-, North- and South-Europe and Oceania (age-standardised rate, ASR >/=7/100 000), followed by North America (5.6/100 000 and lowest (<2/100 000) in Asia and Africa. The mortality rates were highest in Central and South America (0.84 and 0.54 per 100 000, respectively), followed by Eastern and Southern Europe, and Western and Southern Africa. The lowest mortality rates were in Northern Europe, Northern Africa and Eastern Asia (0.16, 0.14, 0.9 per 100 000, respectively). At the country level, incidence rates varied over 100-fold, from 10/100 000 in Norway, Slovenia, Denmark and Germany to </=0.10/100 000 in Gambia, Guinea, Liberia, Lesotho. Mortality rates were highest in Fiji, Argentina and Mexico. Our results indicate a higher mortality burden in countries undergoing economic transitions and reinforce the need for more equitable access to testicular cancer diagnosis and treatment globally.

Zorzi, M. and E. D. L. Urso (2022). "Impact of colorectal cancer screening on incidence, mortality and surgery rates: Evidences from programs based on the fecal immunochemical test in Italy." Dig Liver Dis.

Fecal immunochemical tests (FIT) are among the most commonly used tests for colorectal cancer (CRC) screening programs worldwide. However, no randomised controlled trials have been carried out evaluating the impact of FIT-based screening programs (FIT-progr) on CRC incidence and mortality rates. Italian FIT-progr represent one of the most widespread and established experience worldwide. This paper reviews the evidence on the impact of FIT-progr on CRC incidence, tumor stage at diagnosis, mortality and surgery rates, deriving from Italian routine programs, i.e., outside the research setting. Unfortunately, the application of FIT-progr in Italy can be considered as an unplanned experimental model, due to the differences between Regions, both in health system management and adherence of the target population to the screening programs. The analysis of the manuscripts considered in the review, confirms that FIT-progr are effective in reducing CRC incidence and mortality rates and in improving the rate of endoscopic treatment of early invasive lesions. The review also highlights that FIT-progr are less performing for proximal colon than for distal colon and rectum.

Zou, J., et al. (2022). "Impact of cancer types on COVID-19 infection and mortality risk: a protocol for systematic review and meta-analysis." BMJ Open **12**(7): e058078.

INTRODUCTION: The COVID-19 pandemic has created a huge social and economic burden, and the lifestyles of individuals have significantly changed. In addition, the diagnosis, treatment and management of patients with cancer were greatly affected. Studies have shown that patients with cancer are at a higher risk of COVID-19 infection-related complications, which require aggressive preventive measures. Different types of cancer may have different risks of COVID-19 infection and death, and different preventive care measures are needed for different types of patients with cancer. Here, we designed a protocol for systematic review and meta-analysis to explore the impact of cancer types on COVID-19 infection and mortality risk. METHODS AND ANALYSIS: A systematic search plan will be performed to filter the eligible studies in the seven databases, namely PubMed,

Cochrane search strategy, EMBASE search strategy, SinoMed, China National Knowledge Infrastructure, China Science and Technology Journals Database, and Wanfang database from 2019 to 10 August 2021. Two independent reviewers will choose the eligible studies and extract the data. The risk of bias will be evaluated based on the Newcastle-Ottawa Scale recommended by the Cochrane Collaboration. Finally, a systematic review and meta-analysis will be performed using Review Manager (V.5.3) statistical software. ETHICS AND DISSEMINATION: Formal ethical approval is not required, and the findings will be published in a peer-reviewed journal. PROSPERO REGISTRATION NUMBER: CRD42021271108.

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