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Cancer Biology

MARSLAND PRESS
Multidisciplinary Academic Journal Publisher

Research Literatures of Cancer Risks, Signs, Symptoms, Tests, Treatments

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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.
[Dr. Mark Herbert. **Research Literatures of Cancer Risks, Signs, Symptoms, Tests, Treatments.**Cancer Biology 2023;13(3):82-123]. ISSN: 2150-1041 (print); ISSN: 2150-105X (online). http://www.cancerbio.net 05. doi:10.7537/marscbj130323.05.

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-Razeq, H., et al. (2023). "Management of breast cancer patients with BRCA gene mutations in Jordan: perspectives and challenges." Hosp Pract (1995) **51**(4): 184-191.
BACKGROUND: This paper explores and discusses local challenges oncologists face for diagnosing and managing breast cancer patients with BRCA gene mutations in Jordan. METHODS: A task force involving key opinion leaders, experts in the management of breast cancer, and stakeholders in healthcare systems where genetic testing is available in Jordan discussed current evidence and local real-life practice. The task force then formulated recommendations to achieve better patient outcomes and satisfaction based on evidence-based medicine and their clinical experience in BRCA-mutated breast cancer management. RESULTS AND CONCLUSION: Eligibility of patients for genetic testing, physician acceptance and willingness to integrate genetic testing into routine practice is encouraging but remains restricted by testing availability and financial coverage. Until more data is available, genetic testing should be targeted for breast cancer patients based on tumor subtypes, as well as family and personal history of cancer, as per international guidelines. Whenever possible, genetic testing should aim to detect all actionable genes through a multigene panel including BRCA1/2. Major challenges faced in clinical practice in Jordan include fear of genetic discrimination and social stigmatization, as well as hesitancy toward risk-reducing surgery. Pre-testing counseling is therefore critical to promote acceptance of genetic testing. Since geneticists are in short supply in Jordan, genetic counseling can be offered through a specially trained genetic counselor or through a hybrid system that includes oncologist-based counselling. In addition to cancer prevention, germline genetic testing may assist in the selection of specific anti-cancer therapy, such as PARP inhibitors, in patients with BRCA1/2 mutation. Nationwide initiatives are also needed to ensure access to PARP inhibition therapy and provide financial coverage for genetic screening, mastectomies and reconstructive surgery across Jordan.

Abdel-Razeq, H., et al. (2023). "Pathogenic germline variants in patients with breast cancer: conversations across generations, practices and patients' attitude." Front Genet **14**: 1194075.
Background: Breast cancer susceptibility genes such as BRCA1, BRCA2, PALB2, CHEK2 and many others are increasingly recognized among our patient population. In addition to their impact on treatment decisions of tested patients themselves, identifying at-risk family

members offer opportunities for cancer preventive measures. Methods: This is an observational cross-sectional study of adult breast cancer patients with positive breast-cancer-susceptibility germline variants who received treatment at our institution. Patients with variants of uncertain significance (VUS), or who refused to give consent, were excluded. The data was collected from an eligible sample of breast cancer patients using a structured questionnaire developed by the study team and tested for validity and reliability, as well as a clinical chart review form. Patients were invited to participate in the study during their scheduled oncology clinics visit. Results: 169 patients were enrolled, including 42 (24.9%) with pathogenic/likely pathogenic (P/LP) BRCA1 variants, 84 (49.7%) with BRCA2 and 43 (25.4%) with non-BRCA variants. All patients were female and the mean age was 45 +/- 9.9 years. Among 140 eligible patients, 104 (74.3%) underwent prophylactic mastectomy, while 79 (59.0%) of 134 eligible patients had prophylactic bilateral salpingo-oophorectomy (BSO). Results were communicated with family members by majority (n = 160, 94.7%), including 642 first degree female relatives, and 286 (44.5%) of them have taken no action. Fear of positive test results, cost of testing, unwillingness to undergo preventive measures, and social stigma were cited as barriers to genetic testing in 54%, 50%, 34% and 15%, respectively. Conclusion: Risk-reducing interventions including mastectomy and BSO were carried by majority of patients with P/LP variants. However, though the rate of communication of genetic testing results with family members was high, proper preventive measures were relatively low. Cost and fear of cancer diagnosis, were the leading causes that prevented cascade testing in our cohort.

Akkus, S., et al. (2023). "Autoimmune and paraneoplastic neurological disorders: A review of relevant neuroimaging findings." J Neurol Sci **454**: 120830.
INTRODUCTION: Paraneoplastic neurologic syndromes (PNS) and autoimmune encephalitis (AIE) are immune-mediated disorders. PNS is linked to cancer, while AIE may not Their clinical manifestations and imaging patterns need further elucidation. OBJECTIVE/AIMS: To investigate the clinical profiles, antibody associations, neuroimaging patterns, treatments, and outcomes of PNS and AIE. METHODS: A systematic review of 379 articles published between 2014 and 2023 was conducted. Of the 55 studies screened, 333 patients were diagnosed with either PNS or AIE and tested positive for novel antibodies. Data on demographics, symptoms, imaging, antibodies, cancer associations, treatment, and outcomes were extracted. RESULTS: The study included 333 patients (mean age 54 years, 67% males) with PNS and AIE positive for various novel antibodies. 84% had central nervous system issues like cognitive impairment (53%), rhombencephalitis (17%), and cerebellar disorders (24%). Neuroimaging revealed distinct patterns with high-risk antibodies associated with brainstem lesions in 98%, cerebellar in 91%, hippocampal in 98%, basal ganglia in 75%, and spinal cord in 91%, while low/intermediate-risk antibodies were associated with medial temporal lobe lesions in 71% and other cortical/subcortical lesions in 55%. High-risk antibodies were associated with younger males, deep brain lesions, and increased mortality of 61%, while low/intermediate-risk antibodies were associated with females, cortical/subcortical lesions, and better outcomes with 39% mortality. Associated cancers included seminomas (23%), lung (19%), ovarian (2%), and breast (2%). Treatments included IVIG, chemotherapy, and plasmapheresis. Overall mortality was 25% in this cohort. CONCLUSION: PNS and AIE have distinct clinical and radiological patterns based on antibody profiles. High-risk antibodies are associated with increased mortality while low/intermediate-risk antibodies are associated with improved outcomes. Appropriate imaging and antibody testing are critical for accurate diagnosis.

Anderson, J. R., et al. (2023). "The CryoPop study: Screening for high-grade cervical dysplasia in Karnataka, India." BJOG **130 Suppl 3**(Suppl 3): 158-167.
OBJECTIVE: To describe our experience of screening with visual inspection with acetic acid (VIA) and colposcopy to identify women with high-grade precancerous cervical lesions who were candidates for cryotherapy. Women were screened to determine eligibility for a clinical trial testing the safety and efficacy of a new, simple and inexpensive cryotherapy device (CryoPop(R)) targeted for use in low and middle-income countries (LMICs). DESIGN: Prospective cohort study. SETTING: Primary and urban health centres in Belagavi, Hubballi and Vijayapur, India. POPULATION: Women in the age-group 30-49 years, premenopausal, with no prior hysterectomy and no known HIV infection were eligible for screening. METHODS: Visual inspection with acetic acid was performed on eligible women following informed consent. VIA-positive women were referred for colposcopy and biopsy. Biopsies were read by two pathologists independently, with a third pathologist acting as tie-breaker if needed. MAIN OUTCOME MEASURES: The primary outcome measures were the number/proportion of women screening positive by VIA and the number/proportion of those women screening VIA-positive found to have high-grade cervical lesions on biopsy (cervical intraepithelial neoplasia 2/3 [CIN 2/3]). Demographic variables were compared between

women who screened VIA-positive and those who screened VIA-negative; a separate comparison of demographic and limited reproductive variables was performed between women who had CIN 2/3 on biopsy and those without CIN 2/3 on biopsy. Chi-square or Fisher's exact tests for categorical data and t-tests or analysis of variance for numeric data were used with all tests two-sided and performed at an alpha 0.05 level of statistical significance. RESULTS: A total of 9130 women were screened with VIA between 4 July 2020 and 31 March 2021. The mean age of all women screened was 37 years (standard deviation = 5.6 years) with 6073 of the women (66.5%) in the 30-39 year range. Only 1% of women reported prior cervical cancer screening. A total of 501 women (5.5%) were VIA-positive; of these, 401 women underwent colposcopy. Of those who had colposcopy, 17 (4.2%) had high-grade lesions on biopsy, an additional 164 (40.9%) had low-grade cervical lesions on biopsy or endocervical curettage and one woman (0.2%) was found to have invasive cancer. VIA-positive women were younger and had higher levels of education and income; however, women who were VIA-positive and found to have CIN 2/3 were older, were more likely to be housewives and had higher household income than those without CIN 2/3. CONCLUSION: Despite the COVID-19 pandemic, over 9100 women were screened with VIA for precancerous lesions. However, only 17 (4.2%) were found to have biopsy-proven high-grade cervical lesions, underscoring the subjective performance of VIA as a screening method. Given that this is significantly lower than rates reported in the literature, it is possible that the prevalence of high-grade lesions in this population was impacted by screening a younger and more rural population. This study demonstrates that screening is feasible in an organised fashion and can be scaled up rapidly. However, while inexpensive and allowing for same-day treatment, VIA may be too subjective and have insufficient accuracy clearly to identify lesions requiring treatment, particularly in low-prevalence and low-risk populations, calling into question its overall cost-effectiveness.

Arthur, A., et al. (2023). "A CT-based radiomics classification model for the prediction of histological type and tumour grade in retroperitoneal sarcoma (RADSARC-R): a retrospective multicohort analysis." Lancet Oncol **24**(11): 1277-1286.
BACKGROUND: Retroperitoneal sarcomas are tumours with a poor prognosis. Upfront characterisation of the tumour is difficult, and under-grading is common. Radiomics has the potential to non-invasively characterise the so-called radiological phenotype of tumours. We aimed to develop and independently validate a CT-based radiomics classification model for the prediction of histological type and grade in retroperitoneal leiomyosarcoma and liposarcoma. METHODS: A retrospective discovery cohort was collated at our centre (Royal Marsden Hospital, London, UK) and an independent validation cohort comprising patients recruited in the phase 3 STRASS study of neoadjuvant radiotherapy in retroperitoneal sarcoma. Patients aged older than 18 years with confirmed primary leiomyosarcoma or liposarcoma proceeding to surgical resection with available contrast-enhanced CT scans were included. Using the discovery dataset, a CT-based radiomics workflow was developed, including manual delineation, sub-segmentation, feature extraction, and predictive model building. Separate probabilistic classifiers for the prediction of histological type and low versus intermediate or high grade tumour types were built and tested. Independent validation was then performed. The primary objective of the study was to develop radiomic classification models for the prediction of retroperitoneal leiomyosarcoma and liposarcoma type and histological grade. FINDINGS: 170 patients recruited between Oct 30, 2016, and Dec 23, 2020, were eligible in the discovery cohort and 89 patients recruited between Jan 18, 2012, and April 10, 2017, were eligible in the validation cohort. In the discovery cohort, the median age was 63 years (range 27-89), with 83 (49%) female and 87 (51%) male patients. In the validation cohort, median age was 59 years (range 33-77), with 46 (52%) female and 43 (48%) male patients. The highest performing model for the prediction of histological type had an area under the receiver operator curve (AUROC) of 0.928 on validation, based on a feature set of radiomics and approximate radiomic volume fraction. The highest performing model for the prediction of histological grade had an AUROC of 0.882 on validation, based on a radiomics feature set. INTERPRETATION: Our validated radiomics model can predict the histological type and grade of retroperitoneal sarcomas with excellent performance. This could have important implications for improving diagnosis and risk stratification in retroperitoneal sarcomas. FUNDING: Wellcome Trust, European Organisation for Research and Treatment of Cancer-Soft Tissue and Bone Sarcoma Group, the National Institutes for Health, and the National Institute for Health and Care Research Biomedical Research Centre at The Royal Marsden NHS Foundation Trust and The Institute of Cancer Research.

Atef Abdelsattar Ibrahim, H., et al. (2023). "Glucose indices as inflammatory markers in children with acute surgical abdomen: a cross-sectional study." Ann Med **55**(2): 2248454.
BACKGROUND: Glycaemic dysregulation potentiates the pro-inflammatory response and increases oxidative injury; therefore, preoperative hyperglycaemia is linked

to increased mortalities. In addition, inflammation is accompanied by higher glycated haemoglobin (HbA1c) levels, and the relationship between this and random blood sugar (RBS) could be non-linear. METHODS: This is a cross-sectional study. Non-diabetic paediatric patients with acute surgical abdomen, presenting to the emergency surgical services were enrolled, over a period of 6 months. They were all screened for their random blood sugar and HbA1c levels. RESULTS: Fifty-three cases were studied. The prevalence of glycaemic dysregulation in the enrolled children was high. Abnormal HbA1c was observed in 66% of the study group. Stress hyperglycaemia was observed in 60% of the enrolled children. There was a significant correlation (r = 0.770, p-value: < 0.001) between RBS and the total leucocytic count (TLC). The TLC cutoff value for predicting stress hyperglycaemia was 13,595 cells/mm(3). The cutoff value of RBS for predicting leukocytosis was 111.5 mg/dl. Median RBS level was significantly higher in complicated appendicitis (169.5 mg/dl), compared to uncomplicated appendicitis (118.0 mg/dl). CONCLUSION: HbA1c and RBS could be used as inflammatory markers for surgical acute abdomen and its degree of severity, respectively. HbA1c rises in a considerable number of cases with surgical acute abdomen, irrespective of the disease stage. However, as the disease progresses, the random blood sugar rises due to stress hyperglycaemia, thus becoming a surrogate inflammatory marker.

What is already known on this topic? Preoperative stress hyperglycaemia is common in children, and it is linked to adverse postoperative outcomes. HbA1c could be a marker for inflammation and oxidative stress.What does this study add? HbA1c could be an inflammatory marker for surgical acute abdomen, irrespective of the disease stage, as it had a high prevalence in the enrolled children with an acute surgical abdomen. However, as the disease progresses, the random blood sugar rises due to stress hyperglycaemia, thus becoming a surrogate inflammatory marker, as there is a significant correlation between it and the TLC.How might this study affect research, practice, or policy? The novelty in this study centers around the role of glucose metabolism, as evaluated by random blood sugar and HBA1c, in the diagnostic evaluation and prognostication of inflammation, represented by the surgical acute abdomen. This may invite further research into understanding the underlining mechanisms. The outcome of the clinical management of conditions involving inflammation can be improved by using the proposed biomarkers, as peri/preoperative hyperglycaemia could lead to morbidity and mortality, consequently, as proven, the reliability of those biomarkers facilitates risk assessment and stratification. As both tests are cost-effective and universally available, they can be readily implemented in practice guidelines and departmental policies.

Baena, A., et al. (2023). "Latin America and the Caribbean Code Against Cancer 1st Edition: Medical interventions including hormone replacement therapy and cancer screening." Cancer Epidemiol **86 Suppl 1**: 102446.

Prostate, breast, colorectal, cervical, and lung cancers are the leading cause of cancer in Latin America and the Caribbean (LAC) accounting for nearly 50% of cancer cases and cancer deaths in the region. Following the IARC Code Against Cancer methodology, a group of Latin American experts evaluated the evidence on several medical interventions to reduce cancer incidence and mortality considering the cancer burden in the region. A recommendation to limit the use of HRT was issued based on the risk associated to develop breast, endometrial, and ovarian cancer and on growing concerns related to the over-the-counter and without prescription sales, which in turn bias estimations on current use in LAC. In alignment with WHO breast and cervical cancer initiatives, biennial screening by clinical breast examination (performed by trained health professionals) from the age of 40 years and biennial screening by mammography from the age of 50 years to 74, as well as cervical screening by HPV testing (either self-sampling or provider-sampling) every 5-10 years for women aged 30-64 years, were recommended. The steadily increasing rates of colorectal cancer in LAC also led to recommend colorectal screening by occult blood testing every two years or by endoscopic examination of the colorectum every 10 years for both men and women aged 50-74 years. After evaluating the evidence, the experts decided not to issue recommendations for prostate and lung cancer screening; while there was insufficient evidence on prostate cancer mortality reduction by prostate-specific antigen (PSA) testing, there was evidence of mortality reduction by low-dose computed tomography (LDCT) targeting high-risk individuals (mainly heavy and/or long-term smokers) but not individuals with average risk to whom recommendations of this Code are directed. Finally, the group of experts adapted the gathered evidence to develop a competency-based online microlearning program for building cancer prevention capacity of primary care health professionals.

Banks, J. (2023). "DNA Testing for Preventative Health: Do Outcomes Justify Continued Investment?" IEEE Pulse **14**(4): 19-23.

In The U.K., a heated debate is raging in the genetics community about a not-so-new technology and its role in public health. Cheap genetic tests to discover our ancestry have become familiar consumer products, and

our genes can tell us a lot about our ancestry, so it is an appealing idea that they can tell us about our susceptibility to serious diseases. Polygenic risk scores (PRS)-generated by sequencing multiple parts of a person's DNA-are said by some to hold the key to helping people avoid everything from type 1 diabetes to cardiovascular disease and cancer. This could herald a new era of preventive medicine, and the U.K. is investing heavily, but ultimately, whether or not this a good investment is still being determined.

Blechter, B., et al. (2023). "Polygenic Risk Score, Environmental Tobacco Smoke, and Risk of Lung Adenocarcinoma in Never-Smoking Women in Taiwan." JAMA Netw Open **6**(11): e2339254.
IMPORTANCE: Estimating absolute risk of lung cancer for never-smoking individuals is important to inform lung cancer screening programs. OBJECTIVES: To integrate data on environmental tobacco smoke (ETS), a known lung cancer risk factor, with a polygenic risk score (PRS) that captures overall genetic susceptibility, to estimate the absolute risk of lung adenocarcinoma (LUAD) among never-smokers in Taiwan. DESIGN, SETTING, AND PARTICIPANTS: The analyses were conducted in never-smoking women in the Taiwan Genetic Epidemiology Study of Lung Adenocarcinoma, a case-control study. Participants were recruited between September 17, 2002, and March 30, 2011. Data analysis was performed from January 17 to July 15, 2022. EXPOSURES: A PRS was derived using 25 genetic variants that achieved genome-wide significance ($P < 5 \times 10^{-8}$) in a recent genome-wide association study, and ETS was defined as never exposed, exposed at home or at work, and exposed at home and at work. MAIN OUTCOMES AND MEASURES: The Individualized Coherent Absolute Risk Estimator software was used to estimate the lifetime absolute risk of LUAD in never-smoking women aged 40 years over a projected 40-year span among the controls by using the relative risk estimates for the PRS and ETS exposures, as well as age-specific lung cancer incidence rates for never-smokers in Taiwan. Likelihood ratio tests were conducted to assess an additive interaction between the PRS and ETS exposure. RESULTS: Data were obtained on 1024 women with LUAD (mean [SD] age, 59.6 [11.4] years, 47.9% ever exposed to ETS at home, and 19.5% ever exposed to ETS at work) and 1024 controls (mean [SD] age, 58.9 [11.0] years, 37.0% ever exposed to ETS at home, and 14.3% ever exposed to ETS at work). The overall average lifetime 40-year absolute risk of LUAD estimated using PRS alone was 2.5% (range, 0.6%-10.3%) among women never exposed to ETS. When integrating both ETS and PRS data, the estimated absolute risk was 3.7% (range, 0.6%-14.5%) for women exposed to ETS at home or work and 5.3% (range, 1.2%-12.1%) for women exposed to ETS at home and work. A super-additive interaction between ETS and the PRS ($P = 6.5 \times 10^{-4}$ for interaction) was identified. CONCLUSIONS AND RELEVANCE: This study found differences in absolute risk of LUAD attributed to genetic susceptibility according to levels of ETS exposure in never-smoking women. Future studies are warranted to integrate these findings in expanded risk models for LUAD.

Cameron, J. K., et al. (2023). "Disease mapping: Geographic differences in population rates of interventional treatment for prostate cancer in Australia." PLoS One **18**(11): e0293954.
BACKGROUND: Treatment decisions for men diagnosed with prostate cancer depend on a range of clinical and patient characteristics such as disease stage, age, general health, risk of side effects and access. Associations between treatment patterns and area-level factors such as remoteness and socioeconomic disadvantage have been observed in many countries. OBJECTIVE: To model spatial differences in interventional treatment rates for prostate cancer at high spatial resolution to inform policy and decision-making. METHODS: Hospital separations data for interventional treatments for prostate cancer (radical prostatectomy, low dose rate and high dose rate brachytherapy) for men aged 40 years and over were modelled using spatial models, generalised linear mixed models, maximised excess events tests and k-means statistical clustering. RESULTS: Geographic differences in population rates of interventional treatments were found ($p<0.001$). Separation rates for radical prostatectomy were lower in remote areas (12.2 per 10 000 person-years compared with 15.0-15.9 in regional and major city areas). Rates for all treatments decreased with increasing socioeconomic disadvantage (radical prostatectomy 19.1 /10 000 person-years in the most advantaged areas compared with 12.9 in the most disadvantaged areas). Three groups of similar areas were identified: those with higher rates of radical prostatectomy, those with higher rates of low dose brachytherapy, and those with low interventional treatment rates but higher rates of excess deaths. The most disadvantaged areas and remote areas tended to be in the latter group. CONCLUSIONS: The geographic differences in treatment rates may partly reflect differences in patients' physical and financial access to treatments. Treatment rates also depend on diagnosis rates and thus reflect variation in investigation rates for prostate cancer and presentation of disease. Spatial variation in interventional treatments may aid identification of areas of under-treatment or over-treatment.

Carr, M. J., et al. (2023). "Grade of Primary Cutaneous Leiomyosarcoma Dictates Risk for Metastatic Spread

and Disease-Specific Mortality." Cancer Control **30**: 10732748231206957.
BACKGROUND AND OBJECTIVES: Primary cutaneous leiomyosarcoma (cLMS), a rare, typically intradermal tumor, has previously been reported to exhibit an indolent course of disease with zero-to-low risk of local recurrence or distant metastasis. This study seeks to evaluate recurrence and survival of cLMS patients through study of its clinicopathologic and treatment characteristics. METHODS: All patients included underwent resection of primary cLMS at this institution between 2006 and 2019. A retrospective cohort study analysis of clinicopathologic characteristics, treatment, recurrence, and overall survival was performed. Data was assessed through descriptive statistics and outcome measures assessed by Cox proportional models and log-rank tests. RESULTS: Eighty-eight patients with cLMS were evaluated. The majority were men (n = 68, 77%) and Caucasian (n = 85, 97%), with median age at diagnosis of 66 years (range 20-96). 65% of tumors were located on the extremities, with a median size of 1.3 cm (range .3-15). Assessment revealed low (n = 41, 47%), intermediate (n = 29, 33%), and high (n = 18, 20%) grade tumors, demonstrating extension into subcutaneous tissue in 38/60 (60%), with 3 patients exhibiting extension into muscle (3%). All underwent resection as primary treatment with median 1 cm margins (range .5-2). With median follow-up of 27.5 months (IQR 8-51; range 1-131), no low-grade cases had recurrence or death while there was a recurrence rate of 19.1% (9/47) and death rate of 8.5% (4/47) in intermediate- to high-grade cases. CONCLUSIONS: Primary tumor resection of cLMS provides excellent local control for low-grade tumors as no low-grade cases experienced recurrence. For patients with intermediate- to high-grade tumors, there is potential for local recurrence, distant metastasis, and death, and therefore surveillance following treatment is encouraged.

Chadwick, V., et al. (2023). "A minority of women of childbearing potential are tested for pregnancy before chemoimmunotherapy: An Australian Cancer Centre Experience." Intern Med J.
BACKGROUND: Chemotherapy is potentially harmful to a developing foetus and there is limited data on the foetal impact of chemoimmunotherapy (CIT). Therefore, determining pregnancy status prior to initiation of CIT should be standard of care. AIMS: To determine how many women of childbearing age are tested for pregnancy prior to immunochemotherapy administration. METHODS: A retrospective chart review at a large Australian metropolitan cancer referral centre, including 304 women aged 18 to 51 years with a diagnosis of cancer receiving outpatient-based CIT between May 1 2015 and June 12 2020. We assessed uptake of pregnancy screening and contraception counselling prior to and during first-line CIT. RESULTS: Only 17.3% of CIT cycles (n = 416) screened patients for pregnancy 90 days or prior to administration, and the median time between pregnancy screening and treatment was approximately three weeks. One patient with early breast cancer had a spontaneous miscarriage estimated at 3-4 weeks gestation, and neither the patient nor the treating oncologist was aware of this event. This was also the only patient who had a pregnancy test beyond the first cycle of CIT during their treatment. CONCLUSIONS: Our results highlight a concerningly low rate of pregnancy screening in women of childbearing age receiving CIT. The implication of missing a positive pregnancy test in this group of women could result in foetal complication, accidental miscarriage, potential bleeding risks and avoidable psychosocial stress. This highlights the urgent need for guidelines to mandate pregnancy testing in women of childbearing age receiving CIT and evidence-based implementation tools.

Chapman, G. C., et al. (2023). "Gynecologic cancer care in the first year of the COVID-19 pandemic." Gynecol Oncol **178**: 138-144.
OBJECTIVE: To analyze the impact of the early COVID-19 pandemic on the diagnosis and initiation of treatment for patients with gynecologic cancer. METHODS: Patients diagnosed with gynecologic cancer in the National Cancer Database during 2017-2020 were included. For the first aim, incidence rate ratios were calculated to compare gynecologic cancer diagnosis in the first year of the COVID-19 pandemic to the three years prior, and factors associated with a reduction in diagnosis were identified. For the second aim, patients who experienced an 8-week delay in cancer treatment were compared to those who did not. Multivariate logistic regression was used to identify factors associated with treatment delay. Propensity score analysis was utilized to compare the rate of cancer treatment delay in patients who were diagnosed with COVID-19 to those who were not. RESULTS: The incidence rate ratio of being diagnosed with gynecologic cancer in 2020 versus 2017-2019 was 0.90 (95%CI 0.90-0.91). Factors associated with increased risk of missed or delayed diagnosis in 2020 included cervical cancer, earlier cancer stage, younger age, lower levels of medical comorbidity, and lack of health insurance. In 2020, factors associated with treatment delay included COVID-19 diagnosis (aOR 1.50, 95%CI 1.35-1.67), in addition to race and ethnicity, insurance type, comorbidity, cancer stage, and primary site. The risk of treatment delay remained significantly elevated in patients diagnosed with COVID-19 after propensity-score matching. CONCLUSIONS: Gynecologic cancer diagnosis and timely provision of care were negatively

impacted during the first year of the COVID-19 pandemic, with certain subgroups at elevated risk.

Chen, C., et al. (2023). "Functionalized GD2 Electrochemical Immunosensor to Diagnose Minimum Residual Disease of Bone Marrow in Neuroblastoma Effectively." Biosensors (Basel) **13**(10).
Neuroblastoma (NB) is known as the "king of childhood tumors" due to its highly metastatic, recurrence-prone, and difficult-to-treat characteristics. International Neuroblastoma Risk Grading Group (INRG) has recommended GD2, a disialoganglioside expressed on neuroectodermal tumor cells, as the target for detecting minimal residual disease in bone marrow metastases of high-risk neuroblastoma in children. Therefore, accurately identifying GD2-positive cells is crucial for diagnosing children with high-risk NB. Here, we designed a graphene/AuNP/GD2 Ab-functionalized electrochemical biosensor for GD2 detection. A three-electrode system was processed using a screen-printed technique with a working electrode of indium tin oxide, a counter electrode of carbon, and a reference electrode of silver/silver chloride. Graphene/AuNPs were modified on the indium tin oxide electrode using chronoamperometric scans, and then, the GD2 antibody was modified on the biosensor by electrostatic adsorption to achieve sensitive and specific detection of GD2-positive cells in bone marrow fluid. The results showed that a graphene/AuNP/GD2 Ab-functionalized electrochemical biosensor achieved GD2-positive cell detection in the range of 10(2) cells/mL~10(5) cells/mL by differential pulse voltammetry. Bone marrow fluid samples from 12 children with high-risk NB were retained for testing on our biosensor and showed 100% compliance with the clinical application of the gold-standard immunocytochemical staining technique for detecting GD2-positive cells qualitatively. The GD2-based electrochemical assay can accurately detect children with high-risk NB, providing a rapidly quantitative basis for clinical diagnosis and treatment.

Cheung, T. T., et al. (2023). "The Hong Kong consensus recommendations on the diagnosis and management of pancreatic cystic lesions." Hepatobiliary Surg Nutr **12**(5): 715-735.
BACKGROUND: The finding of pancreatic cystic lesions (PCL) on incidental imaging is becoming increasingly common. International studies report a prevalence of 2.2-44.7% depending on the population, imaging modality and indication for imaging, and the prevalence increases with age. Patients with PCL are at risk of developing pancreatic cancer, a disease with a poor prognosis. This publication summarizes recommendations for the diagnosis and management of PCL and post-operative pancreatic exocrine insufficiency (PEI) from a group of local specialists. METHODS: Clinical evidence was consolidated from narrative reviews and consensus statements formulated during two online meetings in March 2022. The expert panel included gastroenterologists, hepatobiliary surgeons, oncologists, radiologists, and endocrinologists. RESULTS: Patients with PCL require careful investigation and follow-up due to the risk of malignant transformation of these lesions. They should undergo clinical investigation and pancreas-specific imaging to classify lesions and understand the risk profile of the patient. Where indicated, patients should undergo pancreatectomy to excise PCL. Following pancreatectomy, patients are at risk of PEI, leading to gastrointestinal dysfunction and malnutrition. Therefore, such patients should be monitored for symptoms of PEI, and promptly treated with pancreatic enzyme replacement therapy (PERT). Patients with poor response to PERT may require increases in dose, addition of a proton pump inhibitor, and/or further investigation, including tests for pancreatic function. Patients are also at risk of new-onset diabetes mellitus after pancreatectomy; they should be screened and treated with insulin if indicated. CONCLUSIONS: These statements are an accurate summary of our approach to the diagnosis and management of patients with PCL and will be of assistance to clinicians treating these patients in a similar clinical landscape.

Coleman, C., et al. (2023). "Opioid dose risk, clinician and patient characteristics, and adherence to opioid prescribing recommendations in chronic non-cancer pain." J Opioid Manag **19**(5): 413-422.
OBJECTIVE: This study aims to assess associations between morphine-equivalent daily dose (MEDD) of opioids, clinician and patient characteristics, and prescriber adherence to guidelines for long-term opioid therapy (LTOT) in chronic noncancer pain (CNCP) and to elucidate potential relationships associated with increased-risk opioid prescribing. DESIGN: Retrospective cross-sectional study. SETTING: Academic health system's 33 primary care clinics. PATIENTS: Adults (>/=18 years old) prescribed LTOT (10 + outpatient prescriptions in the past year) for CNCP. MAIN OUTCOME MEASURE(S): Electronic health record data on prescribed opioids (for MEDD), clinician/patient characteristics, and adherence rates to LTOT guideline-concordant recommendations. RESULTS: A total of 2,738 patients were eligible, 61.6 percent Lower, 15.7 percent Moderate, and 22.7 percent Higher Risk MEDD (<50, 50-89, and >/=90 mg/day, respectively). Higher MEDD correlated ($p < 0.001$) with Medicare insurance, current cigarette smoking, higher pain intensity and interference scores, and the presence of opioid use disorder diagnoses. Male clinicians more frequently prescribed ($p < 0.001$) and male patients were more likely to be prescribed ($p < 0.001$) higher MEDD

compared to their female counterparts. Higher Risk MEDD was associated with higher coprescribed benzodiazepines (p = 0.015), lower depression screening (p = 0.048), urine drug testing (p = 0.003), comparable active treatment agreement (p = 0.189), opioid misuse risk screening (p = 0.619), and prescription drug monitoring checks (p = 0.203). CONCLUSIONS: This study documented that higher MEDD was associated with risks of worse health outcomes without improved adherence to opioid prescribing guideline recommendations. Enhanced clinician awareness of factors associated with MEDD has the potential to mitigate LTOT risks and improve overall patient care.

D'Ambrosio, L., et al. (2023). "Guideline-Based Follow-Up Outcomes in Patients With Gastrointestinal Stromal Tumor With Low Risk of Recurrence: A Report From the Italian Sarcoma Group." JAMA Netw Open **6**(11): e2341522.
IMPORTANCE: Gastrointestinal stromal tumor (GIST) follow-up is recommended by international guidelines, but data on the role of follow-up in patients with low relapse risk are missing. For these patients, the potential benefit of anticipating recurrence detection should be weighed against psychological burden and radiologic examination loads in terms of costs and radiation exposure. OBJECTIVE: To evaluate the outcomes of guideline-based follow-up in low-risk GIST. DESIGN, SETTING, AND PARTICIPANTS: This multi-institutional retrospective cohort study involving Italian Sarcoma Group reference institutions evaluated patients with GIST who underwent surgery between January 2001 and June 2019. Median follow-up time was 69.2 months. Data analysis was performed from December 15, 2022, to March 20, 2023. Patients with GIST at low risk according to Armed Forces Institute of Pathology criteria were included provided adequate clinical information was available: primary site, size, mitotic index, surgical margins, and 2 or more years of follow-up. EXPOSURES: All patients underwent follow-up according to European Society for Medical Oncology (ESMO) guidelines. MAIN OUTCOMES AND MEASURES: The primary outcome was the number of tests needed to identify a relapse according to ESMO guidelines follow-up plan. Secondary outcomes included relapse rate, relapse timing, disease-free survival (DFS), overall survival (OS), GIST-specific survival (GIST-SS), postrelapse OS, secondary tumor rates, and theoretical ionizing radiation exposure. An exploratory end point, new follow-up schedule proposal for patients with low-risk GIST according to the observed results, was also assessed. RESULTS: A total of 737 patients (377 men [51.2%]; median age at diagnosis, 63 [range, 18-86] years) with low-risk GIST were included. Estimated 5-year survival rates were 95.5% for DFS, 99.8% for GIST-SS, and 96.1% for OS. Estimated 10-year survival rates were 93.4% for DFS, 98.1% for GIST-SS, and 91.0% for OS. Forty-two patients (5.7%) experienced disease relapse during follow-up (9 local, 31 distant, 2 both), of which 9 were detected after 10 or more years. This translated into approximately 1 relapse detected for every 170 computed tomography scans performed, with a median radiation exposure of 80 (IQR, 32-112) mSv per patient. Nongastric primary tumor (hazard ratio [HR], 2.09; 95% CI, 1.14-3.83; P = .02), and KIT mutation (HR, 2.77; 95% CI, 1.05-7.27; P = .04) were associated with a higher risk of relapse. Second tumors affected 187 of 737 patients (25%), of which 56 were detected during follow-up and represented the primary cause of death in these patients. CONCLUSIONS AND RELEVANCE: In this cohort study on patients affected by low-risk GISTs, the risk of relapse was low despite a follow-up across 10 or more years. These data suggest the need to revise follow-up schedules to reduce the anxiety, costs, and radiation exposure of currently recommended follow-up strategy.

Dankai, W., et al. (2023). "Molecular-based classification of endometrial carcinoma in Northern Thailand: impact on prognosis and potential for implementation in resource-limited settings." BMC Womens Health **23**(1): 605.
BACKGROUND: Endometrial carcinoma is molecularly categorized into four subgroups: polymerase-E exonuclease domain-mutant (POLE-mut), mismatch repair-deficient (MMR-d), p53-abnormal (p53-abn), and no specific molecular profile (NSMP). This classification scheme has been included into clinical recommendation for post-operative risk-based management, although there have been few Asian studies on this topic. The present study aimed to evaluate the prevalence and clinical outcomes of endometrial carcinoma using this classification in Northern Thailand and the feasibility of implementation in resource-limited settings. METHODS: Endometrial carcinomas from hysterectomy specimens were classified using immunohistochemistry for MMR proteins and p53, as well as POLE mutation testing. Clinicopathological variables and outcomes were analyzed. The costs of the molecular information-based approach were compared to those incurred by the conventional approach (without molecular classification). RESULTS: Of 138 patients, 52.9% in the NSMP subgroup, 28.2% were in the MMR-d, 13.8% in the p53-abn, and 5.1% in the POLE-mut. After adjusting for other variables, patients with POLE-mut showed the most favorable outcomes, while those with p53-abn had the poorest survival. When estimating the costs for post-operative management, the use of molecular classification resulted in a 10% increase over the conventional approach. However, the cost increased

only by 1% if only POLE testing was used to identify patients for treatment omission. CONCLUSION: In Northern Thailand, endometrial carcinoma had comparable subgroup distribution and prognostic implications to previous reports, supporting the implementation of management guidelines that incorporate molecular information. In resource-limited settings, at least POLE mutation testing in early-stage patients should be considered.

Ding, X., et al. (2023). "Construction of a novel prognostic model in skin cutaneous melanoma based on chemokines-related gene signature." Sci Rep **13**(1): 18172.
Skin cutaneous melanoma, SKCM, is one of the most aggressive treatment-resistant tumours. Despite the fact that the BRAF oncogene and immunological checkpoints such as PD-1/PD-L1 and CTLA-4 have enhanced the therapeutic efficacy of SKCM, the subsequent resistance mechanisms and remedies have raised concerns. Chemokines have a significant role in the immunological milieu of tumor, which may increase the efficacy of checkpoint blockade and serve as a possible therapeutic intervention route. However, there is still no chemokine-based typing and risk model to provide a prognosis and therapeutic efficacy assessment for SKCM patients. In this study, we verified the distinct differences of prognostic stratification as well as immune characteristics between two chemokine-related clusters in SKCM patients. Two clusters of DEGs were discovered to be primarily enriched in B and T cell receptor signaling pathways as well as TNF signaling via NF-kappa-B. Based on 14 prognosis-related DEGs from aforementioned two clusters (CCL8, GBP2, GBP4, SRNG, HLA-DMB, RARRES3, HLA-DQA1, PARP12, APOL3, IRF1, HLA-DRA, UBE2L6, IL2RA and CD38), a chemokine-related 14-gene prognostic model was established. At the same time, researchers explored differences between the low-risk and high-risk groups in clinical traits, the proportion of infiltration of 22 different types of immune cells, and how well medications worked. The risk score model's immunotherapy and prognostic predictions were also confirmed in testing groups. Based on the finding, we can claim that there is a clear link between chemokines and TME in SKCM. The risk score may perform as a trustworthy prediction model, giving therapeutic benefits for both chemotherapy and immunotherapy, as well as being beneficial for clinical decision making in SKCM patients.

Dong, S., et al. (2023). "Sequential high-intensity focused ultrasound treatment combined with chemotherapy for inoperable pancreatic cancer: a retrospective analysis for prognostic factors and survival outcomes." Int J Hyperthermia **40**(1): 2278417.
OBJECTIVE: To evaluate the effect of HIFU (High-Intensity Focused Ultrasound) therapy on the survival and prognosis of patients with inoperable pancreatic cancer, and the clinical application of serological prognostic indicators. METHODS: We retrospectively analyzed the clinicopathological features, laboratory tests and follow-ups of 192 patients. Among the patients, 57 were treated with HIFU prior to chemotherapy (HIFU-priority), and 135 patients received chemotherapy followed by HIFU (HIFU-second). Univariate and multivariate Cox regression analysis was used to determine the prognostic value of tumor inflammation-related serological markers. A nomogram model was established based on the identified prognostic factors. RESULTS: Univariate analysis showed that receiving the treatment regimen in HIFU-priority was a significant protective factor for overall survival (OS, $p < 0.001$). Tumor stage, high C-reactive protein (CRP), high gamma-glutamyl transferase(gammaGT) high carbohydrate antigen 125 (CA125), high neutrophil-to-lymphocyte ratio (NLR), high lymphocyte-to-monocyte ratio (LMR) and liver metastasis were significant risk factors for poor prognosis ($p < 0.05$). CRP combined with normal tumor marker CA125 (CRP + CA125) was associated with longer OS ($p = 0.005$). Multivariate analysis shows that HIFU-priority is a protective factor for OS (Hazard Ratio, HR: 0.38; 95% confidence interval(CI): 0.25-0.57), tumor stage (HR: 1.61; 95% CI: 1.12-2.31), CRP + CA125 (HR: 1.46; 95% CI: 1.02-2.08) and gammaGT (HR: 1.44; 95% CI: 1.04-1.98) are risk factors for OS and serve as independent prognostic factors in the nomogram. CONCLUSION: Early application of HIFU treatment improves the OS of patients with inoperable pancreatic cancer. CRP + CA125 and gammaGT are independent prognostic factors.

Elremeli, M., et al. (2023). "Li-Fraumeni Syndrome, A Rarity Among Rarities: A Case Report and Review of Literature." Cureus **15**(9): e45462.
Li-Fraumeni syndrome (LFS) is a rare inherited cancer susceptibility disorder with a wide tumour spectrum, particularly in children and young adults. Patients with LFS have life-long cancer risk, and the most commonly encountered tumours include soft tissue sarcoma, breast cancer, brain tumours, osteosarcoma, leukaemia and adrenocortical carcinoma. LFS is associated with mutations in the tumour suppressor gene TP53, andnearly two-thirds of families with LFS have this germline mutation. However, the diagnosis of LFS is currently based on recognised strict clinical criteria regardless of the genetic mutation status, as a few families with the clinical characteristics and cancer predisposition of LFS do not have TP53 mutations. Breast cancer is particularly significant among the common malignancies associated with LFS as it is the

most common cancer in women worldwide. We present a case of a 27-year-old woman with unilateral breast cancer, in whom further history revealed a brain tumour at the age of 14 years. Due to the early onset of breast cancer and history of childhood malignancy, we suspected LFS. Genetic testing revealed a TP53 mutation, further suggesting the diagnosis of LFS. This has important implications in managing this patient's breast cancer, as the need for risk-reducing mastectomy and arranging a special surveillance programme. It also has great implications for the patient's family members, especially in terms of psychological impact, particularly when the mutation has been detected in children. Also, there is a need for periodic surveillance, which can help in early diagnosis and timely treatment with a more favourable outcome.

Emeraud, C., et al. (2023). "Emergence and rapid dissemination of highly resistant NDM-14-producing Klebsiella pneumoniae ST147, France, 2022." Euro Surveill **28**(42).
BackgroundSince 2021, an emergence of New Delhi metallo-beta-lactamase (NDM)-14-producing Klebsiella pneumoniae has been identified in France. This variant with increased carbapenemase activity was not previously detected in Enterobacterales.AimWe investigated the rapid dissemination of NDM-14 producers among patients in hospitals in France.MethodsAll NDM-14-producing non-duplicate clinical isolates identified in France until June 2022 (n = 37) were analysed by whole genome sequencing. The phylogeny of NDM-14-producers among all K. pneumoniae sequence type (ST) 147 reported in France since 2014 (n = 431) was performed. Antimicrobial susceptibility testing, conjugation experiments, clonal relationship and molecular clock analysis were performed.ResultsThe 37 NDM-14 producers recovered in France until 2022 belonged to K. pneumoniae ST147. The dissemination of NDM-14-producing K. pneumoniae was linked to a single clone, likely imported from Morocco and responsible for several outbreaks in France. The gene bla (NDM-14) was harboured on a 54 kilobase non-conjugative IncFIB plasmid that shared high homology with a known bla (NDM-1)-carrying plasmid. Using Bayesian analysis, we estimated that the NDM-14-producing K. pneumoniae ST147 clone appeared in 2020. The evolutionary rate of this clone was estimated to 5.61 single nucleotide polymorphisms per genome per year. The NDM-14 producers were highly resistant to all antimicrobials tested except to colistin, cefiderocol (minimum inhibitory concentration 2 mg/L) and the combination of aztreonam/avibactam.ConclusionHighly resistant NDM-14 producing K. pneumoniae can rapidly spread in healthcare settings. Surveillance and thorough investigations of hospital outbreaks are critical to evaluate and limit the dissemination of this clone.

Fantasia, I., et al. (2023). "Late third trimester diagnosis of congenital giant hemangioma complicated by the Kasabach-Merritt phenomen: a case report and literature review." J Matern Fetal Neonatal Med **36**(2): 2274803.
Objective. To describe the case of a large cervical mass diagnosed in the late third trimester with development of Kasabach-Merritt phenomenon (KMP) in the immediate postnatal period, along with a literature review.Methods. Description of case-report and literature search through Medline/Pubmed, performed from inception to December 2022 for articles relating to the pre and postnatal diagnosis of KMP.Results. A 36-year-old multiparous woman was admitted to hospital for contractions at 40 weeks of gestation, in an otherwise uneventful pregnancy. Admission's ultrasound showed the presence of a voluminous mass of 14x15 cm of the posterior side of the neck, highly vascularized, and no signs of hemodynamic imbalance. Postnatally, blood tests showed the presence of severe anemia and thrombocytopenia requiring several transfusions of blood, plasma, platelets and clotting factors. Due to the association of congenital hemangioma and thrombocytopenia a diagnosis of KMP was made. After attempts of conservative treatment, surgical removal was needed to stop the hematological cascade with regression of symptoms. The review of the literature identified 14 articles including 9 cases of prenatally suspected KMP and 6 diagnosed in the immediate postnatal period and without signs of fetal hydrops. Adverse perinatal outcome, in terms of postnatal death/termination of pregnancy, was observed in 67% of cases (6/9) in the prenatally suspected group and 33% of cases in those with a postnatal diagnosis of KMP. Fetal hydrops was present in 83% of cases with adverse perinatal outcome.Conclusions. The Kasabach-Merrit syndrome is a rare condition, which can have a dangerous evolution when it develops in utero or in the immediate postnatal period carrying a risk of perinatal mortality of approximately 50%. Even if the fetus shows no signs of anemia or heart failure, the risk of developing it in the immediate postnatal period is high and should be mentioned to the couple.

Feng, T., et al. (2023). "Outcome and associated factors of high-risk human papillomavirus infection without cervical lesions." BMC Womens Health **23**(1): 599.
OBJECTIVE: To study the outcome of human papillomavirus (HPV) infection in women with cervical pathology results of non-cervical intraepithelial neoplasia (CIN) or cervical cancer and positive high-risk HPV test, as well as analyze the associated risk factors affecting the outcome of infection. METHODS: To investigate the outcome of high-risk (HR)-HPV

infection in the female genital tract and analyze the associated risk factors affecting their outcome, a total of 196 women with positive HR-HPV test results and non-CIN or cervical cancer cervical pathology results were selected for follow-up at the Cervical Disease Clinic of the Obstetrics and Gynecology Hospital, Zhejiang University School of Medicine from January 2017 to March 2020. The follow-up interval was every 6 months, and both cervical cytology (TCT) and HR-HPV testing were performed at each follow-up visit. If the cervical cytology results were normal upon recheck and the HR-HPV test was negative, the woman was considered to be cleared of the HPV infection and was entered into the routine cervical screening population. When the repeat HR-HPV test remained positive after 6 months, the woman was defined as having a persistent HR-HPV infection. If HR-HPV persisted but the TCT results were normal, follow-up was continued. If HR-HPV persisted and the TCT results were abnormal, a colposcopy-guided biopsy was performed immediately. In this situation, if the histological results were still non-CIN or cervical cancer, the follow-up was continued. If the histological results confirmed the development of CIN or invasive cancer, then enter another study follow-up to further track its development and outcome, and the woman commenced the treatment process. The HPV infection clearance time was analyzed by the Kaplan-Meier method, and the comparison of the HPV clearance rate and infection clearance time between each of the different groups was performed using achi(2) test or Fisher's exact test, as appropriate. After the univariate analysis, several significant factors were included in the Cox model and independent risk factors were analyzed. RESULTS: A total of 163 women were enrolled in this study. The median age was 40.0 years (22-67 years) and the median follow-up time was 11.5 months (6-31 months). The spontaneous clearance rate of HR-HPV infection was 51.5%, and the median time to viral clearance was 14.5 months. Age and the initial viral load were high risk factors affecting the spontaneous clearance of HR-HPV infection. The factors significantly associated with HPV clearance rate and time to HPV clearance consisted of menopause and full-term delivery ($P < 0.05$). CONCLUSIONS: In women with normal or low-grade lesions on the cell smear, the spontaneous clearance rate of HR-HPV infection was 51.5% and the time to clearance was 14.5 months. Age and the initial viral load were independent associated factors affecting the spontaneous clearance of HR-HPV infection in the female genital tract. These findings suggest that non-young women or those with high viral loads have a higher rate of persistent HR-HPV infection. Thus, intensive screening should be recommended.

Ferraz, C. (2023). "Molecular testing for thyroid nodules: Where are we now?" Rev Endocr Metab Disord.

Approximately 25% of the fine needle aspiration samples (FNAB) of thyroid nodules are classified as "indeterminate samples", that means, Bethesda III and IV categories. Until the last decade, most of these cases underwent diagnostic surgery, although only a minority (13-34%) confirmed malignancy postoperatively. In view of this, with the objective of improving the preoperative diagnosis in these cases, the molecular tests emerged, which are validated from the diagnostic point of view, presenting good performance, with good diagnostic accuracy, being able to avoid diagnostic surgeries. With the advancement of knowledge of the role of each of the mutations and gene rearrangements in thyroid oncogenesis, molecular markers have left to play only a diagnostic role and have been gaining more and more space both in defining the prognostic role of the tumor, as well as in the indication of target therapy. Thus, the objective of this review is to show how to use the tool of molecular tests, now commercially available in the world, in the management of indeterminate cytological nodules, assessing the pre-test malignancy risk of the nodule, through clinical, ultrasonographic and cytological characteristics, and decide on the benefit of molecular testing for each patient. In addition, to discuss its new and promising prognostic and therapeutic role in thyroid cancer.

Foda, Z. H., et al. (2023). "Preventive strategies in familial and hereditary colorectal cancer." Best Pract Res Clin Gastroenterol **66**: 101840.

Colorectal cancer is a leading cause of cancer-related deaths worldwide. While most cases are sporadic, a significant proportion of cases are associated with familial and hereditary syndromes. Individuals with a family history of colorectal cancer have an increased risk of developing the disease, and those with hereditary syndromes such as Lynch syndrome or familial adenomatous polyposis have a significantly higher risk. In these populations, preventive strategies are critical for reducing the incidence and mortality of colorectal cancer. This review provides an overview of current preventive strategies for individuals at increased risk of colorectal cancer due to familial or hereditary factors. The manuscript includes a discussion of risk assessment and genetic testing, highlighting the importance of identifying at-risk individuals and families. This review describes various preventive measures, including surveillance colonoscopy, chemoprevention, and prophylactic surgery, and their respective benefits and limitations. Together, this work highlights the importance of preventive strategies in familial and hereditary colorectal cancer.

Forrest, L. E., et al. (2023). "Personalising genetic counselling (POETIC) trial: Protocol for a hybrid type II effectiveness-implementation randomised clinical trial of a patient screening tool to improve patient empowerment after cancer genetic counselling." Trials **24**(1): 712.

BACKGROUND: Genetic counselling aims to identify, and address, patient needs while facilitating informed decision-making about genetic testing and promoting empowerment and adaptation to genetic information. Increasing demand for cancer genetic testing and genetic counsellor workforce capacity limitations may impact the quality of genetic counselling provided. The use of a validated genetic-specific screening tool, the Genetic Psychosocial Risk Instrument (GPRI), may facilitate patient-centred genetic counselling. The aim of this study is to assess the effectiveness and implementation of using the GPRI in improving patient outcomes after genetic counselling and testing for an inherited cancer predisposition. METHODS: The PersOnalising gEneTIc Counselling (POETIC) trial is a hybrid type 2 effectiveness-implementation trial using a randomised control trial to assess the effectiveness of the GPRI in improving patient empowerment (primary outcome), while also assessing implementation from the perspective of clinicians and the healthcare service. Patients referred for a cancer risk assessment to the conjoint clinical genetics service of two metropolitan hospitals in Victoria, Australia, who meet the eligibility criteria and consent to POETIC will be randomised to the usual care or intervention group. Those in the intervention group will complete the GPRI prior to their appointment with the screening results available for the clinicians' use during the appointment. Appointment audio recordings, clinician-reported information about the appointment, patient-reported outcome measures, and clinical data will be used to examine the effectiveness of using the GPRI. Appointment audio recordings, health economic information, and structured interviews will be used to examine the implementation of the GPRI. DISCUSSION: The POETIC trial takes a pragmatic approach by deploying the GPRI as an intervention in the routine clinical practice of a cancer-specific clinical genetics service that is staffed by a multidisciplinary team of genetics and oncology clinicians. Therefore, the effectiveness and implementation evidence generated from this real-world health service setting aims to optimise the relevance of the outcomes of this trial to the practice of genetic counselling while enhancing the operationalisation of the screening tool in routine practice. TRIAL REGISTRATION: Australian New Zealand Clinical Trials Registry registration number 12621001582842p. Date of registration: 19th November 2021.

Fowler, J. R., et al. (2023). Cervical Cancer. StatPearls. Treasure Island (FL) ineligible companies. Disclosure: Elizabeth Maani declares no relevant financial relationships with ineligible companies. Disclosure: Charles Dunton declares no relevant financial relationships with ineligible companies. Disclosure: David Gasalberti declares no relevant financial relationships with ineligible companies. Disclosure: Brian Jack declares no relevant financial relationships with ineligible companies.

Cervical cancer continues to rank among the top gynecologic cancers worldwide. According to current data, it is ranked 14th among all cancers and is the 4th most common cancer among women worldwide. Cervical cancer intervention focuses on primary and secondary prevention. Primary prevention and screening are the best methods to decrease the burden of cervical cancer and mortality. In the United States and other developed countries, most screening and diagnostic efforts are directed toward the early identification of high-risk human papillomavirus (HPV) lesions through HPV testing and Papanicolaou (Pap) smears. Although HPV testing is not recommended in women younger than 30 years, low-risk younger women should begin screening with Pap tests at age 21 and continue until age 65, per the United States Preventive Services Task Force (USPSTF) recommendations. Newer recommendations offer 3- to 5-year intervals between screenings based on a patient's prior results and the use of Pap and HPV cotesting. Like many diseases and cancers, disparities exist in screening, early diagnosis, and timely treatment rates. Screening rates are lower in low socioeconomic and low-resource areas with racial, ethnic, and age variations. Studies show women with obesity and chronic disease may have lower cervical and breast cancer screening rates. A study of ethnic minority women in the United Kingdom reports several barriers to screening, including lack of awareness, fear, embarrassment, shame, and low perceived risk. Another study reviewing the barriers for Haitian women revealed socioeconomic barriers, language barriers, and a limited understanding of health and disease. In the United States, cervical cancer mortality is disproportionately higher in black women. As cervical cancer is a sexually transmitted infection (STI), it is preventable, and the global incidence can be reduced through targeted education, screening, and intervention. Since 2006, vaccination has been available for the prevention of cervical cancer. Vaccination can improve cancer death rates in populations with higher mortality rates and in developing countries where resources may not be available for routine screening.

Fu, Z., et al. (2023). "Predicting multiple linear stapler firings in double stapling technique with an MRI-based deep-learning model." Sci Rep **13**(1): 18906.

Multiple linear stapler firings is a risk factor for anastomotic leakage (AL) in laparoscopic low anterior resection (LAR) using double stapling technique (DST) anastomosis. In this study, our objective was to establish the risk factors for >/= 3 linear stapler firings, and to create and validate a predictive model for >/= 3 linear stapler firings in laparoscopic LAR using DST anastomosis. We retrospectively enrolled 328 mid-low rectal cancer patients undergoing laparoscopic LAR using DST anastomosis. With a split ratio of 4:1, patients were randomly divided into 2 sets: the training set (n = 260) and the testing set (n = 68). A clinical predictive model of >/= 3 linear stapler firings was constructed by binary logistic regression. Based on three-dimensional convolutional networks, we built an image model using only magnetic resonance (MR) images segmented by Mask region-based convolutional neural network, and an integrated model based on both MR images and clinical variables. Area under the curve (AUC), sensitivity, specificity, accuracy, positive predictive value (PPV), and Youden index were calculated for each model. And the three models were validated by an independent cohort of 128 patients. There were 17.7% (58/328) patients received >/= 3 linear stapler firings. Tumor size >/= 5 cm (odds ratio (OR) = 2.54, 95% confidence interval (CI) = 1.15-5.60, p = 0.021) and preoperative carcinoma embryonic antigen (CEA) level > 5 ng/mL [OR = 2.20, 95% CI = 1.20-4.04, p = 0.011] were independent risk factors associated with >/= 3 linear stapler firings. The integrated model (AUC = 0.88, accuracy = 94.1%) performed better on predicting >/= 3 linear stapler firings than the clinical model (AUC = 0.72, accuracy = 86.7%) and the image model (AUC = 0.81, accuracy = 91.2%). Similarly, in the validation set, the integrated model (AUC = 0.84, accuracy = 93.8%) performed better than the clinical model (AUC = 0.65, accuracy = 65.6%) and the image model (AUC = 0.75, accuracy = 92.1%). Our deep-learning model based on pelvic MR can help predict the high-risk population with >/= 3 linear stapler firings in laparoscopic LAR using DST anastomosis. This model might assist in determining preoperatively the anastomotic technique for mid-low rectal cancer patients.

Galkin, V. N., et al. (2023). "[Anatomical resection for non-small cell lung cancer: cardiopulmonary exercise testing in assessing the risk of respiratory complications]." Khirurgiia (Mosk)(10): 88-97.
OBJECTIVE: To assess the role of cardiopulmonary exercise testing in examination of patients with high risk of respiratory complications in anatomical resections for non-small cell lung cancer. MATERIAL AND METHODS: A non-randomized retrospective single-center study was devoted to immediate results of surgical treatment of patients with NSCLC between December 2020 and April 2021. Median age of patients was 65 (84; 30) years, male-to-female ratio - 129 (57%)/98 (43%). All patients were examined according to a unified algorithm recommended by the American (ATS) and European (ESTS) societies of thoracic surgeons. At the first stage, we analyzed airflow rate and performed non-invasive exercise tests (6-minute walk and/or stair test). Resections of lungs were performed in 231 patients, anatomic lung resections - in 227 patients (lobectomy - 199, bilobectomy - 4, segmentectomy - 17, pneumonectomy - 7). We excluded 4 patients who underwent non-anatomic lung resections (marginal resections). RESULTS: Among 236 patients referred for anatomical lung resections, 34 (14.4%) ones were selected for cardiopulmonary testing. Selection was based on low exercise tolerance and/or severe decrease in predictive respiratory parameters (FEV<50%). Patients were divided into 4 groups depending on peak oxygen consumption. There were 5 (2%), 10 (29.4%), 11 (32.3%) and 8 (23.5%) patients with extremely high, high, moderate and low risk of respiratory complications, respectively. Surgeries were performed for IA1 (n=6), IA2 (n=50), IA3 (n=37), IB (n=31), IIA (n=19), IIB (n=37), IIIA (n=25) and IIIB (n=4) stages. The overall incidence of postoperative complications was 23% (95% CI: 18-28.8). Complications Clavien-Dindo grade I, IIIA, IIIB, IVA, IVB and V prevailed in both groups. Median postoperative hospital-stay (6 (6; 8) vs. 7 (6; 8) days) and time of pleural drainage (4 (2; 5) vs. 3 (3; 4) days) were similar. Organ-sparing procedures prevailed in the main group (5 (26%) out of 19 (95% CI: 11.81-48.8) vs. 12 (6.7%) out of 180 (95% CI: 3.8-11.3)). Overall mortality (n=231) was 1.7% (95% CI: 0.7-4.4). Mortality throughout the first postoperative year was 24% (95% CI: 12.2-42.1) and 7.4% (95% CI: 4.2-11.3), respectively. CONCLUSION: Cardiopulmonary exercise testing makes it possible to objectively assess exercise tolerance and identify high-risk patients for respiratory complications. These data are valuable when planning the treatment of patients with non-small cell lung cancer.

Garman, K. S., et al. (2023). "Helicobacter pylori testing prior to or at gastric cancer diagnosis and survival in a diverse US patient population." Gastric Cancer.
BACKGROUND: Gastric cancer (GC) accounts for the greatest disparity in cancer mortality between Black and White Americans. Although clinical trials have shown that Helicobacter pylori (Hp) treatment reduces risk of GC, Hp testing and treatment is not consistently performed in the US, and may offer an opportunity to improve survival. METHODS: In a diverse retrospective cohort of 99 GC cases diagnosed at Duke University from 2002-2020 (57% Black; 43% white), we examined the association of Hp testing and treatment prior to or at cancer diagnosis with overall survival using

Cox regression analyses to calculate adjusted hazards ratios (HRs) and 95% confidence intervals (CIs). RESULTS: Overall, 62% of patients were tested for Hp prior to or at GC diagnosis. Of those, 25% tested positive and were treated < 1 year prior to or at diagnosis, 15% tested positive and were treated >/= 1 year prior to diagnosis, 6% tested positive without evidence of treatment, and 54% tested negative. Compared to never tested, Hp testing and treatment < 1 year prior to or at diagnosis was associated with a significantly reduced likelihood of death (HR 0.21, 95% CI 0.08-0.58). The benefit of any Hp test and treat prior to or at GC diagnosis was significant even among stage IV patients only (HR, 0.22; 95% CI 0.05-0.96). CONCLUSIONS: These findings support Hp testing and treatment for patients at risk of or diagnosed with GC, and suggest Hp treatment may provide an opportunity to reduce GC mortality disparities in the US.

Gimeno-Valiente, F., et al. (2023). "Sequencing paired tumor DNA and white blood cells improves circulating tumor DNA tracking and detects pathogenic germline variants in localized colon cancer." ESMO Open **8**(6): 102051.
BACKGROUND: In the setting of localized colon cancer (CC), circulating tumor DNA (ctDNA) monitoring in plasma has shown potential for detecting minimal residual disease (MRD) and predicting a higher risk of recurrence. With the tumor-only sequencing approach, however, germline variants may be misidentified as somatic variations, precluding the possibility of tracking in up to 11% of patients due to a lack of known somatic mutations. In this study, we assess the potential value of adding white blood cells (WBCs) to tumor tissue sequencing to enhance the accuracy of sequencing results. PATIENTS AND METHODS: A total of 148 patients diagnosed with localized CC were prospectively recruited at the Hospital Clinico Universitario in Valencia (Spain). Employing a custom 29-gene panel, sequencing was conducted on tumor tissue, plasma and corresponding WBCs. Droplet digital PCR and amplicon-based NGS were performed on plasma samples post-surgery to track MRD. Oncogenic somatic variants were identified by annotating with COSMIC, OncoKB and an internal repository of pathogenic mutations database. A variant prioritization analysis, mainly characterized by the match of oncogenic mutations with the evidence levels defined in OncoKB, was carried out to select specific targeted therapies. RESULTS: Utilizing paired tumor and WBCs sequencing, we identified somatic mutations in all patients (100%) within our cohort, compared to 89% using only tumor tissue. Consequently, the top 10 most frequently mutated genes for plasma monitoring were altered. The sequencing of WBCs identified 9% of patients with pathogenic mutations in the germline, with APC and TP53 being the most frequently mutated genes. Additionally, mutations in genes related to clonal hematopoiesis of indeterminate potential were detected in 27% of the cohort, with TP53, KRAS, and KMT2C being the most frequently altered genes. There were no observed differences in the sensitivity of monitoring MRD using ddPCR or amplicon-based NGS (p = 1). Ultimately, 41% of the patients harbored potentially targetable alterations at diagnosis. CONCLUSION: The germline testing method not only enhanced sequencing results and raised the proportion of patients eligible for plasma monitoring, but also uncovered the existence of pathogenic germline variations, thereby aiding in the identification of patients at a higher risk of hereditary cancer syndromes.

Grant, R. C., et al. (2023). "Machine Learning-Based Early Warning Systems for Acute Care Utilization During Systemic Therapy for Cancer." J Natl Compr Canc Netw **21**(10): 1029-1037 e1021.
BACKGROUND: Emergency department visits and hospitalizations frequently occur during systemic therapy for cancer. We developed and evaluated a longitudinal warning system for acute care use. METHODS: Using a retrospective population-based cohort of patients who started intravenous systemic therapy for nonhematologic cancers between July 1, 2014, and June 30, 2020, we randomly separated patients into cohorts for model training, hyperparameter tuning and model selection, and system testing. Predictive features included static features, such as demographics, cancer type, and treatment regimens, and dynamic features, such as patient-reported symptoms and laboratory values. The longitudinal warning system predicted the probability of acute care utilization within 30 days after each treatment session. Machine learning systems were developed in the training and tuning cohorts and evaluated in the testing cohort. Sensitivity analyses considered feature importance, other acute care endpoints, and performance within subgroups. RESULTS: The cohort included 105,129 patients who received 1,216,385 treatment sessions. Acute care followed 182,444 (15.0%) treatments within 30 days. The ensemble model achieved an area under the receiver operating characteristic curve of 0.742 (95% CI, 0.739-0.745) and was well calibrated in the test cohort. Important predictive features included prior acute care use, treatment regimen, and laboratory tests. If the system was set to alarm approximately once every 15 treatments, 25.5% of acute care events would be preceded by an alarm, and 47.4% of patients would experience acute care after an alarm. The system underestimated risk for some treatment regimens and potentially underserved populations such as females and non-English speakers. CONCLUSIONS: Machine learning warning systems can detect patients at risk for

acute care utilization, which can aid in preventive intervention and facilitate tailored treatment. Future research should address potential biases and prospectively evaluate impact after system deployment.

Guo, X., et al. (2023). "The Diagnostic Value of Serum TGF-beta1, p2PSA Combined with PSA in Prostate Cancer." Altern Ther Health Med.
OBJECTIVE: To investigate the diagnostic value of transforming growth factor-beta1 (TGF-beta1), prostate-specific antigen isomer 2 (p2PSA) combined with a prostate-specific antigen (PSA) in prostate cancer (PCa). METHODS: From October 1, 2019 to September 1, 2022 we enrolled a total of 90 patients with PCa90 patients with PCa in the urology department of our hospital were selected as the PCa group, 90 patients with benign prostatic hyperplasia (BPH) were selected as the BPH group, and 90 healthy people were selected as a healthy control group. The levels of TGF-beta1, p2PSA and PSA in serum were detected, and the differences in TGF-beta1, p2PSA and PSA levels among the three groups and PCa patients with different pathological parameters were compared. Univariate and Logistic regression analyses were used to analyze the independent risk factors affecting the occurrence of PCa. With pathological results as the 'gold standard', the diagnostic efficacy of TGF-beta1, p2PSA and PSA alone and their combination for PCa was analyzed by the receiver operating characteristic (ROC) curve. RESULTS: The levels of serum PSA, p2PSA, and TGF-beta1 in the PCa group were higher than those in the BPH group and control group (P < .001), and those in BPH group were higher than those in the control group (P < .001). The serum indexes of PCa group increased with the increase of Glerson grade and TNM stage (P < .001). The serum indexes of patients with lymph and bone metastasis were significantly higher than those without lymph and bone metastasis (P < .001). Logistic regression analysis showed that PSA, p2PSA and TGF-beta1 were independent risk factors for PCa (P < .001). The area under the ROC curve (AUC) of PSA, p2PSA, TGF-beta1 and combined detection were 0.738, 0.862, 0.821 and 0.932, respectively. The AUC of combined detection was greater than that of single detection (P < .001). CONCLUSION: The expression levels of serum TGF-beta1, p2PSA and PSA are related to PCa and are independent risk factors for PCa. The combined detection of the three groups can improve the diagnostic efficacy of PCa. Combined testing improves diagnostic accuracy for prostate cancer, allows for early intervention, and improves patient survival and confidence in treatment options. This will significantly improve the clinical management of prostate cancer. Future studies could explore other biomarkers or molecular indicators to further improve the accuracy of diagnosis and grading of prostate cancer. Additionally, differences between different populations and subtypes can be studied to better understand the heterogeneity of prostate cancer.

Gupta, I., et al. (2023). "Changes in Prognostic Beliefs of Patients With Metastatic Cancer and Their Association With Changing Health Status." J Natl Compr Canc Netw **21**(10): 1021-1028 e1028.
BACKGROUND: Patients' prognostic beliefs are known to influence treatment decisions. However, the evolution of these beliefs over an extended period in patients with metastatic cancer is understudied. We assessed longitudinal changes in prognostic beliefs and investigated their association with patients' changing health status. METHODS: We surveyed a cohort of 600 patients with solid metastatic cancer every 9 months, up to 54 months. At each time point, we assessed whether patients believed their current treatments would cure them (responses classified as accurate, inaccurate, or uncertain belief) and tested the association of their response with symptom burden and recent unplanned hospital admission. RESULTS: Only 29% of patients had accurate prognostic belief at baseline, and 24% of patients changed from having accurate to uncertain/inaccurate belief at some point during follow-up. Patients who experienced greater symptom burden were less likely to report inaccurate (relative risk ratio [RRR], 0.87; 95% CI, 0.84-0.90) or uncertain prognostic belief (RRR, 0.90; 95% CI, 0.87-0.92), whereas those with a recent unplanned hospital admission were more likely to report inaccurate (RRR, 2.71; 95% CI, 1.48-4.94) or uncertain belief (RRR, 2.34; 95% CI, 1.34-4.07) compared with accurate belief. An increase in symptom burden was associated with change toward accurate belief (RRR, 1.75; 95% CI, 1.33-2.31) as opposed to no change. CONCLUSIONS: In our study of long-term changes in prognostic beliefs among patients with metastatic cancer, reported prognostic beliefs were unstable, changed from accurate to inaccurate/uncertain and vice versa, and were associated with their changing health status. Our findings imply that conversations about goals of care must occur regularly to factor in these changes.

Guzeloz, Z., et al. (2023). "Dose Volume and Liver Function Test Relationship following Radiotheraphy for Right Breast Cancer: A Multicenter Study." Curr Oncol **30**(10): 8763-8773.
OBJECTIVE: The liver is a critical organ at risk during right breast radiotherapy (RT). Liver function tests (LFTs) such as alanine aminotransferase (ALT), aspartate aminotransferase (AST), and gamma-glutamyl transferase (GGT) serve as biochemical markers for hepatobiliary damage. In this multicenter cross-sectional study, the effects of liver dose-volume on changes in LFTs pre- and post-RT in patients treated for

right breast cancer were evaluated. MATERIALS AND METHODS: Between January 2019 and November 2022, data from 100 patients who underwent adjuvant right breast RT across three centers were retrospectively assessed. Target volumes and normal structures were contoured per the RTOG atlas. Patients were treated with a total dose of 50 Gy in 25 fractions to the CTV, followed by a boost to the tumor bed where indicated. The percentage change in LFT values in the first two weeks post-RT was calculated. Statistics were analyzed with SPSS version 22 software, with significance set at $p < 0.05$. Statistical correlation between liver doses (in cGy) and the volume receiving specific doses (Vx in cc) on the change in LFTs were analyzed using Kolmogorov-Smirnov, Mann-Whitney U test. RESULTS: The median age among the 100 patients was 56 (range: 29-79). Breast-conserving surgery was performed on 75% of the patients. The most common T and N stages were T1 (53%) and N0 (53%), respectively. None of the patients had distant metastasis or simultaneous systemic treatment with RT. A total of 67% of the treatments utilized the IMRT technique and 33% VMAT. The median CTV volume was 802 cc (range: 214-2724 cc). A median boost dose of 10 Gy (range: 10-16 Gy) was applied to 28% of the patients with electrons and 51% with IMRT/VMAT. The median liver volume was 1423 cc (range: 825-2312 cc). Statistical analyses were conducted on a subset of 57 patients for whom all three LFT values were available both pre- and post-RT. In this group, the median values for AST, ALT, and GGT increased up to 15% post-RT compared to pre-RT, and a median liver D(mean) below 208 cGy was found significant. While many factors can influence LFT values, during RT planning, attention to liver doses and subsequent regular LFT checks are crucial. CONCLUSION: Due to factors such as anatomical positioning, planning technique, and breast posture, the liver can receive varying doses during right breast irradiation. Protecting patients from liver toxicity secondary to RT is valuable, especially in breast cancer patients with a long-life expectancy. Our study found that, even in the absence of any systemic treatment or risk factors, there was an average increase of nearly 15% in enzymes, indicating acute liver damage post-RT compared with pre-RT. Attention to liver doses during RT planning and regular follow-up with LFTs is essential.

Horakova, Z., et al. (2023). "Current status and future perspectives of oral HPV testing in the diagnosis and monitoring of oropharyngeal cancer. A review." Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub.
HPV16 status in oropharyngeal cancer (OPC) is an important prognostic factor. Its determination, based on immunistochemical analysis of p16 oncoprotein requires an invasive biopsy. Thus, alternative methods are being sought. Determining oral HPV16 status appears to be a promising alternative. However, it is not used routinely. This prompted us to perform a systematic literature review enabling us to evaluate the diagnostic and predictive ability of this approach. Thirty-four relevant studies were finally selected. For determination of HPV status in OPC, the calculated average sensitivity and specificity for oral sampling was 74% and 91%, respectively, with p16 tumour tissue marker being the gold standard. The method appears to be valuable in monitoring treatment response as well as the biological activity of the tumour, enabling early detection of persistent or relapsing carcinoma sufficiently long before its clinical and/or radiological manifestation. It can also contribute to identification of the primary tumour in cases of metastases of unknown origin. Last but not least, the screening HPV oral testing would help to identify individuals with persistent HPV oral infection who are at increased risk of development of OPC.

Hu, S., et al. (2023). "Mental health outcomes in a population-based cohort of patients with prostate cancer." J Natl Cancer Inst.
BACKGROUND: Few studies have evaluated mental health disorders comprehensively among patients with prostate cancer on long-term follow-up. The primary aim of our study was to assess the incidence of mental health disorders among patients with prostate cancer compared with a general population cohort. A secondary aim was to investigate potential risk factors for mental health disorders among patients with prostate cancer. METHODS: Cohorts of 18 134 patients with prostate adenocarcinomas diagnosed between 2004 and 2017 and 73470 men without cancer matched on age, birth state, and follow-up time were identified. Mental health diagnoses were identified from electronic health records and statewide health-care facilities data. Cox proportional hazard models were used to estimate hazard ratios. All statistical tests were 2-sided. RESULTS: The hazard ratios for mood disorders, including depression, among prostate cancer survivors increased for all follow-up periods compared with the general population. The hazard ratios for any mental illness increased with Hispanic, Black, or multiple races; people who were underweight or obese; those with advanced prostate cancer; and those undergoing their first course cancer treatment. We also observed statistically significantly increased hazard ratios for mental health disorders among patients with lower socioeconomic status ($P < .0001$) and increasing duration of androgen-deprivation therapy ($P = .0348$). Prostate cancer survivors had a 61% increased hazard ratio for death with a depression diagnosis. CONCLUSION: Prostate cancer diagnosis was associated with a higher risk of mental health disorders

compared with the general population, which was observed as long as 10-16 years after cancer diagnosis. Providing long-term mental health support may be beneficial to increasing life expectancy for patients with prostate cancer.

Ismail, A., et al. (2023). "Frontiers of Ovarian Carcinosarcoma." Curr Treat Options Oncol.
Ovarian carcinosarcoma (OCS), also known as a malignant mixed Mullerian tumour (MMMT), is a rare and aggressive form of cancer that accounts for less than 5% of ovarian cancers. It is characterized by high morbidity and mortality rates, with a median overall survival (OS) of less than 2 years. Several factors, including advancing age, nulliparity, reduced lactation rates, decreased use of oral contraceptive pills, genetic mutations in BRCA (breast cancer) genes, and the use of assisted reproductive technology, may increase the risk of OCS. Poor prognostic factors include an advanced stage at diagnosis, older age, lymph node metastasis, suboptimal surgical cytoreduction, the presence of heterologous features on histopathology, and increased expression of vascular endothelial growth factor (VEGF), tumour protein p53, and p53 alongside Wilms tumour 1 (WT1). The main treatment approach for OCS is cytoreductive surgery followed by platinum-based chemotherapy, although immunotherapy is showing promise. Homologous recombination deficiency (HRD) testing may enhance outcomes by enabling personalized immunotherapy and targeted therapies for specific patient groups, thereby reducing unnecessary side effects and healthcare costs. However, there is currently a lack of standardised treatment regimens for OCS patients, with most studies consisting of case reports and a shortage of suitable comparator groups. This article aims to provide clinicians with information on the epidemiology, risk factors, prognostic factors, and latest therapeutic advancements in OCS.

Kasteler, R., et al. (2023). "Longitudinal assessment of lung function in Swiss childhood cancer survivors-A multicenter cohort study." Pediatr Pulmonol.
OBJECTIVE: Childhood cancer survivors are at risk for pulmonary morbidity due to exposure to lung-toxic treatments, including specific chemotherapeutics, radiotherapy, and surgery. Longitudinal data on lung function and its change over time are scarce. We investigated lung function trajectories in survivors over time and the association with lung-toxic treatments. METHODS: This retrospective, multicenter cohort study included Swiss survivors diagnosed between 1990 and 2013 and exposed to lung-toxic chemotherapeutics or thoracic radiotherapy. Pulmonary function tests (PFTs), including forced expiration volume in the first second (FEV1), forced vital capacity (FVC), FEV1/FVC, total lung capacity, and diffusion capacity of the lung for carbon monoxide, were obtained from hospital charts. We calculated z-scores and percentage predicted, described lung function over time, and determined risk factors for change in FEV1 and FVC using multivariable linear regression. RESULTS: We included 790 PFTs from 183 survivors, with a median age of 12 years at diagnosis and 5.5 years of follow-up. Most common diagnosis was lymphoma (55%). Half (49%) of survivors had at least one abnormal pulmonary function parameter, mainly restrictive (22%). Trajectories of FEV1 and FVC started at z-scores of -1.5 at diagnosis and remained low throughout follow-up. Survivors treated with thoracic surgery started particularly low, with an FEV1 of -1.08 z-scores (-2.02 to -0.15) and an FVC of -1.42 z-scores (-2.27 to -0.57) compared to those without surgery. CONCLUSION: Reduced pulmonary function was frequent but mainly of mild to moderate severity. Nevertheless, more research and long-term surveillance of this vulnerable population is needed.

Kindt, I. S., et al. (2023). "The risk of bleeding and perforation from sigmoidoscopy or colonoscopy in colorectal cancer screening: A systematic review and meta-analyses." PLoS One **18**(10): e0292797.
INTRODUCTION: Physical harm from Colorectal Cancer Screening tends to be inadequately measured and reported in clinical trials. Also, studies of ongoing Colorectal Cancer Screening programs have found more frequent and severe physical harm from screening procedures, e.g., bleeding and perforation, than reported in previous trials. Therefore, the objectives of the study were to systematically review the evidence on the risk of bleeding and perforation in Colorectal Cancer Screening. DESIGN: Systematic review with descriptive statistics and random-effects meta-analyses. METHODS: We systematically searched five databases for studies investigating physical harms related to Colorectal Cancer Screening. We assessed the internal and the external validity using the ROBINS-I tool and the GRADE approach. Harm estimates was calculated using mixed Poisson regression models in random-effect meta-analyses. RESULTS: We included 89 studies. Reporting and measurement of harms was inadequate in most studies. In effect, the risk of bias was critical in 97.3% and serious in 98.3% of studies. All GRADE ratings were very low. Based on severe findings with not-critical risk of bias and 30 days follow-up, the risk of bleedings per 100,000 people screened were 8 [2;24] for sigmoidoscopy, 229 [129;408] for colonoscopy following fecal immunochemical test, 68 [39;118] for once-only colonoscopy, and 698 [443;1045] for colonoscopy following any screening tests. The risk of perforations was 88 [56;138] for colonoscopy following fecal immunochemical test and 53 [25;112] for once-only colonoscopy. There were no

findings within the subcategory severe perforation with long-term follow-up for colonoscopy following any screening tests and sigmoidoscopy. DISCUSSION: Harm estimates varied widely across studies, reporting and measurement of harms was mostly inadequate, and the risk of bias and GRADE ratings were very poor, collectively leading to underestimation of harm. In effect, we consider our estimates of perforation and bleeding as conservative, highlighting the need for better reporting and measurement in future studies. TRIAL REGISTRATION: PROSPERO registration number: CRD42017058844.

Kobat, H., et al. (2023). "Smoking, Diabetes Mellitus, and Previous Cardiovascular Disease as Predictors of Anticancer Treatment-Induced Cardiotoxicity in Non-Small-Cell Lung Cancer: A Real-World Study." Clin Lung Cancer.
PURPOSE: Cardiotoxicity is a common and under-reported side effect of tyrosine-kinase inhibitors (TKI) and immune checkpoint inhibitors (ICI). Baseline risk factors may help in risk-stratifying patients at increased risk of cardiotoxicity. This real-world study investigated the effects of baseline risk factors in cardiotoxicity on patients with non-small-cell lung cancer (NSCLC) treated with TKIs and ICIs. METHODS: This is a retrospective study carried out at The Royal Marsden Hospital, UK. Newly diagnosed patients with localized or metastatic NSCLC who received anticancer therapy with TKIs and/or ICIs were eligible. Patients who received only chemotherapy were excluded. Patients were followed up from the time of diagnosis until death or discharge. The relationship between cardiotoxicity and risk factors were tested by logistic regression. RESULTS: Of 88/451 (19.5%) patients developed cardiotoxicity. Risk factors hypothesized to have a causal relationship with anticancer treatment-induced cardiotoxicity were analyzed. Cardiotoxicity risk was increased with prior diabetes mellitus (OR = 1.93, 95% CI, 1.04-3.61, P = .038), history of smoking (OR = 1.91, 95% CI, 1.13-3.22, P = .016) and presence of baseline cardiovascular disease (OR = 2.03, 95% CI, 1.13-3.64, P = .018). The risk of developing cardiotoxicity increased in patients for smokers with diabetes mellitus (OR = 3.03, 95% CI, 1.40-6.55, P < .01) and for smokers with previous cardiovascular disease (OR = 1.99, 95% CI, 1.03-3.84, P = .041). CONCLUSION: Diabetes mellitus, smoking and baseline cardiovascular disease may synergistically contribute to cardiotoxicity when a patient is exposed to potentially cardiotoxic anticancer agents. Risk stratification at baseline may improve cardio-oncology care.

Kou, J., et al. (2023). "Effects of Adjuvant Radiation Plus Chemotherapy on Survival Outcomes in Stage III C Endometrial Cancer According to Histology: Analysis of Data from the Surveillance, Epidemiology, and End Results Database." Technol Cancer Res Treat **22**: 15330338231208610.
Purpose: To evaluate the survival benefit of radiation plus chemotherapy in adult females with stage IIIC endometrial cancer and to investigate whether the benefit varies according to histology. Methods: Data from adult females with International Federation of Gynecology and Obstetrics (FIGO) stage IIIC endometrial cancer, who underwent at least total hysterectomy between 2010 and 2015, were obtained from the Surveillance, Epidemiology, and End Results (SEER) database. Adjuvant treatments were categorized as chemotherapy alone, chemotherapy with external beam radiation therapy (EBRT), chemotherapy with vaginal brachytherapy (VBT), or chemotherapy with EBRT+VBT. Multivariate Cox regression models, Kaplan-Meier curves, and log-rank tests were used to assess the association between treatment modality and overall survival (OS). Results: In total, 2138 cases were identified: stage IIIC1 (n = 1299 [60.8%]) and stage IIIC2 (n = 839 [39.2%]). Median OS for all patients was 48 (interquartile range [IQR] 28-70) months. Regarding adjuvant treatment, 40.5% of patients underwent chemotherapy only, followed by chemotherapy with EBRT (35.5%). Stage IIIC patients treated with chemotherapy plus radiation exhibited a significantly reduced risk for death from endometrial cancer in both univariate and multivariate analyses (P < 0.001). However, when stratified according to histology, OS also differed according to treatment modality when analyzing each histological type; combination therapy was no longer significantly different from chemotherapy alone for any histology (clear cell and carcinosarcoma). Combination therapy was associated with improved OS in patients with IIIC1 and IIIC2 disease. Similar associations were observed in patients with high-grade stage IIIC endometrioids. However, for low-grade tumors, combination therapy was no longer associated with reduced risk for death compared with chemotherapy alone. Conclusion: For patients with stage IIIC endometrial cancer, combined treatment with radiation and chemotherapy was associated with improved OS compared with chemotherapy alone. However, no survival benefit was found, and radiotherapy may be unnecessary in patients with low-grade endometrioids.

Krauze, A. V., et al. (2023). "Revisiting Concurrent Radiation Therapy, Temozolomide, and the Histone Deacetylase Inhibitor Valproic Acid for Patients with Glioblastoma-Proteomic Alteration and Comparison Analysis with the Standard-of-Care Chemoirradiation." Biomolecules **13**(10).
BACKGROUND: Glioblastoma (GBM) is the most common brain tumor with an overall survival (OS) of

less than 30% at two years. Valproic acid (VPA) demonstrated survival benefits documented in retrospective and prospective trials, when used in combination with chemo-radiotherapy (CRT). PURPOSE: The primary goal of this study was to examine if the differential alteration in proteomic expression pre vs. post-completion of concurrent chemoirradiation (CRT) is present with the addition of VPA as compared to standard-of-care CRT. The second goal was to explore the associations between the proteomic alterations in response to VPA/RT/TMZ correlated to patient outcomes. The third goal was to use the proteomic profile to determine the mechanism of action of VPA in this setting. MATERIALS AND METHODS: Serum obtained pre- and post-CRT was analyzed using an aptamer-based SOMAScan((R)) proteomic assay. Twenty-nine patients received CRT plus VPA, and 53 patients received CRT alone. Clinical data were obtained via a database and chart review. Tests for differences in protein expression changes between radiation therapy (RT) with or without VPA were conducted for individual proteins using two-sided t-tests, considering p-values of <0.05 as significant. Adjustment for age, sex, and other clinical covariates and hierarchical clustering of significant differentially expressed proteins was carried out, and Gene Set Enrichment analyses were performed using the Hallmark gene sets. Univariate Cox proportional hazards models were used to test the individual protein expression changes for an association with survival. The lasso Cox regression method and 10-fold cross-validation were employed to test the combinations of expression changes of proteins that could predict survival. Predictiveness curves were plotted for significant proteins for VPA response (p-value < 0.005) to show the survival probability vs. the protein expression percentiles. RESULTS: A total of 124 proteins were identified pre- vs. post-CRT that were differentially expressed between the cohorts who received CRT plus VPA and those who received CRT alone. Clinical factors did not confound the results, and distinct proteomic clustering in the VPA-treated population was identified. Time-dependent ROC curves for OS and PFS for landmark times of 20 months and 6 months, respectively, revealed AUC of 0.531, 0.756, 0.774 for OS and 0.535, 0.723, 0.806 for PFS for protein expression, clinical factors, and the combination of protein expression and clinical factors, respectively, indicating that the proteome can provide additional survival risk discrimination to that already provided by the standard clinical factors with a greater impact on PFS. Several proteins of interest were identified. Alterations in GALNT14 (increased) and CCL17 (decreased) (p = 0.003 and 0.003, respectively, FDR 0.198 for both) were associated with an improvement in both OS and PFS. The pre-CRT protein expression revealed 480 proteins predictive for OS and 212 for PFS (p < 0.05), of which 112 overlapped between OS and PFS. However, FDR-adjusted p values were high, with OS (the smallest p value of 0.586) and PFS (the smallest p value of 0.998). The protein PLCD3 had the lowest p-value (p = 0.002 and 0.0004 for OS and PFS, respectively), and its elevation prior to CRT predicted superior OS and PFS with VPA administration. Cancer hallmark genesets associated with proteomic alteration observed with the administration of VPA aligned with known signal transduction pathways of this agent in malignancy and non-malignancy settings, and GBM signaling, and included epithelial-mesenchymal transition, hedgehog signaling, Il6/JAK/STAT3, coagulation, NOTCH, apical junction, xenobiotic metabolism, and complement signaling. CONCLUSIONS: Differential alteration in proteomic expression pre- vs. post-completion of concurrent chemoirradiation (CRT) is present with the addition of VPA. Using pre- vs. post-data, prognostic proteins emerged in the analysis. Using pre-CRT data, potentially predictive proteins were identified. The protein signals and hallmark gene sets associated with the alteration in the proteome identified between patients who received VPA and those who did not, align with known biological mechanisms of action of VPA and may allow for the identification of novel biomarkers associated with outcomes that can help advance the study of VPA in future prospective trials.

Kurniawan, A. A. and U. Maimunah (2023). "A Very Young Adult Female Patient with Hepatitis B Flare: A Case Report." Acta Med Indones **55**(3): 320-326.

Hepatitis B virus (HBV) infection is a major global health problem. It can cause chronic infection and put people at high risk of death from cirrhosis and liver cancer. This study aims to present a case of chronic hepatitis B flare in a very young adult patient. An 18-year-old previously healthy female presented with jaundice developing in one week, following the previous complaints of nausea, vomiting, abdominal pain, loss of appetite, and tiredness for about three months. The patient had no risk factors for getting HBV infection, but her HBsAg-positive mother was probably an inactive HBV carrier. The hepatitis B serological testing revealed HBsAg positivity, anti-HBs seronegativity, HBeAg positivity, anti-HBe seronegativity, anti-HBc IgM seronegativity, and high levels of HBV DNA detected > 1.70 x 108 IU/mL. There was a sharp increase in serum ALT to >/= 5-fold ULN. The abdominal ultrasonography revealed a hepatitis feature, unremarkable portal venous flow, and an extrahepatic biliary system. The liver transient elastography revealed 15.6 kPa of liver stiffness, which was in accordance with the F3-F4 fibrosis stage. These features were typical of a hepatitis B flare, the HBeAg-positive chronic hepatitis

B, previously known as the immune reactive phase. A long-term nucleos(t)ide analog therapy was programmed with Tenofovir alafenamide 25 mg daily.

Le, A., et al. (2023). "Self-Collection for Primary HPV Testing: Perspectives on Implementation From Federally Qualified Health Centers." Prev Chronic Dis **20**: E93.
INTRODUCTION: Primary testing for high-risk human papillomavirus (HPV) by self-collection could result in higher rates of cervical cancer screening. Federally qualified health centers (FQHCs) in the US serve a large proportion of women who have low income and no health insurance and are medically underserved - risk factors for being insufficiently screened for cervical cancer. Although the implementation of self-collection for HPV testing is not yet widespread, health care entities need to prepare for its eventual approval by the US Food and Drug Administration. We conducted focus groups and interviews among clinical and administrative staff and leadership to gather data on key logistical concerns that must be addressed before implementing self-collection for HPV testing in FQHCs. METHODS: We identified focus group and interview participants from 6 FQHCs in North Carolina. We conducted focus groups with clinical and administrative staff (N = 45) and semistructured interviews with chief executive officers, senior-level administrators, chief medical officers, and clinical data managers (N = 24). Transcripts were coded by using codebooks derived from research questions and notes taken during data collection. Themes emerged on implementation of self-collection for HPV testing. We applied the constructs from the Consolidated Framework for Implementation Research (CFIR) to themes to identify domains of potential barriers and facilitators to implementation. RESULTS: Clinical personnel reported that offering self-collection for HPV testing is acceptable and feasible and can increase cervical cancer screening rates. Uncertainties emerged about accuracy of results, workflow disruptions, financial implications, and effects on clinic quality measures. CONCLUSION: Implementing self-collection for HPV testing was considered feasible and acceptable by participants. However, important health service delivery considerations, including financial implications, must be addressed before integrating self-collection for HPV testing into the standard of care.

Lee, H., et al. (2023). "Semi-quantitative FDG parameters predict survival in multiple myeloma patients without autologous stem cell transplantation." Cancer Imaging **23**(1): 104.
BACKGROUND: F-18 fluorodeoxyglucose positron emission tomography/computed tomography (FDG PET/CT) is useful in multiple myeloma (MM) for initial workup and treatment response evaluation. Herein, we evaluated the prognostic value of semi-quantitative FDG parameters for predicting the overall survival (OS) of MM patients with or without autologous stem cell transplantation (ASCT). METHODS: Study subjects comprised 227 MM patients who underwent baseline FDG PET/CT. Therein, 123 underwent ASCT while 104 did not. Volumes of interest (VOIs) of bones were drawn on CT images using a threshold of 150 Hounsfield units. FDG parameters of maximum standardized uptake value (SUVmax), mean SUV (SUVmean), metabolic tumor volume (MTV), total lesion glycolysis (TLG), and number of focal lesions (FLs) were measured. Kaplan-Meier survival analysis with log-rank tests and Cox proportional hazards regression analyses were performed for overall survival (OS). RESULTS: In the ASCT cohort, R-ISS stage, MTV, and TLG were associated with survival. In the non-ASCT cohort, however, R-ISS stage was not associated with patient outcomes. In contrast, high SUVmax, SUVmean, MTV, TLG, and FL could predict worse OS (hazard ratio [HR] = 2.569, 2.649, 2.506, 2.839, and 1.988, respectively). Importantly, combining FDG parameters with R-ISS stage provided a new risk classification system that discriminated worse OS in the non-ASCT cohort significantly better than did R-ISS stage alone. CONCLUSIONS: In the non-ASCT cohort, semi-quantitative FDG parameters were significant predictors of worse OS. Furthermore, combining FDG parameters with R-ISS stage may provide a new risk staging system that can better stratify the survival of MM patients without ASCT.

Leslie, S. W., et al. (2023). Prostate Cancer. StatPearls. Treasure Island (FL) ineligible companies. Disclosure: Taylor Soon-Sutton declares no relevant financial relationships with ineligible companies. Disclosure: Anu R I declares no relevant financial relationships with ineligible companies. Disclosure: Hussain Sajjad declares no relevant financial relationships with ineligible companies. Disclosure: Larry Siref declares no relevant financial relationships with ineligible companies.
Worldwide, prostate cancer is the most commonly diagnosed male malignancy and the fifth leading cause of cancer death in men. This amounted to 1,414,249 newly diagnosed cases and 375,000 deaths worldwide yearly from this disease in 2020. Globally, prostate cancer is the most commonly diagnosed malignancy in more than fifty percent of countries (112 of 185). Fortunately, most prostate cancers tend to grow slowly and are low-grade with relatively low risk and limited aggressiveness. There are no initial or early symptoms in most cases, but late symptoms may include fatigue due to anemia, bone pain, paralysis from spinal metastases, and renal failure from bilateral ureteral

obstruction. Diagnosis is primarily based on prostate-specific antigen (PSA) testing and transrectal ultrasound-guided (TRUS) prostate tissue biopsies, although PSA testing for screening remains controversial. Newer diagnostic modalities include free and total PSA levels, PCA3 urine testing, Prostate Health Index scoring (PHI), the"4K" test, exosome testing, genomic analysis, MRI imaging, PIRADS scoring, and MRI-TRUS fusion guided biopsies. When the cancer is limited to the prostate, it is considered localized and potentially curable. If the disease has spread to the bones or elsewhere outside the prostate, pain medications, bisphosphonates, rank ligand inhibitors, hormonal treatment, chemotherapy, radiopharmaceuticals, immunotherapy, focused radiation, and other targeted therapies can be used. Outcomes depend on age, associated health problems, tumor histology, and the extent of cancer.

Li, D., et al. (2023). "Diagnostic value of inflammatory indicators for surgical site infection in patients with breast cancer." Front Cell Infect Microbiol **13**: 1286313.
BACKGROUND: Breast cancer is the most commonly diagnostic cancer in women worldwide. The main treatment for these patients is surgery. However, there is a high incidence of surgical site infection (SSI) in breast cancer patients. The aim of this study was to identify effective infection-related diagnostic markers for timely diagnosis and treatment of SSI. METHODS: This retrospective study included 263 breast cancer patients who were treated between July 2018 and March 2023 at the Shandong Cancer Hospital and Institute. We analyzed differences between the SSI group and control group and differences before and during infection in the SSI group. Finally, we tested the distribution of pathogenic microorganisms and their susceptibility to antibiotics. RESULTS: Compared with preoperative inflammatory indicators, white blood cells (WBC), neutrophils (NEU), absolute neutrophil count to the absolute lymphocyte count (NLR), D2 polymers (D-Dimer) and fibrinogen (FIB) were significantly increased, while lymphocytes (LYM), albumin (ALB) and prealbumin (PA) were significantly decreased in the SSI group. Compared with uninfected patients, WBC, NEU, NLR and FIB were significantly increased, ALB and PA were significantly decreased in SSI patients, while LYM and D-Dimer did not differ significantly. The distribution of infection bacteria in SSI patients showed that the proportion of patients with Staphylococcus aureus infection was as high as 70.41%; of those patients, 19.33% had methicillin-resistant Staphylococcus aureus (MRSA) infection. The area under the curves (AUCs) of the receiver operating curves (ROCs) for WBC, NEU, NLR, FIB, ALB and PA were 0.807, 0.811, 0.730, 0.705, 0.663 and 0.796, respectively. The AUCs for other inflammatory indicators were not statistically significant. There was no significant difference in antibiotic resistance for Staphylococcus aureus when compared to that of gram-positive bacteria. The resistance of gram-positive bacteria to ceftriaxone (CRO), cefoxitin (FOX), chloramphenicol (CHL), minocycline (MNO) and tetracycline (TCY) was lower than that of gram-negative bacteria, while the resistance to gentamicin (GEN) was higher. CONCLUSION: This study demonstrated that WBC, NEU, NLR, FIB and PA have good predictive value for identifying patients at risk of SSI. The cut-off values of inflammatory indicators can be helpful in the prevention and diagnosis of SSI.

Li, Y., et al. (2023). "CT-based nomogram for early identification of T790M resistance in metastatic non-small cell lung cancer before first-line epidermal growth factor receptor-tyrosine kinase inhibitors therapy." Eur Radiol Exp **7**(1): 64.
BACKGROUND: To evaluate the value of computed tomography (CT) radiomics in predicting the risk of developing epidermal growth factor receptor (EGFR) T790M resistance mutation for metastatic non-small lung cancer (NSCLC) patients before first-line EGFR-tyrosine kinase inhibitors (EGFR-TKIs) therapy. METHODS: A total of 162 metastatic NSCLC patients were recruited and split into training and testing cohort. Radiomics features were extracted from tumor lesions on nonenhanced CT (NECT) and contrast-enhanced CT (CECT). Radiomics score (rad-score) of two CT scans was calculated respectively. A nomogram combining two CT scans was developed to evaluate T790M resistance within up to 14 months. Patients were followed up to calculate the time of T790M occurrence. Models were evaluated by area under the curve at receiver operating characteristic analysis (ROC-AUC), calibration curve, and decision curve analysis (DCA). The association of the nomogram with the time of T790M occurrence was evaluated by Kaplan-Meier survival analysis. RESULTS: The nomogram constructed with the rad-score of NECT and CECT for predicting T790M resistance within 14 months achieved the highest ROC-AUCs of 0.828 and 0.853 in training and testing cohorts, respectively. The DCA showed that the nomogram was clinically useful. The Kaplan-Meier analysis showed that the occurrence time of T790M difference between the high- and low-risk groups distinguished by the rad-score was significant ($p < 0.001$). CONCLUSIONS: The CT-based radiomics signature may provide prognostic information and improve pretreatment risk stratification in EGFR NSCLC patients before EGFR-TKIs therapy. The multimodal radiomics nomogram further improved the capability. RELEVANCE STATEMENT: Radiomics based on NECT and CECT images can effectively identify and stratify the risk of T790M resistance before

the first-line TKIs treatment in metastatic non-small cell lung cancer patients. KEY POINTS: * Early identification of the risk of T790M resistance before TKIs treatment is clinically relevant. * Multimodel radiomics nomogram holds potential to be a diagnostic tool. * It provided an imaging surrogate for identifying the pretreatment risk of T790M.

Lim, J., et al. (2023). "Machine learning classification of polycystic ovary syndrome based on radial pulse wave analysis." BMC Complement Med Ther **23**(1): 409.
BACKGROUND: Patients with Polycystic ovary syndrome (PCOS) experienced endocrine disorders that may present vascular function changes. This study aimed to classify and predict PCOS by radial pulse wave parameters using machine learning (ML) methods and to provide evidence for objectifying pulse diagnosis in traditional Chinese medicine (TCM). METHODS: A case-control study with 459 subjects divided into a PCOS group and a healthy (non-PCOS) group. The pulse wave parameters were measured and analyzed between the two groups. Seven supervised ML classification models were applied, including K-Nearest Neighbors (KNN), Support Vector Machine (SVM), Decision Trees, Random Forest, Logistic Regression, Voting, and Long Short Term Memory networks (LSTM). Parameters that were significantly different were selected as input features and stratified k-fold cross-validations training was applied to the models. RESULTS: There were 316 subjects in the PCOS group and 143 subjects in the healthy group. Compared to the healthy group, the pulse wave parameters h3/h1 and w/t from both left and right sides were increased while h4, t4, t, As, h4/h1 from both sides and right t1 were decreased in the PCOS group ($P < 0.01$). Among the ML models evaluated, both the Voting and LSTM with ensemble learning capabilities, demonstrated competitive performance. These models achieved the highest results across all evaluation metrics. Specifically, they both attained a testing accuracy of 72.174% and an F1 score of 0.818, their respective AUC values were 0.715 for the Voting and 0.722 for the LSTM. CONCLUSION: Radial pulse wave signal could identify most PCOS patients accurately (with a good F1 score) and is valuable for early detection and monitoring of PCOS with acceptable overall accuracy. This technique can stimulate the development of individualized PCOS risk assessment using mobile detection technology, furthermore, gives physicians an intuitive understanding of the objective pulse diagnosis of TCM. TRIAL REGISTRATION: Not applicable.

Lin, C. C. and Y. N. Her (2023). "Demoralization in cancer survivors: an updated systematic review and meta-analysis for quantitative studies." Psychogeriatrics.
BACKGROUND: Demoralization can cause impairments across all life aspects of cancer patients. Cancer patients are also vulnerable during their survivorship. The purpose of this review is to examine the risk of demoralization and associated risk factors among cancer survivors who have completed their primary anti-cancer treatment or time since diagnosis >/=5 years without recurrence. METHODS: We searched databases of PubMed, Cochrane, Embase, PsycINFO and ClinicalTrial.gov to identify eligible studies which reported the demoralization level among cancer survivors. A random-effect meta-analysis model was used for calculating mean demoralization level. Heterogeneity was evaluated by I(2) statistics. Funnel plots and Egger's regression tests were performed for checking publication bias. We used one-study-removed method for sensitivity analysis. Subgroup analysis was also done to examine the difference of demoralization level between cancer types. Meta-regression was performed to reveal risk factors of demoralization. RESULTS: A meta-analysis of 12 articles involving 2902 cancer survivors was conducted. The mean demoralization score among cancer survivors was 25.98 (95% CI: 23.53-28.43). Higher demoralization level was seen in participants with older age, higher female ratio, higher married/living together status ratio and higher patient health questionnaire-9 score. The literature review revealed correlations between demoralization and suicide risk, anxiety and quality of life. No consistent correlation between demoralization and post-traumatic stress symptoms could be seen. CONCLUSIONS: High demoralization level is noticed among cancer survivors. Risks for females, elder patients or breast cancer survivors are identified. More longitudinal or interventional studies for cancer survivors' demoralization are expected in the future.

Liu, B., et al. (2023). "Lung and bone metastases patterns in limb osteosarcoma: Surgical treatment of primary site improves overall survival." Medicine (Baltimore) **102**(42): e35671.
Osteosarcoma (OS) is one of the most prevalent malignant bone tumors. The proportion of patients with limb OS was relatively high. Lung metastasis (LM) and bone metastasis are the first and second most common metastatic types of OS, respectively. A total of 270 new cases of LM, 55 new cases of bone metastases (BM), and 36 new cases of lung and BM were diagnosed in the surveillance, epidemiology and end results database from 2010 to 2019. Univariate and multivariate logistic regression analyses were used to identify the risk factors for lung and/or BM, and Cox regression analyses were performed to identify the prognostic factors for lung and/or BM. Kaplan-Meier curves and log-rank tests were used to analyze the overall survival of limb OS patients with lung and/or BM. Female sex, telangiectatic

OS type, central OS type, T3 stage, N1 stage, BM, surgical treatments, radiotherapy and chemotherapy were significantly correlated with LM. T3 stage, LM, liver metastases, and radiotherapy significantly correlated with BM. The small cell OS type, T2 stage, T3 stage, N1 stage, liver metastases, and radiotherapy were significantly correlated with lung and BM. Among limb OS patients with LM, the mean survival months of older age, black race, N1 stage, BM, brain metastases, no surgery, and no chemotherapy were lower than those of the control group. In limb OS patients with LM and BM, the mean survival months in the no surgery group was lower than in the surgery group. T stage and radiotherapy significantly influence the occurrence of limb OS with lung and/or BM. Surgery at the primary site has been shown to be effective in improving the survival rate of patients with lung and/or BM.

Liu, S., et al. (2023). "Prognosis, Risk Factors and Clinical Features of Intraocular Recurrence in Primary Vitreoretinal Lymphoma." Ophthalmol Retina.
PURPOSE: To investigate the clinical features, risk factors, and prognosis of the intraocular recurrence in primary vitreoretinal lymphoma (PVRL). DESIGN: Retrospective case-control study. PARTICIPANTS: 97 eyes of 51 patients diagnosed with PVRL between 2011/12 and 2021/1 were enrolled in this study. 14 patients among them had experienced intraocular recurrence. METHODS: Date on demographic and ophthalmic characteristics, results of diagnostic tests, treatments, prognosis of intraocular recurrence and non-recurrence PVRL patients were collected and compared. Multivariate logistic regression was used to identify independent risk factors. And receiver operating characteristic curve was conducted to determine the cut-off values. MAIN OUTCOME MEASURES: Clinical features and risk factors. RESULTS: 14 (19 eyes) of 51 PVRL patients had intraocular recurrences, resulting in a recurrence rate of 27.5% over a mean follow-up period of 42.5 months. No difference was observed in central nervous system lymphoma (CNSL) relapse rate (54.3% vs. 64.3%, p=0.523) and median time to CNSL (36.5 95%CI [24.6-48.3] vs. 37.3 95%CI [24.8-49.8], p=0.777) between intraocular non-recurrence and intraocular recurrence groups. Furthermore, there were no statistically significant difference in the survival outcomes, such as mortality (28.6% vs. 29.7%, p=1.000) and median overall survival (70.8 95%CI [54.0-87.7] vs. 59.2 95%CI [44.8-73.6], p=0.297), between these two groups. Younger onset age (odds ratio [OR] 0.90, 95% confidence intervals [CI] 0.84-0.98, p=0.010), isolated PVRL (OR 35.3, 95%CI 2.08-600.0, p=0.014), and no history of intravitreal chemotherapy (OR 7.72, 95%CI 1.37-43.6, p=0.021) were identified as independent risk factors for intraocular recurrences. Of the patients with intraocular recurrence, 23.6% were asymptomatic and were diagnosed during routine follow-up. The rate of interleukin-10 (IL-10) /IL-6>1 was significantly lower than that at diagnosis (43.8% vs. 92.3%, p=0.008). However, the rate of IL-10>/=50 pg/mL was high (81.3%) and not significantly different from that at diagnosis (92.3%, p=0.606). CONCLUSIONS: This study did not identify an impact of intraocular recurrence on CNS manifestations or survival outcomes in patients with PVRL. Younger patients have a higher risk of intraocular recurrence, and combined systemic and intravitreal chemotherapy may reduce intraocular recurrence. Regular ophthalmic follow-up and IL-10 testing are recommended to detect intraocular recurrence.

Liu, S., et al. (2023). "Identification and validation of a ferroptosis-related signature for prediction of the prognosis and tumor microenvironment in patients with chromophobe renal cell carcinoma." BMC Cancer **23**(1): 1079.
BACKGROUND: Ferroptosis is a novel form of regulated cell death that is different from other forms, which has an important role in tumor growth inhibition. The purpose of this study was to construct and validate a prognostic signature related to ferroptosis in chromophobe renal cell carcinoma (ChRCC) and to explore its role in immune cell infiltration and systemic therapy. METHODS: The gene expression profiles of ChRCC patients obtained from The Cancer Genome Atlas (TCGA) database were used to identify differentially expressed prognostic ferroptosis-related genes (FRGs) by univariate Cox proportional hazards analyses. Ferroptosis molecular subtypes were obtained by consensus clustering analysis. The FRG-based signature in the training set was established by least absolute shrinkage and selection operator analysis and verified in the testing set. The association between molecular subtypes and the prognostic signature and immune microenvironment was explored to predict responses to immunotherapy. Immunohistochemistry was used to verify expression of the FRG-based signature externally. RESULTS: ChRCC patients were divided into two FRG subtypes. Two FRGs (TFRC and SLC7A11) were identified to construct the prognostic signature. The high-risk group and cluster 2 had worse overall survival than the low-risk group and cluster 1, respectively. The low-risk group and cluster 1 had higher levels of immune cell infiltration and expression of MHC and immune checkpoint molecules than the high-risk group and cluster 2. The risk score was a predictor of overall survival and had a good predictive ability, which was verified in the testing set and evaluated by ROC and calibration curves. The high-risk group had a higher tumor mutation burden. The different sensitivities of targeted drugs in patients with different risks were evaluated. External immunohistochemical

analysis showed that TFRC and SLC7A11 were highly expressed in tumor tissues compared with para-cancer normal tissues, and the expression level was significantly associated with a more advanced stage and worse cancer-specific survival. CONCLUSIONS: An FRG signature was identified and validated to predict the clinicopathological features and prognosis of ChRCC. A significant association between the signature and immune cell infiltration, immune checkpoint expression, and drug response is helpful to guide comprehensive treatment of ChRCC.

Lopes David, B. B., et al. (2023). "Cost Evaluation Analysis of Genetic Testing and Tailored Adjuvant Imatinib in Patients With Resected High-Risk GI Stromal Tumors: The Brazilian Perspective." JCO Glob Oncol **9**: e2300070.
PURPOSE: Mutations of the KIT gene are the molecular hallmark of most GI stromal tumors (GISTs). Imatinib has revolutionized GIST treatment. Adjuvant imatinib for 3 years is the standard of care for high-risk resected GIST. However, the GIST molecular biologic profile has found different responses to this approach. Despite this, genetic testing at diagnosis is not a routine and empirical adjuvant imatinib remains the rule. Barriers to genetic profiling include concerns about the cost and utility of testing. This analysis aims to determine whether targeted genetic testing reduces costs as an ancillary tool for a limited-resource scenario instead of adjuvant empirical imatinib in patients with resected high-risk GIST. METHODS: The cost evaluation analysis of molecular testing for GIST was based on the Cost of Preventing an Event (COPE), considering the Number Needed to Treat and the costs of each test compared with the cost of 3-year empirical adjuvant imatinib and real treatment costs (median number of cycles) from the public and private Brazilian Healthcare System's perspective. The analysis compared the costs of the molecular tests (broad next-generation sequencing [NGS], GS Infinity DNA/RNA assay, and targeted NGS: GS Focus GIST and the Fleury GIST Tumor DNA sequencing panel), costs of drug acquisition, considering discounts (imatinib mesylate and Glivec), and the costs of supportive care. RESULTS: In both scenarios, public and private, regardless of the use of imatinib or Glivec, tailoring adjuvant treatment reduced costs, irrespective of the number of cycles. The only exception was the combination of the broad NGS test and imatinib in the Public Healthcare System. CONCLUSION: The molecularly tailored adjuvant imatinib reduced costs considering the COPE of available NGS tests for both the public and private Brazilian health care systems.

Luckett, R., et al. (2023). "Triage of HPV positivity in a high HIV prevalence setting: A prospective cohort study comparing visual triage methods and HPV genotype restriction in Botswana." Int J Gynaecol Obstet.
OBJECTIVE: Guidelines for effective triage following positive primary high-risk human papillomavirus (HPV) screening in low- and middle-income countries with high human immunodeficiency virus (HIV)-prevalence have not previously been established. In the present study, we evaluated the performance of three triage methods for positive HPV results in women living with HIV (WLHIV) and without HIV in Botswana. METHODS: We conducted baseline enrollment of a prospective cohort study from February 2021 to August 2022 in South-East District, Botswana. Non-pregnant women aged 25 or older with an intact cervix and no prior diagnosis of cervical cancer were systematically consented for enrollment, with enrichment of the cohort for WLHIV. Those who consented completed a questionnaire and then collected vaginal self-samples for HPV testing. Primary HPV testing for 15 individual genotypes was conducted using Atila AmpFire(R) HPV assay. Those with positive HPV results returned for a triage visit where all underwent visual inspection with acetic acid (VIA), colposcopy, and biopsy. Triage strategies with VIA, colposcopy and 8-type HPV genotype restriction (16/18/31/33/35/45/52/58), separately and in combination, were compared using histopathology as the gold standard in diagnosing cervical intraepithelial neoplasia (CIN) 2 or worse (CIN2+). RESULTS: Among 2969 women enrolled, 1480 (50%) tested HPV positive. The cohort included 1478 (50%) WLHIV; 99% were virologically suppressed after a mean of 8 years on antiretroviral therapy. In total, 1269 (86%) women had histopathology data for analysis. Among WLHIV who tested positive for HPV, 131 (19%) of 688 had CIN2+ compared with 71 (12%) of 581 in women without HIV. Screening by 8-type HPV genotype restriction was more sensitive as triage to detect CIN2+ in WLHIV 87.79% (95% CI: 80.92-92.85) and women without HIV 85.92% (95% CI: 75.62-93.03) when compared with VIA (WLHIV 62.31% [95% CI: 53.39-70.65], women without HIV 44.29% [95% CI: 32.41-56.66]) and colposcopy (WLHIV 70.77% [95% CI: 62.15-78.41], women without HIV 45.71% [95% CI: 33.74-58.06]). However, 8-type HPV genotype restriction had low specificity in WLHIV of 30.88% (95% CI: 27.06-34.90) and women without HIV 37.06% (95% CI: 32.85-41.41). These results were similar when CIN3+ was used as the outcome. When combining 8-type HPV genotype restriction with VIA as the triage strategy, there was improved specificity to detect CIN2+ in WLHIV of 81.65% (95% CI: 78.18-84.79) but dramatically reduced sensitivity of 56.15% (95% CI: 47.18-64.84). CONCLUSIONS: Eight-type HPV genotype restriction is a promising component of effective triage for HPV positivity. However, novel triage strategies in LMICs

with high HIV prevalence may be needed to avoid the trade-off between sensitivity and specificity with currently available options. CLINICAL TRIALS REGISTRATION: This study is registered on Clinicaltrials.gov no. NCT04242823, https://clinicaltrials.gov/ct2/show/NCT04242823.

Luining, W. I., et al. (2023). "Optimization and validation of 18F-DCFPyL PET radiomics-based machine learning models in intermediate- to high-risk primary prostate cancer." PLoS One **18**(11): e0293672. INTRODUCTION: Radiomics extracted from prostate-specific membrane antigen (PSMA)-PET modeled with machine learning (ML) may be used for prediction of disease risk. However, validation of previously proposed approaches is lacking. We aimed to optimize and validate ML models based on 18F-DCFPyL-PET radiomics for the prediction of lymph-node involvement (LNI), extracapsular extension (ECE), and postoperative Gleason score (GS) in primary prostate cancer (PCa) patients. METHODS: Patients with intermediate- to high-risk PCa who underwent 18F-DCFPyL-PET/CT before radical prostatectomy with pelvic lymph-node dissection were evaluated. The training dataset included 72 patients, the internal validation dataset 24 patients, and the external validation dataset 27 patients. PSMA-avid intra-prostatic lesions were delineated semi-automatically on PET and 480 radiomics features were extracted. Conventional PET-metrics were derived for comparative analysis. Segmentation, preprocessing, and ML methods were optimized in repeated 5-fold cross-validation (CV) on the training dataset. The trained models were tested on the combined validation dataset. Combat harmonization was applied to external radiomics data. Model performance was assessed using the receiver-operating-characteristics curve (AUC). RESULTS: The CV-AUCs in the training dataset were 0.88, 0.79 and 0.84 for LNI, ECE, and GS, respectively. In the combined validation dataset, the ML models could significantly predict GS with an AUC of 0.78 ($p<0.05$). However, validation AUCs for LNI and ECE prediction were not significant (0.57 and 0.63, respectively). Conventional PET metrics-based models had comparable AUCs for LNI (0.59, $p>0.05$) and ECE (0.66, $p>0.05$), but a lower AUC for GS (0.73, $p<0.05$). In general, Combat harmonization improved external validation AUCs (-0.03 to +0.18). CONCLUSION: In internal and external validation, 18F-DCFPyL-PET radiomics-based ML models predicted high postoperative GS but not LNI or ECE in intermediate- to high-risk PCa. Therefore, the clinical benefit seems to be limited. These results underline the need for external and/or multicenter validation of PET radiomics-based ML model analyses to assess their generalizability.

Luo, Z., et al. (2023). "Association Between Socioeconomic Status and Adherence to Fecal Occult Blood Tests in Colorectal Cancer Screening Programs: Systematic Review and Meta-Analysis of Observational Studies." JMIR Public Health Surveill **9**: e48150. BACKGROUND: Screening adherence is important in reducing colorectal cancer (CRC) incidence and mortality. Disparity in CRC screening adherence was observed in populations of different socioeconomic status (SES), but the direction and strength of the association remained unclear. OBJECTIVE: We aimed to systematically review all the observational studies that have analyzed the association between SES and adherence to organized CRC screening based on fecal occult blood tests. METHODS: We systematically reviewed the studies in PubMed, Embase, and Web of Science and reference lists of relevant reviews from the inception of the database up until June 7, 2023. Individual SES, neighborhood SES, and small-area SES were included, while any SES aggregated by geographic areas larger than neighbors were excluded. Studies assessing SES with any index or score combining indicators of income, education, deprivation, poverty, occupation, employment, marital status, cohabitation, and others were included. A random effect model meta-analysis was carried out for pooled odds ratios (ORs) and relative risks for adherence related to SES. RESULTS: Overall, 10 studies, with a total of 3,542,379 participants and an overall adherence rate of 64.9%, were included. Compared with low SES, high SES was associated with higher adherence (unadjusted OR 1.73, 95% CI 1.42-2.10; adjusted OR 1.53, 95% CI 1.28-1.82). In the subgroup of nonindividual-level SES, the adjusted association was significant (OR 1.57, 95% CI 1.26-1.95). However, the adjusted association was insignificant in the subgroup of individual-level SES (OR 1.46, 95% CI 0.98-2.17). As for subgroups of the year of print, not only was the unadjusted association significantly stronger in the subgroup of early studies (OR 1.97, 95% CI 1.59-2.44) than in the subgroup of late studies (OR 1.43, 95% CI 1.31-1.56), but also the adjusted one was significantly stronger in the early group (OR 1.86, 95% CI 1.43-2.42) than in the late group (OR 1.26, 95% CI 1.14-1.39), which was consistent and robust. Despite being statistically insignificant, the strength of the association seemed lower in studies that did not adjust for race and ethnicity (OR 1.31, 95% CI 1.21-1.43) than the overall estimate (OR 1.53, 95% CI 1.28-1.82). CONCLUSIONS: The higher-SES population had higher adherence to fecal occult blood test-based organized CRC screening. Neighborhood SES, or small-area SES, was more competent than individual SES to be used to assess the association between SES and adherence. The disparity in adherence between the high SES and the low SES narrowed along with the development of interventions

and the improvement of organized programs. Race and ethnicity were probably important confounding factors for the association.

Ma, Y., et al. (2023). "Investigating High-risk Factors, Precise Diagnosis, and Treatment of Castration-Resistant Prostate Cancer (CRPC)." Comb Chem High Throughput Screen.
BACKGROUND: The treatment of metastatic castration-resistant prostate cancer (mCRPC) in the actual world currently presents difficulties. In light of this, it is crucial to investigate high-risk factors for the progression of advanced prostate cancer and to identify methods for delaying the onset of CRPC. AIMS: This study aimed to explore the high-risk factors that impact the progression of prostate cancer and emphasize the significance of precise diagnosis and treatment based on etiological classification in the clinical management of castration-resistant prostate cancer. METHODS: A retrospective analysis was conducted on 277 newly diagnosed cases of PCa treated with endocrine therapy. A follow-up was done on prostate-specific antigen (PSA) levels and testosterone. Additionally, a prospective analysis was performed on the clinical data of 60 patients with CRPC. Following the principle of '4W1H', 30 patients were included in the precision treatment group for a second biopsy and related tests, while another 30 patients were included in the conventional treatment group. The therapeutic effect and prognosis of the two groups were observed. RESULTS: Distant metastasis (HR = 1.879, 95% CI: 1.311 ~ 2.694, P = 0.001), PSA nadir &gt 0.2 ng/mL (HR = 1.843, 95% CI: 1.338 ~ 2.540, P = 0.001), testosterone nadir &gt 20 ng/dL (HR = 1.403, 95% CI: 1.035 ~ 1.904, P = 0.029), and time to testosterone nadir &gt 6 months (HR = 1.919, 95% CI: 1.364 ~ 2.701, P = 0.001) were risk factors for the progression to CRPC. Patients in the CRPC group were treated with precision therapy and conventional therapy based on their molecular subtyping. The precision treatment group showed a significantly prolonged median PSA progression-free survival compared to the conventional treatment group (16.0 months vs. 13.0 months, P=0.025). The median radiographic progression-free survival was also significantly extended in the precision treatment group compared to the conventional treatment group (21.0 months vs. 16.0 months, P=0.042). CONCLUSION: Patients with prostate cancer diagnosed with distant metastasis at initial presentation require early intervention. Close monitoring of PSA and serum testosterone changes is necessary during the process of endocrine therapy. After entering the CRPC stage, the etiological classification precision treatment can improve the therapeutic effect and improve the prognosis of patients.

Manfredi, C., et al. (2023). "Prostate Cancer in Transgender Women: Epidemiology, Clinical Characteristics, and Management Challenges." Curr Oncol Rep.
PURPOSE OF REVIEW: To systematically review the evidence on prostate cancer (PCa) in transgender women (TGW). RECENT FINDINGS: A total of 25 studies were included. Fourteen articles were case reports or case series describing 21 TGW with PCa; 11 papers focused primarily on assessing the incidence or screening of PCa in TGW. The median (range) age of patients with PCa was 63 (45-78) years. Median (range) PSA at diagnosis was 7.5 (0.4-1710) ng/mL. Prostate biopsy detected ISUP 3-5 in 10 (67%) cases. T3-4 stages were described in 7 (64%) patients. Three (14.3%) cases of nodal involvement and 2 (9.5%) of metastases were reported at diagnosis. First-line therapy included radical prostatectomy or radiotherapy +/- androgen deprivation therapy in 14 (74 %) subjects. Median (range) follow-up was 24 (2-120) months. A good response to first-line therapy was recorded in 8 (47.1%) cases. Median (range) incidence of PCa in TGW was 44.1 (4.34-140) cases per 100,000 person-years. PCa was significantly less frequent in TGW than in cisgender males (HR 0.4, 95% CI 0.2-0.9). Risk of death after PCa diagnosis was significantly higher in TGW compared to cisgender males (HR 1.91, 95% CI 1.06-3.45). TGW had lower lifetime PSA rates (48% vs. 64.6%, p = 0.048) than cisgender males. Few cases of PCa in TGW are currently reported. PCa seems significantly less frequent in TGW than in cisgender males; however, some data suggest a possible higher mortality in this cohort. TGW appear to have less access to PSA testing than cisgender men.

Miyamori, D., et al. (2023). "Impact of the COVID-19 pandemic on the mortality among patients with colorectal cancer in Hiroshima, Japan: A large cancer registry study." Cancer Med **12**(21): 20554-20563.
BACKGROUND: This retrospective cohort study aimed to evaluate the impact of the COVID-19 pandemic on colorectal cancer care and mortality using a large cancer registry in Hiroshima Prefecture, Japan. The study aimed to estimate the all-cause mortality rates within 1 year of diagnosis among colorectal cancer patients diagnosed during the pandemic period (2020 and 2021) compared to those diagnosed during the pre-pandemic period (2018 and 2019). METHODS: The day of diagnosis was set as Day 0 and Cox regression models were utilized to estimate crude hazard ratios (HRs) and adjusted HRs, accounting for age, sex, cancer stage, and treatment status. Two sensitivity analyses of overall survival were performed with different cutoffs of the pre-pandemic/pandemic periods and year-to-year comparisons. Subgroup analyses were performed using likelihood ratio tests. RESULTS: A total of 15,085 colorectal cancer patients were included, with 6499

eligible for follow-up. A median age of included patients was 72 years old, of which 59% were male. The distribution of cancer stages showed little variation between the pre-pandemic and pandemic periods. With a median follow-up of 177 days, the number of events was 316/3111 (173 events per 1000 person-years [E/1000PY], 95% confidence interval [CI]: 154-192 E/1000PY) in the pre-pandemic period, and 326/2746 (245 E/1000PY, 95% CI: 220-274 E/1000PY) in the pandemic period (crude HR: 1.42, 95% CI: 1.22-1.66; adjusted HR: 1.25, 95% CI: 1.07-1.46). The two sensitivity analyses and subgroup analyses consistently supported these findings. CONCLUSIONS: The study revealed an increased colorectal cancer mortality during the pandemic period, suggesting a continuous impact of the COVID-19 pandemic on the known and unknown risk factors for colorectal cancer for several years. Further studies are necessary to mitigate the adverse effects on patient outcomes.

Onate-Ocana, L. F., et al. (2023). "Multivariate Prognostic Models for Patients with Stages I and Ii Colon Carcinoma: a Strobe-Compliant Retrospective Cohort Study." Rev Invest Clin **75**(5): 259-271.
BACKGROUND: Colorectal cancer is the most frequent gastrointestinal malignancy worldwide. The value of adjuvant treatment is controversial in Stages I and II. OBJECTIVE: The aim of this study was to construct post-operative prognostic models applicable to patients with stages I-II colon carcinoma (CC). METHODS: This is a retrospective cohort study of patients with Stage I-II CC treated over a 25-year period. Exposure was defined as clinical, histopathological, and immunohistochemical factors (including CDX2 and MUC2 expression). Patients were randomly allocated to either a "modeling set" or a "validation set". Factors associated with recurrence, disease-free survival (DFS), and overall survival (OS) were defined in the "modeling set". Their performances were tested in the "validation set". RESULTS: From a total of 556 recruited patients, 339 (61%) were allocated to the "modeling set" and 217 (39%) to the "validation set". Three models explaining recurrence, DFS, and OS were described. Tumor location in the left colon (Hazards ratio [HR] = 1.57; 95% Confidence interval [CI] 0.99-2.48), lymphocyte (HR = 0.46; 96% CI 0.27-0.88) and monocyte (HR = 0.99; 95% CI 0.99-1) counts, neutrophil/platelet ratio (HR = 1.3; 95% CI 0.74-2.3, and HR = 2.3; 95% CI 1.3-4.1; for second and third category, respectively), albumin/monocyte ratio (HR = 0.43; 95% CI 0.21-0.87), and microscopic residual disease after surgery (HR = 8.7; 95% CI 3.1-24) were independently associated with OS. T classification and expression of CDX2 and/or MUC2 were not independently associated with recurrence or prognosis. CONCLUSION: These models are simple and readily available, and distinguish the risk and prognosis in patients with CC stages I and II; these models require cheaper processes than the use of more sophisticated molecular biology techniques. They may guide either the need for adjuvant therapy versus post-operative surveillance only, as well as aid in the design of clinical trials.

Ortblad, K. F., et al. (2023). "Measuring the performance of HIV self-testing at private pharmacies in Kenya: a cross-sectional study." J Int AIDS Soc **26**(10): e26177.
INTRODUCTION: HIV self-testing (HIVST) has the potential to support daily oral pre-exposure prophylaxis (PrEP) delivery in private pharmacies, but many national guidelines have not approved HIVST for PrEP dispensing. In Kenya, pharmacy providers are permitted to deliver HIVST, but often do not have the required certification to deliver rapid diagnostic testing (RDT). We estimated the performance of provider-delivered HIVST compared to RDT, the standard of care for PrEP delivery, at private pharmacies in Kenya to inform decisions on the use of HIVST for PrEP scale-up. METHODS: At 20 pharmacies in Kisumu County, we trained pharmacy providers (pharmacists and pharmaceutical technologists) on blood-based HIVST use and client assistance (if requested). We recruited pharmacy clients purchasing sexual and reproductive health-related products (e.g. condoms) and enrolled those >/=18 years with self-reported behaviours associated with HIV risk. Enrolled clients received HIVST with associated provider counselling, followed by RDT by a certified HIV testing services (HTS) counsellor. Pharmacy providers and clients independently interpreted HIVST results prior to RDT (results interpreted only by the HTS counsellor). We calculated the sensitivity and specificity of pharmacy provider-delivered HIVST compared to HTS counsellor-administered RDT. RESULTS: Between March and June 2022, we screened 1691 clients and enrolled 1500; 64% (954/1500) were female and the median age was 26 years (IQR 22-31). We additionally enrolled 40 providers; 42% (17/40) were pharmacy owners and their median years of experience was 6 (IQR 4-10). The majority (79%, 1190/1500) of clients requested provider assistance with HIVST and providers spent a median of 20 minutes (IQR 15-43) with each HIVST client. The sensitivity of provider-delivered HIVST at the pharmacy was high when interpreted by providers (98.5%, 95% CI 97.8%, 99.1%) and clients (98.8%, 95% CI 98.0%, 99.3%), as was the specificity of HIVST in this setting (provider-interpretation: 96.9%, 95% CI 89.2%, 99.6%; client-interpretation: 93.8%, 95% CI 84.8%, 98.3%). CONCLUSIONS: When compared to the national HIV testing algorithm, provider-delivered blood-based HIVST at private pharmacies in Kenya performed well. These findings

suggest that blood-based HIVST may be a useful tool to support PrEP initiation and continuation at private pharmacies and potentially other community-based delivery settings.

Pan, B., et al. (2023). "Nomogram prediction of the 70-gene signature (MammaPrint) binary and quartile categorized risk using medical history, imaging features and clinicopathological data among Chinese breast cancer patients." J Transl Med **21**(1): 798.
BACKGROUND: The 70-gene signature (70-GS, MammaPrint) test has been recommended by the main guidelines to evaluate prognosis and chemotherapy benefit of hormonal receptor positive human epidermal receptor 2 negative (HR + /Her2-) early breast cancer (BC). However, this expensive assay is not always accessible and affordable worldwide. Based on our previous study, we established nomogram models to predict the binary and quartile categorized risk of 70-GS. METHODS: We retrospectively analyzed a consecutive cohort of 150 female patients with HR + /Her2- BC and eligible 70-GS test. Comparison of 40 parameters including the patients' medical history risk factors, imaging features and clinicopathological characteristics was performed between patients with high risk (N = 62) and low risk (N = 88) of 70-GS test, whereas risk calculations from established models including Clinical Treatment Score Post-5 years (CTS5), Immunohistochemistry 3 (IHC3) and Nottingham Prognostic Index (NPI) were also compared between high vs low binary risk of 70-GS and among ultra-high (N = 12), high (N = 50), low (N = 65) and ultra-low (N = 23) quartile categorized risk of 70-GS. The data of 150 patients were randomly split by 4:1 ratio with training set of 120 patients and testing set 30 patients. Univariate analyses and multivariate logistic regression were performed to establish the two nomogram models to predict the the binary and quartile categorized risk of 70-GS. RESULTS: Compared to 70-GS low-risk patients, the high-risk patients had significantly less cardiovascular co-morbidity ($p = 0.034$), more grade 3 BC ($p = 0.006$), lower progesterone receptor (PR) positive percentage ($p = 0.007$), more Ki67 high BC (>/= 20%, $p < 0.001$) and no significant differences in all the imaging parameters of ultrasound and mammogram. The IHC3 risk and the NPI calculated score significantly correlated with both the binary and quartile categorized 70-GS risk classifications (both $p < 0.001$). The area under curve (AUC) of receiver-operating curve (ROC) of nomogram for binary risk prediction were 0.826 (C-index 0.903, 0.799-1.000) for training and 0.737 (C-index 0.785, 0.700-0.870) for validation dataset respectively. The AUC of ROC of nomogram for quartile risk prediction was 0.870 (C-index 0.854, 0.746-0.962) for training and 0.592 (C-index 0.769, 0.703-0.835) for testing set. The prediction accuracy of the nomogram for quartile categorized risk groups were 55.0% (likelihood ratio tests, $p < 0.001$) and 53.3% ($p = 0.04$) for training and validation, which more than double the baseline probability of 25%. CONCLUSIONS: To our knowledge, we are the first to establish easy-to-use nomograms to predict the individualized binary (high vs low) and the quartile categorized (ultra-high, high, low and ultra-low) risk classification of 70-GS test with fair performance, which might provide information for treatment choice for those who have no access to the 70-GS testing.

Parida, P., et al. (2023). "Circulating cell-free DNA as a diagnostic and prognostic marker for cervical cancer." Int J Gynecol Cancer.
Circulating cell-free DNA (cfDNA) is a promising tool for liquid biopsy-based tests. cfDNA has been reported to help in the diagnosis, quantification of minimal residual disease, prognosis, and identification of mutations conferring resistance in various types of cancers. Cervical cancer is the fourth most common cancer among women worldwide. High-risk human papillomavirus (hr-HPV) infections have been associated with almost all cervical cancers. Lack of HPV vaccines in national vaccination programs and irregular screening strategies in nations with low or moderate levels of human development index have led to cervical cancer becoming the second leading cause of cancer mortality in women. As HPV integration and overexpression of E6/E7 oncoprotein are crucial steps in the development of cancer, HPV cfDNA could potentially be used as a specific biomarker for the detection of cervical cancer. Many studies have used HPV cfDNA and other gene mutations or mRNA expression profiles for diagnosis and disease surveillance in patients with cervical cancer at various stages of disease progression. In this review we present an overview of different studies discussing the utility of cfDNA in cervical cancer and summarize the evidence supporting its potential use in diagnosis and treatment monitoring.

Parikh, P. M., et al. (2023). "Practical Clinical Consensus Guidelines for the Management of Cancer Associated Anemia in Low- and Middle-Income Countries." South Asian J Cancer **12**(2): 93-99.
Purvish M. ParikhCancer-associated anemia (CAA) remains a major unmet need that compromises overall survival (OS) and quality of life (QoL). Currently, available guidelines do not take into consideration the unique challenges in low- and middle-income countries (LMIC). Our CAA patients have to battle preexisting impaired nutritional status, depleted body iron stores, financial limitations, and difficulty in having easily accessible affordable healthcare. Hence, we fulfilled the need of guidelines for LMIC. A group of subject experts

were put together, given background literature, met in a face-to-face discussion, voted using Delphi process, and finally agreed on the contents of this guideline document. As many as 50% of cancer patients will have significant anemia (hemoglobin < 10 g/dL) at initial diagnosis. It is most commonly seen with gastrointestinal malignancies, head and neck cancers, and acute leukemias. The hemoglobin falls further after initiation of cancer directed therapy, due to chemotherapy itself or heightened nutritional deficiency. Its evaluation should include tests for complete blood count, red blood cell morphology, reticulocyte count, Coombs test, and levels of vitamin B12 and folic acid. Iron status should be monitored using test to measure serum iron, total iron binding capacity, transferring saturation, and serum ferritin levels. A minimum of 50% of cancer patients with anemia require iron supplements. The preferred mode of therapy is with intravenous (IV) iron using ferric carboxymaltose (FCM). Most patients respond satisfactorily to single dose of 1000 mg. It is also safe and does not require use of a test dose. Significant anemia is found in at least half of all cancer patients in India, South Asian Association for Regional Cooperation region, and other LMIC countries. Its awareness among healthcare professionals will prevent it from remaining undiagnosed (in up to 70% of all cancer patients) and adversely affecting OS and QoL. The benefits of treating them with IV iron therapy are quick replenishment of iron stores, hemoglobin returning to normal, better QoL, and avoiding risk of infections/reactions with blood transfusions. Many publications have proven the value of single-dose FCM in such clinical situations. CAA has been proven to be an independent prognostic factor that adversely affects both QoL and OS in cancer patients. Use of FCM as single IV dose of 1000 mg is safe and effective in the majority of patients with CAA.

Pozorski, V., et al. (2023). "Neutrophil-to-eosinophil ratio as a biomarker for clinical outcomes in advanced stage melanoma patients treated with anti-PD-1 therapy." Pigment Cell Melanoma Res **36**(6): 501-511.
Neutrophil-to-lymphocyte ratios (NLR) and eosinophil counts are associated with improved survival in melanoma patients treated with immune checkpoint inhibitors, but no study has investigated neutrophil-to-eosinophil ratios (NER) as a predictive indicator in this population. In this retrospective study evaluating anti-PD-1 treated patients with advanced melanoma, progression-free survival (PFS), overall survival (OS), objective response rates (ORR), and risk of high-grade (grade >/=3) immune-related adverse events (irAEs) were compared between groups defined by median pretreatment NLR and NER as well as median NLR and NER at 1-month post-treatment. Lower baseline NLR and NER were associated with improved OS [HR: 0.504, 95% CI: 0.328-0.773, p = .002 and HR: 0.442, 95% CI: 0.288-0.681, p < .001, respectively] on univariate testing. After accounting for multiple covariates, our multivariate analysis found that lower pretreatment NER was associated with better ORR (by irRECIST) (OR: 2.199, 95% CI: 1.071-4.582, p = .033) and improved OS (HR: 0.480, 95% CI: 0.296-0.777, p = .003). Baseline NLR, 1-month NLR, and 1-month NER were not associated with ORR, PFS, or OS outcomes; but 1-month NER correlated with lower risk of grade >/=3 irAEs (OR: 0.392, 95% CI: 0.165-0.895, p = .029). Our findings suggest baseline NER merits additional investigation as a novel prognostic marker for advanced melanoma patients receiving anti-PD-1-based regimens.

Rajagopal, R., et al. (2023). "Prognostic significance of molecular subgroups in survival outcome for children with medulloblastoma in Malaysia." Front Oncol **13**: 1278611.
INTRODUCTION: Advancements in genomic profiling led to the discovery of four major molecular subgroups in medulloblastoma (MB), which have now been incorporated into the World Health Organization classification of central nervous system tumors. The current study aimed to determine the prognostic significance of the MB molecular subgroups among children in Malaysia. METHODS: We assembled MB samples from children <18 years between January 2003 and June 2017 from four pediatric oncology centers in Malaysia. MB was sub-grouped using 850k DNA methylation testing at German Cancer Research Centre, Heidelberg, Germany. RESULTS: Fifty samples from patients diagnosed and treated as MB were identified. Two (4%) of the 50 patients' tumor DNA samples were insufficient for analysis. Of the remaining 48 patients, 41 (85%) samples were confirmed as MB, while for 7 (15%) patients, DNA methylation classification results were discrepant with the histopathological diagnosis of MB, with various other diagnoses. Of the 41 MB patients, 15 patients were stratified as standard-risk (SR), 16 patients as high-risk (HR), and ten as infants (age <3 years old). Molecular subgrouping of the whole cohort revealed four (14%) WNT, 11 (27%) SHH, 10 (24%) Group 3, and 16 (39%) Group 4. Treatment abandonment rates for older children and infants were 22.5% and 10%, respectively. After censoring treatment abandonment, for SR patients, the 5-year event-free survival (EFS) and overall survival (OS) were 43.1% +/- 14.7% and 46.9 +/- 15.6%, respectively, while in HR, 5-year EFS and OS were both 63.6% +/- 14.5%. Infants had a 5-year EFS and OS of 55.6% +/- 16.6% and 66.7% +/- 15.7%, respectively. WNT tumors had the best 5y-OS, followed by Group 3, Group 4, and SHH in children >/=3 years old. In younger children, SHH MB patients showed favorable outcomes. CONCLUSION: The study

highlights the importance of DNA methylation profiling for diagnostic accuracy. Most infants had SHH MB, and their EFS and OS were comparable to those reported in high-income countries. Due to the relatively small cohort and the high treatment abandonment rate, definite conclusions cannot be made regarding the prognostic significance of molecular subgroups of MB. Implementing this high-technology investigation would assist pathologists in improving the diagnosis and provide molecular subgrouping of MB, permitting subgroup-specific therapies.

Ren, Y., et al. (2023). "Ultrasound-guided thermal ablation for papillary thyroid microcarcinoma: the devil is in the details." Int J Hyperthermia **40**(1): 2278823.
Thermal ablation (TA) has harvested favorable outcomes in treating low-risk papillary thyroid microcarcinoma (PTMC). Preoperative assessment, intraoperative procedures and postoperative follow-up are all closely linked with the success and safety of TA on PTMC. However, many details in these aspects have not been systematically reviewed. This review firstly described the influence of preoperative assessment, especially for the risk of lymph node metastasis (LNM), as well as the molecular testing on the selection of TA for PTMC. Besides, we also summarized the experiences in treating special PTMC cases by TA, like multifocal lesions, PTMC located in the isthmus or adjacent to the dorsal capsule. At last, we discussed the follow-up strategies, the influence of the thyroid-stimulating hormone (TSH) level on the prognosis of PTMCs, and the management for recurrent cases. In conclusion, the procedures during the entire perioperative period should be standardized to improve the outcomes of TA in treating PTMC patients.

Roebothan, A., et al. (2023). "Specialty Care and Counselling about Hereditary Cancer Risk Improves Adherence to Cancer Screening and Prevention in Newfoundland and Labrador Patients with BRCA1/2 Pathogenic Variants: A Population-Based Retrospective Cohort Study." Curr Oncol **30**(10): 9367-9381.
Pathogenic variants (PVs) in BRCA1 and BRCA2 increase the lifetime risks of breast and ovarian cancer. Guidelines recommend breast screening (magnetic resonance imaging (MRI) and mammogram) or risk-reducing mastectomy (RRM) and salpingo-oophorectomy (RRSO). We sought to (1) characterize the population of BRCA1/2 PV carriers in Newfoundland and Labrador (NL), (2) evaluate risk-reducing interventions, and (3) identify factors influencing screening and prevention adherence. We conducted a retrospective study from a population-based provincial cohort of BRCA1/2 PV carriers. The eligibility criteria for risk-reducing interventions were defined for each case and patients were categorized based on their level of adherence with recommendations. Chi-squared and regression analyses were used to determine which factors influenced uptake and level of adherence. A total of 276 BRCA1/2 PV carriers were identified; 156 living NL biological females composed the study population. Unaffected females were younger at testing than those with a cancer diagnosis (44.4 years versus 51.7 years; $p = 0.002$). Categorized by eligibility, 61.0%, 61.6%, 39.0%, and 75.7% of patients underwent MRI, mammogram, RRM, and RRSO, respectively. Individuals with breast cancer were more likely to have RRM (64.7% versus 35.3%; $p < 0.001$), and those who attended a specialty hereditary cancer clinic were more likely to be adherent to recommendations (73.2% versus 13.4%; $p < 0.001$) and to undergo RRSO (84.1% versus 15.9%; $p < 0.001$). Nearly 40% of the female BRCA1/2 PV carriers were not receiving breast surveillance according to evidence-based recommendations. Cancer risk reduction and uptake of breast imaging and prophylactic surgeries are significantly higher in patients who receive dedicated specialty care. Organized hereditary cancer prevention programs will be a valuable component of Canadian healthcare systems and have the potential to reduce the burden of disease countrywide.

Ross, E. L., et al. (2023). "Estimated Average Treatment Effect of Psychiatric Hospitalization in Patients With Suicidal Behaviors: A Precision Treatment Analysis." JAMA Psychiatry.
IMPORTANCE: Psychiatric hospitalization is the standard of care for patients presenting to an emergency department (ED) or urgent care (UC) with high suicide risk. However, the effect of hospitalization in reducing subsequent suicidal behaviors is poorly understood and likely heterogeneous. OBJECTIVES: To estimate the association of psychiatric hospitalization with subsequent suicidal behaviors using observational data and develop a preliminary predictive analytics individualized treatment rule accounting for heterogeneity in this association across patients. DESIGN, SETTING, AND PARTICIPANTS: A machine learning analysis of retrospective data was conducted. All veterans presenting with suicidal ideation (SI) or suicide attempt (SA) from January 1, 2010, to December 31, 2015, were included. Data were analyzed from September 1, 2022, to March 10, 2023. Subgroups were defined by primary psychiatric diagnosis (nonaffective psychosis, bipolar disorder, major depressive disorder, and other) and suicidality (SI only, SA in past 2-7 days, and SA in past day). Models were trained in 70.0% of the training samples and tested in the remaining 30.0%. EXPOSURES: Psychiatric hospitalization vs nonhospitalization. MAIN OUTCOMES AND MEASURES: Fatal and nonfatal SAs within 12 months of ED/UC visits were identified

in administrative records and the National Death Index. Baseline covariates were drawn from electronic health records and geospatial databases. RESULTS: Of 196 610 visits (90.3% men; median [IQR] age, 53 [41-59] years), 71.5% resulted in hospitalization. The 12-month SA risk was 11.9% with hospitalization and 12.0% with nonhospitalization (difference, -0.1%; 95% CI, -0.4% to 0.2%). In patients with SI only or SA in the past 2 to 7 days, most hospitalization was not associated with subsequent SAs. For patients with SA in the past day, hospitalization was associated with risk reductions ranging from -6.9% to -9.6% across diagnoses. Accounting for heterogeneity, hospitalization was associated with reduced risk of subsequent SAs in 28.1% of the patients and increased risk in 24.0%. An individualized treatment rule based on these associations may reduce SAs by 16.0% and hospitalizations by 13.0% compared with current rates. CONCLUSIONS AND RELEVANCE: The findings of this study suggest that psychiatric hospitalization is associated with reduced average SA risk in the immediate aftermath of an SA but not after other recent SAs or SI only. Substantial heterogeneity exists in these associations across patients. An individualized treatment rule accounting for this heterogeneity could both reduce SAs and avert hospitalizations.

Schutte, W., et al. (2023). "[Prevention, Diagnosis, Therapy, and Follow-up of Lung Cancer - Interdisciplinary Guideline of the German Respiratory Society and the German Cancer Society - Abridged Version]." Pneumologie **77**(10): 671-813.
The current S3 Lung Cancer Guidelines are edited with fundamental changes to the previous edition based on the dynamic influx of information to this field:The recommendations include de novo a mandatory case presentation for all patients with lung cancer in a multidisciplinary tumor board before initiation of treatment, furthermore CT-Screening for asymptomatic patients at risk (after federal approval), recommendations for incidental lung nodule management , molecular testing of all NSCLC independent of subtypes, EGFR-mutations in resectable early stage lung cancer in relapsed or recurrent disease, adjuvant TKI-therapy in the presence of common EGFR-mutations, adjuvant consolidation treatment with checkpoint inhibitors in resected lung cancer with PD-L1 >/= 50%, obligatory evaluation of PD-L1-status, consolidation treatment with checkpoint inhibition after radiochemotherapy in patients with PD-L1-pos. tumor, adjuvant consolidation treatment with checkpoint inhibition in patients withPD-L1 >/= 50% stage IIIA and treatment options in PD-L1 >/= 50% tumors independent of PD-L1status and targeted therapy and treatment option immune chemotherapy in first line SCLC patients.Based on the current dynamic status of information in this field and the turnaround time required to implement new options, a transformation to a "living guideline" was proposed.

Schuurman, T. N., et al. (2023). "Optimising follow-up strategy based on cytology and human papillomavirus after fertility-sparing surgery for early stage cervical cancer: a nationwide, population-based, retrospective cohort study." Lancet Oncol.
BACKGROUND: The optimal follow-up strategy to detect recurrence after fertility-sparing surgery for early stage cervical cancer is unknown. Tailored surveillance based on individual risks could contribute to improved efficiency and, subsequently, reduce costs in health care. The aim of this study was to establish the predictive value of cervical cytology and high-risk human papillomavirus (HPV) testing to detect recurrent cervical intraepithelial neoplasia grade 2 or worse (CIN2+; including recurrent cervical cancer) after fertility-sparing surgery. METHODS: In this nationwide, population-based, retrospective cohort study, we used data from the Netherlands Cancer Registry and the Dutch Nationwide Pathology Databank. All patients aged 18-40 years with cervical cancer of any histology who received fertility-sparing surgery (ie, large loop excision of the transformation zone, conisation, or trachelectomy) between Jan 1, 2000, and Dec 31, 2020, were included. Pathology data from diagnosis, treatment, and during follow-up were analysed. The primary and secondary outcomes were the cumulative incidence of recurrent CIN2+ and recurrence-free survival, overall and stratified by results for cytology and high-risk HPV. FINDINGS: 1548 patients were identified, of whom 1462 met the inclusion criteria. Of these included patients, 19 568 pathology reports were available. The median age at diagnosis was 31 years (IQR 30-35). After a median follow-up of 6.1 years (IQR 3.3-10.8), recurrent CIN2+ was diagnosed in 128 patients (cumulative incidence 15.0%, 95% CI 11.5-18.2), including 52 patients (cumulative incidence 5.4%, 95% CI 3.7-7.0) with recurrent cervical cancer. The overall 10-year recurrence-free survival for CIN2+ was 89.3% (95% CI 87.4-91.3). By cytology at first follow-up visit within 12 months after fertility-sparing surgery, 10-year recurrence-free survival for CIN2+ was 92.1% (90.2-94.1) in patients with normal cytology, 84.6% (77.4-92.3) in those with low-grade cytology, and 43.1% (26.4-70.2) in those with high-grade cytology. By high-risk HPV status at first follow-up visit within 12 months after surgery, 10-year recurrence-free survival for CIN2+ was 91.1% (85.3-97.3) in patients who were negative for high-risk HPV and 73.6% (58.4-92.8) in those who were positive for high-risk HPV. Cumulative incidence of recurrent CIN2+ within 6 months after any follow-up visit (6-24 months) in patients negative for

high-risk HPV with normal or low-grade cytology was 0.0-0.7% and with high-grade cytology was 0.0-33.3%. Cumulative incidence of recurrence in patients positive for high-risk HPV with normal or low-grade cytology were 0.0-15.4% and with high-grade cytology were 50.0-100.0%. None of the patients who were negative for high-risk HPV without high-grade cytology, at 6 months and 12 months, developed recurrence. INTERPRETATION: Patients who are negative for high-risk HPV with normal or low-grade cytology at 6-24 months after fertility-sparing surgery, could be offered a prolonged follow-up interval of 6 months. This group comprises 80% of all patients receiving fertility-sparing surgery. An interval of 12 months seems to be safe after two consecutive negative tests for high-risk HPV with an absence of high-grade cytology, which accounts for nearly 75% of all patients who receive fertility-sparing surgery. FUNDING: KWF Dutch Cancer Society.

Semba, R., et al. (2023). "Short-term prognosis of low-risk prostate cancer patients is favorable despite the presence of pathological prognostic factors: a retrospective study." BMC Urol **23**(1): 174.
BACKGROUND: Prostate cancer patients with pathological prognostic factors have a poor prognosis, but it is unclear whether pathological prognostic factors are associated with prognosis limited to low-risk patients with good prognosis according to NCCN guidelines. The present study examined whether prognosis is influenced by pathological prognostic factors using radical prostatectomy (RP) specimens from low-risk patients. METHODS: We evaluated diagnostic accuracy by examining biochemical recurrence (BCR)-free survival with respect to clinical and pathological prognostic factors in 419 all-risk patients who underwent RP. Clinical prognostic factors included age, prostate-specific antigen (PSA) levels, PSA density, and risk stratification, while pathological prognostic factors included grade group, lymphovascular space invasion, extraprostatic extension, surgical margins, seminal vesicle invasion, intraductal carcinoma of the prostate (IDCP), and pT. In a subsequent analysis restricted to 104 low-risk patients, survival curves were estimated for pathological prognostic factors using the Kaplan-Meier method and compared using log-rank and generalized Wilcoxon tests. RESULTS: In the overall risk analysis, the presence of pathological prognostic factors significantly shortened BCR-free survival ($p < 0.05$). Univariable analysis revealed that PSA density, risk categories, and pathological prognostic factors were significantly associated with BCR-free survival, although age and PSA were not. In multivariable analysis, age, risk categories, grade group, IDCP, and pT significantly predicted BCR-free survival ($p < 0.05$). Conversely, no statistically significant differences were found for any pathological prognostic factors in low-risk patients. CONCLUSIONS: In low-risk patients, pathological prognostic factors did not affect BCR-free survival, which suggests that additional treatment may be unnecessary even if pathological prognostic factors are observed in low-risk patients with RP.

Senore, C., et al. (2023). "Rationale for organized Colorectal cancer screening programs." Best Pract Res Clin Gastroenterol **66**: 101850.
Colorectal cancer (CRC) is a major health problem and it is expected that the number of persons diagnosed with CRC and CRC-related deaths will continue to increase. However, recent years have shown reductions in CRC incidence and mortality particularly among individuals aged 50 years and older which can be attributed to screening, improvements in patients' management, closer adherence to treatment guideline recommendations and a higher utilization of curative surgery, chemotherapy and radiotherapy. The International Agency for Research on Cancer has concluded that there has been sufficient evidence that biennially screening using a stool-test or once-only endoscopy screening reduces CRC-related mortality. In Europe, between 2008 and 2018, nine countries have successfully implemented a population-based organized program and another six are in the roll-out phase. Population-based organized programs show higher screening participation rates and lower lack of compliance to follow-up testing after a positive screen test compared to opportunistic screening. Moreover, organized programs aim to provide high quality screening thereby reducing the risk of the harms of screening, including over-screening, and complications of screening, and poor follow-up of those who test positive. We describe how population-based organized CRC screening programs are preferred, since they reflect a more appropriate utilization of available resources, reduce inequities in access, and can integrate interventions addressing barriers to screening at the individual and health system levels.

Stollberg, S. M., et al. (2023). "Are Tumor Marker Tests Applied Appropriately in Clinical Practice? A Healthcare Claims Data Analysis." Diagnostics (Basel) **13**(21).
Tumor markers (TM) are crucial in the monitoring of cancer treatment. However, inappropriate requests for screening reasons have a high risk of false positive and negative findings, which can lead to patient anxiety and unnecessary follow-up examinations. We aimed to assess the appropriateness of TM testing in outpatient practice in Switzerland. We conducted a retrospective cohort study based on healthcare claims data. Patients who had received at least one out of seven TM tests

(CEA, CA19-9, CA125, CA15-3, CA72-4, Calcitonin, or NSE) between 2018 and 2021 were analyzed. Appropriate determinations were defined as a request with a corresponding cancer-related diagnosis or intervention. Appropriateness of TM determination by patient characteristics and prescriber specialty was estimated by using multivariate analyses. A total of 51,395 TM determinations in 36,537 patients were included. An amount of 41.6% of all TM were determined appropriately. General practitioners most often determined TM (44.3%) and had the lowest number of appropriate requests (27.8%). A strong predictor for appropriate determinations were requests by medical oncologists. A remarkable proportion of TM testing was performed inappropriately, particularly in the primary care setting. Our results suggest that a considerable proportion of the population is at risk for various harms associated with misinterpretations of TM test results.

Takayama, T., et al. (2023). "Clinical Guidelines for Diagnosis and Management of Cowden Syndrome/PTEN Hamartoma Tumor Syndrome in Children and Adults-Secondary Publication." J Anus Rectum Colon **7**(4): 284-300.
Cowden syndrome (CS)/PTEN hamartoma tumor syndrome (PHTS) is a rare autosomal dominantly inherited condition caused by germline pathogenesis. It is associated with multiple hamartomatous lesions occurring in various organs and tissues, including the gastrointestinal tract, skin, mucous membranes, breast, thyroid, endometrium, and brain. Macrocephaly or multiple characteristic mucocutaneous lesions commonly develop in individuals in their 20s. This syndrome is occasionally diagnosed in childhood due to the occurrence of multiple gastrointestinal polyps, autism spectrum disorders, and intellectual disability. CS/PHTS can be diagnosed taking the opportunity of multigene panel testing in patients with cancer. Appropriate surveillance for early diagnosis of associated cancers is required because patients have a high risk of cancers including breast, thyroid, colorectal, endometrial, and renal cancers. Under these circumstances, there is growing concern regarding the management of CS/PHTS in Japan, but there are no available practice guidelines. To address this situation, the guideline committee, which included specialists from multiple academic societies, was organized by the Research Group on Rare and Intractable Diseases granted by the Ministry of Health, Labour, and Welfare, Japan. The present clinical guidelines explain the principles in the diagnosis and management of CS/PHTS, together with four clinical questions and the corresponding recommendations, incorporating the concept of the Grading of Recommendations Assessment, Development, and Evaluation system. Herein, we present an English version of the guideline, some of which have been updated, to promote seamless implementation of accurate diagnosis and appropriate management of pediatric, adolescent, and adult patients with CS/PHTS.

Thipsanthiah, K., et al. (2023). "Factors Affecting Non-Histologically Proven Invasive Cancer of the Uterine Cervix that Had an Abnormal Pap Smear: Results of the CCS Program." Asian Pac J Cancer Prev **24**(10): 3429-3436.
BACKGROUND: Cervical cancer (CC) ranks fourth among cancers diagnosed around the world, but early detection and treatment can reduce invasive cervical cancer and mortality. Screening programs (CCSP), such as the one covering Thailand's 75 provinces, use histology to confirm cases. The study determined the incidence rate (IR) and investigated the factors associated with non-histologically proven invasive cancer of the uterine cervix (non-HPICUC) with an abnormal pap smear from the CCSP at Mahasarakham Hospital, Thailand. METHODS: The CCSP was used to analyse a retrospective cohort of 288 women between 30 and 60 years of age. All abnormal pap smears were followed up until April 30, 2022. We estimated the IR and assessed the relationship between various independent variables and non-HPICUC using the generalised linear model (GLM) for testing association data. We reported the adjusted RR and 95% confidence intervals (95%CI). RESULTS: 260 non-HPICUC cases had abnormal CCSP pap smears for an overall IR of 90.0 (95% CI: 86.3 - 93.2). After adjusting the model for all variables, age at recruitment and pregnancy had a statistically significant association with non-HPICUC (p-value < 0.05). We found that the risk of non-HPICUC increased 1.02 times for every 20-year increment in age compared to below that age (adjusted RR=1.02, 95% CI: 1.01 - 1.04). Pregnancy at risk for non-HPICUC was 0.89 times compared to non-pregnancy (adjusted RR=0.89, 95% CI: 0.80 - 0.99). Pathological vaginal discharge (PVD) did not have a statistically significant association with non-HPICUC (p-value = 0.094); notwithstanding, women with PVD had 1.08 times the risk of non-HPICUC compared to women without PVD (adjusted RR=1.08, 95% CI: 0.97 - 1.20). CONCLUSIONS: Based on an abnormal pap smear from the CCS Program at Mahasarakham Hospital Thailand, age and pregnancy are associated with an increased risk of non-HPICUC. High-risk groups with abnormal pap smears should be targeted for CC campaigns.

Thomas, M., et al. (2023). "Case Report of Seronegative Cancer-Associated Retinopathy in a Patient with Small Cell Lung Carcinoma." Case Rep Oncol **16**(1): 791-796.

Cancer-associated retinopathy (CAR) is a rare paraneoplastic syndrome characterized by autoimmune destruction of photoreceptor cells. It is associated with several tumor types, including small cell lung carcinoma (SCLC). Corticosteroids have been the mainstay treatment for CAR, although no therapeutic standard has truly been established. A 66-year-old female with significant smoking history and age-related macular degeneration (ARMD) presented with rapidly declining bilateral visual acuity. Ophthalmologic examination findings appeared consistent with the known diagnosis of ARMD but did not otherwise present a clear alternative etiology. Imaging with a computed tomography (CT) scan revealed a right hilar mass which was confirmed to be limited stage SCLC based on a subsequent biopsy and further imaging with a positron emission tomography/computed tomography (PET/CT) scan. Antibody testing was negative for anti-recoverin antibodies. The patient experienced a complete response to chemoradiation with cisplatin and etoposide; however, her ocular symptoms did not respond to a combined treatment approach with corticosteroids, plasmapheresis, and intravenous immunoglobulin (IVIG). While CAR represents a rare condition in SCLC, cases that are seronegative for anti-recoverin are even less common. Further, the diagnosis of CAR by ophthalmologic examination may be more challenging in patients with pre-existing ocular diseases, such as macular degeneration. Clinicians should have suspicion for paraneoplastic blindness in patients with known risk factors for malignancy, whose ocular symptoms are inconsistent with exam findings.

Uldbjerg, E. M., et al. (2023). "Diagnostic Workup, Treatment Patterns, and Clinical Outcomes in Early-Stage IB-IIIA Non-Small-Cell Lung Cancer Patients in Denmark." Cancers (Basel) **15**(21).

Despite recent improvements in early-stage non-small-cell lung cancer (NSCLC), disease relapse remains challenging. Moreover, real-world evidence on long-term follow-up of disease-free survival (DFS) and recurrence patterns in a large, unselected cohort of early-stage NSCLC patients is lacking. This cohort study aimed to assess clinical characteristics, diagnostic workup, treatment, survival, and risk of disease relapse among early-stage NSCLC patients. Adult patients with stage IB, II, or IIIA NSCLC diagnosed and/or treated at Aarhus University Hospital in Denmark from January 2010 to December 2020 were included and followed-up until May 2021. Comprehensive clinical data were collected from electronic medical records of eligible patients and linked to Danish register data. The study population comprised 1341 early-stage NSCLC patients: 22%, 40%, and 38% were diagnosed with stage IB, II, and IIIA disease, respectively. In total, 42% of patients were tested for epidermal growth factor receptor (EGFR), of whom 10% were EGFR-mutation-positive (EGFRm(+)). Half of all patients received surgery, and nine percent of patients received stereotactic body radiation therapy (SBRT). Disease-free survival 5 years post-diagnosis was 49%, 42%, and 22% for stage IB, II, and stage IIIA patients, respectively. DFS improved over time both for patients treated with surgery and SBRT. However, disease relapse remained a challenge, with approximately 40% of stage IIIA having relapsed 3 years post-diagnosis. This study contributes important knowledge that puts clinical trials on new perioperative treatment modalities for early-stage NSCLC patients into perspective. Our findings cover an essential evidence gap on real-world DFS and recurrence dynamics, confirming that despite an improvement in DFS over time and across different treatment modalities, disease relapse remains a monumental challenge. Therefore, better treatment strategies are needed.

Ulrikh, E., et al. (2023). "Gestational Trophoblastic Disease with Coexisting Progressing Pregnancy: Personalised Treatment Modalities." Int J Clin Pract **2023**: 5502317.

PURPOSE: Gestational trophoblastic disease (GTD) coexisting with a steadily progressing pregnancy is an extremely rare condition presented in the literature as a single case or case series of successful delivery. The purpose of this study was to describe five cases of GTD and present possible management strategies for such patients. METHODS: Clinical data of five pregnancies with coexisting GTD were identified within the Almazov National Medical Research Centre from 2018 to 2021. RESULTS: Three cases of multiple pregnancies with complete hydatidiform moles and two cases of singleton pregnancies with intraplacental choriocarcinoma and invasive hydatidiform moles were identified. Three pregnancies were prolonged and ended with preterm deliveries. Malignant transformation of the GTD accounted for 60% of the cases. The condition of newborns was based on the level of prematurity and functional immaturity, and in all cases, it was aggravated by anemia. CONCLUSION: GTD coexisting with progressing pregnancy is threatened by the risks of preterm delivery, miscarriage, hemorrhage, and disease progression and requires monitoring in a multidisciplinary clinic experienced in the management of patients with malignant tumors during pregnancy. In cases of prolonged pregnancy against the background of GTD, we suggest the following monitoring during pregnancy: pelvic, abdominal ultrasound/MRI (without contrast), prenatal invasive fetal karyotype testing in cases of singleton pregnancy, lung X-ray/CT with uterine shielding, weekly assessment of beta-hCG levels, and dynamic monitoring of the fetus. The following postnatal monitoring should be performed: morphological examination of the placenta, weekly

assessment of beta-hCG levels up to normalization, then monthly assessment up to six months, and control of beta-hCG level of the newborn.

Van Buren, I., et al. (2023). "Survival Among Veterans Receiving Steroids for Immune-Related Adverse Events After Immune Checkpoint Inhibitor Therapy." JAMA Netw Open **6**(10): e2340695.
IMPORTANCE: Systemic steroids are commonly used to manage immune-related adverse events (irAEs), but it remains unclear whether they may undermine immune checkpoint inhibitor (ICI) therapy outcomes. Few studies have assessed the impact of steroid timing and its association with continuation or cessation of ICI therapy. OBJECTIVE: To characterize how systemic steroids and steroid timing for irAEs are associated with survival in patients receiving ICI therapy. DESIGN, SETTING, AND PARTICIPANTS: This multicenter retrospective cohort study encompassed veterans receiving ICI for cancer between January 1, 2010, and December 31, 2021. Data analysis was conducted September 8, 2023. EXPOSURES: Identifiable primary diagnosis of cancer. Patients were categorized into 3 cohorts: those receiving no steroids, systemic steroids for irAEs, and steroids for non-irAE-associated reasons. All eligible patients received 1 or more doses of an ICI (atezolizumab, avelumab, cemiplimab, durvalumab, ipilimumab, nivolumab, or pembrolizumab). Eligible patients in the steroid group received at least 1 dose (intravenous, intramuscular, or oral) of dexamethasone, hydrocortisone, methylprednisolone, prednisone, or prednisolone. Steroid use at baseline for palliation or infusion prophylaxis or delivered as a single dose was deemed to be non-irAE associated. All other patterns of steroid use were assumed to be for irAEs. MAIN OUTCOMES AND MEASURES: The primary outcome was overall survival, with a 5-year follow-up after ICI initiation. Kaplan-Meier survival analyses were performed with pairwise log-rank tests to determine significance. Risk was modeled with Cox proportional hazard regression. RESULTS: The cohort consisted of 20 163 veterans receiving ICI therapy including 12 221 patients (mean [SD] age, 69.5 [8.0] years; 11 830 male patients [96.8%]; 9394 White patients [76.9%]) who received systemic steroids during ICI treatment and 7942 patients (mean [SD] age, 70.3 [8.5] years; 7747 male patients [97.5%]; 6085 White patients [76.6%]) who did not. Patients with an irAE diagnosis had significantly improved overall survival (OS) compared with those without (median [IQR] OS, 17.4 [6.6 to 48.5] months vs 10.5 [3.5 to 36.8] months; adjusted hazard ratio, 0.84; 95% CI, 0.81-0.84; P < .001). For patients with irAEs, systemic steroids for irAEs were associated with significantly improved survival compared with those who received steroids for non-irAE-related reasons or no steroid treatment (median [IQR] OS, 21.3 [9.3 to 58.2] months vs 13.6 [5.5 to 33.7] months vs 15.8 [4.9 to not reached] months; P <.001). However, among those who received steroids for irAEs, early steroid use (<2 months after ICI initiation) was associated with reduced relative survival benefit vs later steroid use, regardless of ICI continuation or cessation following steroid initiation (median [IQR] OS after ICI cessation 4.4 [1.9 to 19.5] months vs 16.0 [8.0 to 42.2] months; median [IQR] OS after ICI continuation, 16.0 [7.1 to not reached] months vs 29.2 [16.5 to 53.5] months; P <.001). CONCLUSIONS AND RELEVANCE: This study suggests that steroids for irAE management may not abrogate irAE-associated survival benefits. However, early steroid administration within 2 months of ICI initiation is associated with shorter survival despite continuation of ICI therapy.

van den Berge, B. A., et al. (2023). "Patient-Perceived Hand Function Can Predict Treatment for Dupuytren Disease." Plast Reconstr Surg **152**(5): 867e-875e.
BACKGROUND: Web-based patient-reported outcome measures (PROMs) could help surgeons remotely assess the need for examination and subsequent treatment of patients with Dupuytren disease (DD). The authors studied whether the Unite Rhumatologique des Affections de la Main (URAM) and the Michigan Hand Questionnaire (MHQ) could predict DD treatment. METHODS: In this prospective cohort study, the authors compared MHQ and URAM scores of treated patients with those of untreated patients. For the treatment group, the authors selected a score closest to 1 year before treatment. For controls, the authors randomly selected a score. The authors also tested the predictive value of a 1-year change score between 15 months and 6 weeks before treatment. The primary outcome measure was DD treatment. The predictive value was determined using the area under the curve (AUC). An AUC greater than 0.70 was considered good predictive ability; 0.70 to 0.50, poor predictive ability; and less than 0.50, no predictive ability. RESULTS: The authors included 141 patients for the MHQ analysis and 145 patients for the URAM analysis. The AUC of the MHQ and URAM scores measured 1 year before treatment were 0.80 (95% CI, 0.71 to 0.88) and 0.75 (95% CI, 0.68 to 0.82), respectively. The 1-year change score resulted in an AUC less than 0.60 for both questionnaires. CONCLUSIONS: The results show that both the MHQ and URAM score measured around 1 year before treatment can predict treatment for DD. If future studies show that telemonitoring of patients with DD with PROMs is also cost-effective, web-based PROMs could optimize patient care and effectiveness of DD treatment. CLINICAL QUESTION/LEVEL OF EVIDENCE: Risk, III.

Vichapat, V., et al. (2023). "Impact of Waiting Times on Mortality in Advanced Stage Non-Small Cell Lung Cancer: A 10-Year Retrospective Cohort Study in Thailand." Asian Pac J Cancer Prev **24**(10): 3419-3428.
OBJECTIVE: This study investigated the relationship between mortality and waiting times from diagnosis to first treatment while also considering other important risk factors associated with mortality. METHODS: This is a cohort study including 497 patients diagnosed with advanced stage non-small cell lung cancer (NSCLC) between 1st January 2012 and 31st December 2021. The risk factors and waiting periods were analysed to determine their association with mortality. The waiting periods were recorded based on the timeline of patient visits, including the time between the 1st visit and imaging, the time between the 1st visit and tissue diagnosis, the time between the procedure and tissue diagnosis, the time between tissue diagnosis and treatment and the time from the 1st visit until treatment. The data were assessed using Cox regression with time-varying covariates. RESULTS: Waiting time for tissue diagnosis had a modest effect on mortality, a waiting time of more than four weeks indicated poor prognosis both in univariate and multivariate analyses [HR 1.48 (95%CI 1.18-1.87), p = < 0.01), adjusted HR 1.007 (95%CI 1.002-1.010), p = 0.02]. Waiting time for other services was not shown to be associated with mortality. The mortality rate was 3 times higher in patients with poor ECOG performance status than good ECOG performance [adjusted HR 3.17(2.04-4.91)]. Patients with EGFR sensitizing mutation who were treated with EGFR TKI therapy had a lower risk of lung cancer death compared to those being treated with chemotherapy [adjusted HR 0.49 (0.33-0.72)]. CONCLUSION: Molecular testing for EGFR sensitizing mutation and the TKI treatment were fundamental changes that assisted in improving survival rates for patients diagnosed with advanced stage lung cancer over the 10-year period. However, poor ECOG performance status remained a strong risk factor for lung cancer death. Longer waiting time for tissue diagnosis might indicate a poor prognosis.

Voidazan, S., et al. (2023). "Assessing the Level of Knowledge and Experience Regarding Cervical Cancer Prevention and Screening among Roma Women in Romania." Medicina (Kaunas) **59**(10).
Background and Objectives: Romania ranks among the countries with a particularly high rate of mortality that can be prevented through prevention programs, screening, early detection, and prompt care. Cervical cancer (CC) is a major cause of these preventable deaths, affecting individuals from marginalized and rural regions, as well as the Roma population. The purpose of this article was to identify accurate and consistent information about the Roma population on the risk of CC, as well as the importance of understanding the causes of the disease and awareness of the available prevention methods. Materials and Methods: A cross-sectional study was conducted using a self-administered questionnaire applied only to Roma women in Romania. Results: We enrolled 759 patients in this study. These were divided into two groups: Group 1 comprised 289 (38.1%) women who had been tested for HPV infection, while Group 2 included 470 (61.9%) women who had never been tested for HPV infection. Characterization of women in Group 1: mostly aged between 25 and 54 years, with high school education, married, who started sexual activity under the age of 18 years, with only one sexual partner, and had over five pregnancies. Regarding contraceptive methods, 35.7% of women do not know or use any contraceptive method, and 32.2% use hormonal contraceptives. Two thirds of the women tested had heard of HPV, and 19.7% were vaccinated against HPV with at least 2-3 doses. A percentage of 8.7 had a diagnosis of CC, compared to those who were not tested (p-0.0001), whereas 63% of the tested women did not know much about CC, as opposed to 85.7% of the group of untested women. Conclusions: Cervical cancer (CC) continues to be a public health concern in Romania, particularly among vulnerable groups. Promoting campaigns to raise awareness for HPV vaccination and CC screening are necessary to reduce the associated mortality and morbidity.

Winters-Stone, K. M., et al. (2023). "Identifying trajectories and predictors of chemotherapy-induced peripheral neuropathy symptoms, physical functioning, and falls across treatment and recovery in adults treated with neurotoxic chemotherapy: the PATTERN observational study protocol (NCT05790538)." BMC Cancer **23**(1): 1087.
BACKGROUND: Chemotherapy-induced peripheral neuropathy (CIPN) is a debilitating and dose-limiting side effect of systemic cancer therapy. In many cancer survivors, CIPN persists after treatment ends and is associated with functional impairments, abnormal gait patterns, falls, and diminished quality of life. However, little is known regarding which patients are most likely to develop CIPN symptoms that impair mobility and increase fall risk, when this risk develops, or the optimal timing of early intervention efforts to mitigate the impact of CIPN on functioning and fall risk. This study will address these knowledge gaps by (1) characterizing trajectories of symptoms, functioning, and falls before, during, and after treatment in adults prescribed neurotoxic chemotherapy for cancer; and (2) determining the simplest set of predictors for identifying individuals at risk for CIPN-related functional decline and falls. METHODS: We will enroll 200 participants into a prospective, observational study before initiating chemotherapy and up to 1 year after completing

chemotherapy. Eligible participants are aged 40-85 years, diagnosed with stage I-III cancer, and scheduled to receive neurotoxic chemotherapy. We perform objective assessments of vibratory and touch sensation (biothesiometry, tuning fork, monofilament tests), standing and dynamic balance (quiet stance, Timed-Up-and-Go tests), and upper and lower extremity strength (handgrip dynamometry, 5-time repeated chair stand test) in the clinic at baseline, every 4-6 weeks during chemotherapy, and quarterly for 1 year post-chemotherapy. Participants wear devices that passively and continuously measure daily gait quality and physical activity for 1 week after each objective assessment and self-report symptoms (CIPN, insomnia, fatigue, dizziness, pain, cognition, anxiety, and depressive symptoms) and falls via weekly electronic surveys. We will use structural equation modeling, including growth mixture modeling, to examine patterns in trajectories of changes in symptoms, functioning, and falls associated with neurotoxic chemotherapy and then search for distinct risk profiles for CIPN. DISCUSSION: Identifying simple, early predictors of functional decline and fall risk in adults with cancer receiving neurotoxic chemotherapy will help identify individuals who would benefit from early and targeted interventions to prevent CIPN-related falls and disability. TRIAL REGISTRATION: This study was retrospectively registered with ClinicalTrials.gov (NCT05790538) on 3/30/2023.

Wolf, B., et al. (2023). "Desmoplasia in cervical cancer is associated with a more aggressive tumor phenotype." Sci Rep **13**(1): 18946.
In cancer of the uterine cervix, the role of desmoplasia, i.e., peritumoral stromal remodeling characterized by fibroblast activation and increased extracellular matrix deposition, is not established. We conducted a retrospective cohort study based on data from 438 patients who had undergone surgical treatment for cervical cancer as part of the prospective Leipzig Mesometrial Resection study between 1999 and 2021. Using non-parametric tests, Kaplan-Meier plotting, and Cox regression modeling, we calculated the prognostic impact of desmoplasia and its association with other risk factors. Desmoplasia was present in 80.6% of cases and was associated with a higher frequency of lymphovascular space involvement (76.5 vs. 56.5%, $p < 0.001$) and venous infiltration (14.4 vs. 2.4%, $p < 0.001$). Lymph node metastasis (23.0 vs. 11.8%, $p < 0.05$) and parametrial involvement (47.3 vs. 17.6%, $p < 0.0001$) were also more common in patients with desmoplasia. The presence of desmoplasia was associated with inferior overall (80.2% vs. 94.5% hazard ratio [HR] 3.8 [95% CI 1.4-10.4], $p = 0.002$) and recurrence-free survival (75.3% vs. 87.3%, HR 2.3 [95% CI 1.2-4.6], $p = 0.008$). In addition, desmoplasia was associated with significantly less peritumoral inflammation (rho - 0.43, $p < 0.0001$). In summary, we link desmoplasia to a more aggressive phenotype of cervical cancer, reduced peritumoral inflammation, and inferior survival.

Wu, Y., et al. (2023). "Immunobiological signatures and the emerging role of SPP1 in predicting tumor heterogeneity, malignancy, and clinical outcomes in stomach adenocarcinoma." Aging (Albany NY) **15**(20): 11588-11610.
BACKGROUND: Immunotherapy, as a form of immunobiological therapy, represents a promising approach for enhancing patients' immune responses. This work aims to present innovative ideas and insights for prognostic assessment and clinical treatment of stomach adenocarcinoma (STAD) by leveraging immunobiological signatures. METHODS: We employed weighted gene co-expression network analysis (WGCNA) and unsupervised clustering analysis to identify hub genes. These hub genes were utilized to construct a prognostic risk model, and their impact on the tumor microenvironment (TME) and DNA variations was assessed using large-scale STAD patient cohorts. Additionally, we conducted transfection experiments with plasmids to investigate the influence of SPP1 on the malignancy of HGC27 and NCI-N87 cells. RESULTS: Unsupervised clustering of 12 immune-related genes (IRGs) revealed three distinct alteration patterns with unique molecular phenotypes, clinicopathological characteristics, prognosis, and TME features. Using LASSO and multivariate Cox regression analyses, we identified three hub genes (MMP12, SPP1, PLAU) from the IRGs to establish a risk signature. This IRG-related risk model significantly stratified the prognosis risk among STAD patients in the training (n = 522), testing (n = 521), and validation (n = 300) cohorts. Notably, there were discernible differences in therapy responses and TME characteristics, such as tumor purity and lymphocyte infiltration, between the risk model groups. Subsequently, a nomogram that incorporates the IRG signature and clinicopathological factors demonstrated superior sensitivity and specificity in predicting outcomes for STAD patients. Furthermore, down-regulation of SPP1, as observed after siRNA transfection, significantly inhibited the proliferation and migration abilities of HGC27 and NCI-N87 cells. CONCLUSIONS: In summary, this study highlights the critical role of immune-related signatures in STAD and offers novel insights into prognosis indicators and immunotherapeutic targets for this condition. SPP1 emerges as an independent prognostic factor for STAD and appears to regulate STAD progression by influencing the immune microenvironment.

Xu, Y., et al. (2023). "Exploration of an Prognostic Signature Related to Endoplasmic Reticulum Stress in

Colorectal Adenocarcinoma and Their Response Targeting Immunotherapy." Technol Cancer Res Treat **22**: 15330338231212073.
Background: Endoplasmic reticulum (ER) stress plays a pro-apoptotic role in colorectal adenocarcinoma (COAD). This study aimed to develop a novel ER-stress-related prognostic risk model for COAD and provide support for COAD cohorts with different risk score responses to immune checkpoint inhibitor therapies. Methods: TCGA-COAD and GSE39582 were included in this prospective study. Univariate and multivariate Cox analyses were performed to identify prognostic ER stress-related genes (ERSGs). Accordingly, the immune infiltration landscape and immunotherapy response in different risk groups were assessed. Finally, the expression of prognostic genes in 10 normal and 10 COAD tissue samples was verified using reverse transcription-quantitative polymerase chain reaction. Results: Eight prognostic genes were selected to establish an ERSG-based signature in the training set of the TCGA-COAD cohort. The accuracy of this was confirmed using a testing set of TCGA-COAD and GSE39582 cohorts. Gene set variation analysis indicated that differential functionality in high-low-risk groups was related to immune-related pathways. Corresponding to this, CD36, TIMP1, and PTGIS were significantly associated with 19 immune cells with distinct proportions between the different risk groups, such as central memory CD4T cells and central memory CD8T cells. Moreover, the risk score was considered effective for predicting the clinical response to immunotherapy, and the immunotherapy response was significantly and negatively correlated with the risk score of individuals with COAD. Furthermore, the immune checkpoint inhibitor treatment was less effective in the high-risk group, where the expression levels of PD-L1 and tumor immune dysfunction and exclusion scores in the high-risk group were significantly increased. Finally, the experimental results demonstrated that the expression trends of prognostic genes in clinical samples were consistent with the results from public databases. Conclusion: Our study established a novel risk signature to predict the COAD prognosis of patients and provide theoretical support for the clinical treatment of COAD.

Xue, M., et al. (2023). "Profiling risk factors for separation of infection complications in patients with gastrointestinal and nodal diffuse large B-cell lymphoma." BMC Infect Dis **23**(1): 711.
OBJECTIVE: To identify risk factors for infection complications in patients with gastrointestinal diffuse large B-cell lymphoma (GI-DLBCL) and nodal DLBCL (N-DLBCL) during treatment, respectively. METHODS: Total 51 GI-DLBCL patients and 80 N-DLBCL patients were included after retrieving clinical data from a single medical center in the past ten years. Logistic regression analysis was utilized to analyze patients' data, including baseline demographics, treatments and laboratory values, to determine independent risk factors of infection in these patients. RESULTS: Total 28 of 51 patients (54.9%) in the GI-DLBCL group and 52 of 80 patients (65%) in the N-DLBCL group were observed infection events during treatment. A multivariate logistic regression model revealed that Ann-arbor stage IV (P = 0.034; odds ratio [OR]: 10.635; 95% confidence interval [CI]: 1.152-142.712), extra-nodal lesions >/= 2 (P = 0.041; OR: 23.116; 95%CI: 1.144-466.949) and high serum lactate dehydrogenase (LDH) at the time of diagnosis (LDH > 252U/L; P = 0.033; OR: 6.058; 95%CI: 1.159-31.659) were independent risk factors for the development of infection in patients with GI-DLBCL after systemic treatment. In the N-DLBCL group, high serum C-reactive protein (CRP) (P = 0.027; OR: 1.104; 95%CI: 1.011-1.204) and a low platelet count (P = 0.041; OR: 0.991; 95%CI: 0.982-1.000) at routine blood tests just before infection occurred were identified as significant risk factors related to infection events during treatment. CONCLUSIONS: Discordant independent risk factors induced infection may be present during the treatment in patients with GI-DLBCL and N-DLBCL. Close monitoring these risk factors is likely an effective strategy to prevent microbial infections in these patients.

Yaghoubi, M. A., et al. (2023). "The Prognostic Role of Corticosteroid Administration in Hospitalized Patients with Severe COVID-19: A Cross-sectional Study." Recent Adv Inflamm Allergy Drug Discov **17**(2): 152-157.
BACKGROUND AND OBJECTIVE: The COVID-19 pandemic is a recent global issue with no established consensus on treatments. Therefore, the aim of this study was to assess the impact of corticosteroid (CS) pulses on the prognosis of COVID-19 patients admitted to hospitals. METHODS: In this retrospective single-center cross-sectional study, we used hospital records of all consecutive patients aged 18 years or older admitted to the hospital from July 23rd to September 23rd, 2021. All patients included in the study had confirmed SARS-CoV-2 infection using polymerase chain reaction (PCR) testing and required hospitalization. Demographic and clinical information, as well as patient outcomes, were collected. Treatment details, including the type(s), cumulative doses, and duration of administered corticosteroids, were also recorded. CS pulse therapy was defined as the daily administration of 24 mg or more of dexamethasone or its equivalents. RESULTS: A total of 500 patients with COVID-19 were included in this study, comprising 122 patients who received CS pulse therapy and 378 patients who did not. A higher mortality rate was observed in patients receiving CS pulse therapy

(42.6%) compared to the other group (28%) (p =0.04). Additionally, logistic regression analysis showed an increased mortality risk in patients receiving CS pulse therapy in the crude model (OR=1.54, 95% CI: 1.01-2.27, p <0.01). However, after adjusting for confounding factors, such as mechanical ventilation and ICU admission, the results were reversed (OR=0.21, 95% CI: 0.07-0.62, p <0.01). ; Conclusion: In the findings of the current study, treatment with CS pulses was shown to significantly enhance recovery in patients with non-severe COVID-19.

Yu, G., et al. (2023). "Development and validation of web calculators to predict early recurrence and long-term survival in patients with duodenal papilla carcinoma after pancreaticoduodenectomy." BMC Cancer **23**(1): 1129.
BACKGROUND: Duodenal papilla carcinoma (DPC) is prone to relapse even after radical pancreaticoduodenectomy (PD) (including robotic, laparoscopic and open approach). This study aimed to develop web calculators to predict early recurrence (ER) (within two years after surgery) and long-term survival in patients with DPC after PD. METHODS: Patients with DPC after radical PD were included. Univariate and multivariate logistic regression analyses were used to identify independent risk factors. Two web calculators were developed based on independent risk factors in the training cohort and then tested in the validation cohort. RESULTS: Of the 251 patients who met the inclusion criteria, 180 and 71 patients were enrolled in the training and validation cohorts, respectively. Multivariate logistic regression analysis revealed that tumor size [Odds Ratio (OR) 1.386; 95% confidence interval (CI) 1070-1.797; P = 0.014]; number of lymph node metastasis (OR 2.535; 95% CI 1.114-5.769; P = 0.027), perineural invasion (OR 3.078; 95% CI 1.147-8.257; P = 0.026), and tumor differentiation (OR 3.552; 95% CI 1.132-11.152; P = 0.030) were independent risk factors for ER. Nomogram based on the above four factors achieved good C-statistics of 0.759 and 0.729 in predicting ER in the training and the validation cohorts, respectively. Time-dependent ROC analysis (timeROC) and decision curve analysis (DCA) revealed that the nomogram provided superior diagnostic capacity and net benefit compared with single variable. CONCLUSIONS: This study developed and validated two web calculators that can predict ER and long-term survival in patients with DPC with high degree of stability and accuracy.

Yu, Y., et al. (2023). "Machine learning radiomics of magnetic resonance imaging predicts recurrence-free survival after surgery and correlation of LncRNAs in patients with breast cancer: a multicenter cohort study." Breast Cancer Res **25**(1): 132.
BACKGROUND: Several studies have indicated that magnetic resonance imaging radiomics can predict survival in patients with breast cancer, but the potential biological underpinning remains indistinct. Herein, we aim to develop an interpretable deep-learning-based network for classifying recurrence risk and revealing the potential biological mechanisms. METHODS: In this multicenter study, 1113 nonmetastatic invasive breast cancer patients were included, and were divided into the training cohort (n = 698), the validation cohort (n = 171), and the testing cohort (n = 244). The Radiomic DeepSurv Net (RDeepNet) model was constructed using the Cox proportional hazards deep neural network DeepSurv for predicting individual recurrence risk. RNA-sequencing was performed to explore the association between radiomics and tumor microenvironment. Correlation and variance analyses were conducted to examine changes of radiomics among patients with different therapeutic responses and after neoadjuvant chemotherapy. The association and quantitative relation of radiomics and epigenetic molecular characteristics were further analyzed to reveal the mechanisms of radiomics. RESULTS: The RDeepNet model showed a significant association with recurrence-free survival (RFS) (HR 0.03, 95% CI 0.02-0.06, P < 0.001) and achieved AUCs of 0.98, 0.94, and 0.92 for 1-, 2-, and 3-year RFS, respectively. In the validation and testing cohorts, the RDeepNet model could also clarify patients into high- and low-risk groups, and demonstrated AUCs of 0.91 and 0.94 for 3-year RFS, respectively. Radiomic features displayed differential expression between the two risk groups. Furthermore, the generalizability of RDeepNet model was confirmed across different molecular subtypes and patient populations with different therapy regimens (All P < 0.001). The study also identified variations in radiomic features among patients with diverse therapeutic responses and after neoadjuvant chemotherapy. Importantly, a significant correlation between radiomics and long non-coding RNAs (lncRNAs) was discovered. A key lncRNA was found to be noninvasively quantified by a deep learning-based radiomics prediction model with AUCs of 0.79 in the training cohort and 0.77 in the testing cohort. CONCLUSIONS: This study demonstrates that machine learning radiomics of MRI can effectively predict RFS after surgery in patients with breast cancer, and highlights the feasibility of non-invasive quantification of lncRNAs using radiomics, which indicates the potential of radiomics in guiding treatment decisions.

Yu, Y., et al. (2023). "A large-scale study integrating nutritional indicators and clinicopathological parameters to evaluate prognosis, follow-up, and postoperative chemotherapy decisions in rectal cancer patients." Support Care Cancer **31**(12): 686.

OBJECTIVE: The aim of this study was to evaluate the role of nutritional indicators and clinicopathological parameters in predicting the progression and prognosis for pathological stage II-III rectal cancer (RC) patients without neoadjuvant radiotherapy. In addition, we sought to explore the high-risk population who may require postoperative chemotherapy. METHODS: A total of 894 consecutive RC patients were enrolled in this study. Univariate and multivariate Cox analysis were performed to identify the independent risk factors for PFS and OS. The nomogram and calibration curves were conducted according to multivariable analysis result. Kaplan-Meier survival curves and log-rank tests were performed for different groups. Finally, random survival forest (RSF) model was developed to predict the probability of progression. RESULTS: Our results revealed that CEA level, pathological stage, tumor deposit, and PNI were independently associated with PFS in RC patients. Similarly, the results indicated that CEA level, pathological stage, tumor deposit, PNI, and NRI were independently associated with OS. RSF model revealed that group 1 had the highest risk of progression at the 12th month of follow-up, group 2 had the highest risk of progression at the 15th month of follow-up, while group 3 had the highest risk of progression at the 9th month of follow-up. Besides, subgroup analysis suggested that the high-risk group needs postoperative adjuvant chemotherapy, while patients in the low- and moderate-risk groups may not need postoperative adjuvant chemotherapy. Finally, we validated our results with the SEER database. CONCLUSIONS: In conclusion, we demonstrated that preoperative nutritional indicator and clinicopathological parameters could act as auxiliary prognostication tools for RC patients without neoadjuvant radiotherapy. We also established follow-up strategies for different groups of patients. Collectively, incorporating nutritional assessment into risk stratification for RC resection is crucial and should be an integral part of preoperative planning.

Yuan, K., et al. (2023). "Novel diagnostic biomarkers of oxidative stress, immune- infiltration characteristics and experimental validation of SERPINE1 in colon cancer." Discov Oncol **14**(1): 206.

BACKGROUND: Colon cancer (CC) is a prevalent malignant tumor that affects the colon in the gastrointestinal tract. Its aggressive nature, strong invasiveness, and rapid progression make it a significant health concern. In addition, oxidative stress can lead to the production of reactive oxygen species (ROS) that surpass the body's antioxidant defense capacity, causing damage to proteins, lipids, and DNA, potentially promoting tumor development. However, the relationship between CC and oxidative stress requires further investigation. METHODS: We collected gene expression data and clinical data from 473 CC patients from The Cancer Genome Atlas (TCGA) dataset. Additionally, we obtained 433 oxidative stress genes from Genecards (https://www.genecards.org/). Using univariate, multivariate, and LASSO Cox regression analyses, we developed predictive models for oxidative stress-related genes in CC patients. To validate the models, we utilized data from the Gene Expression Omnibus (GEO) database. We assessed the accuracy of the models through various techniques, including the creation of a nomogram, receiver operating characteristic curve (ROC) analysis, and principal component analysis (PCA). The Cytoscape program was utilized to identify hub genes among differentially expressed genes (DEGs) in tumor patients using the TCGA dataset. Subsequently, we conducted survival analysis, clinical relevance analysis, and immune cell relevance analysis for the intersected genes obtained by combining the hub genes with the genes from the predictive models. Moreover, we investigated the mRNA expression and potential functions of these intersected genes using a range of experimental approaches. RESULTS: In both the TCGA and GSE17538 datasets, patients classified as high-risk had significantly shorter overall survival compared to those in the low-risk group (TCGA: $p < 0.001$; GSE17538: $p = 0.010$). As a result, we decided to further investigate the role of SERPINE1. Our survival analysis revealed that patients with high expression of SERPINE1 had a significantly lower probability of survival compared to those with low expression ($p < 0.05$). Additionally, our clinical correlation analysis showed a significant relationship between SERPINE1 expression and T, N, and M stages, as well as tumor grade. Furthermore, our immune infiltration correlation analysis demonstrated notable differences in multiple immune cells between the high- and low-expression groups of SERPINE1. To validate our findings, we conducted experimental tests and observed that knocking down SERPINE1 in colon cancer cells resulted in significant reductions in cell viability and proliferation. Interestingly, we also noticed an increase in oxidative stress parameters, such as ROS and MDA levels, while the levels of reduced GSH decreased upon SERPINE1 knockdown. These findings suggest that the antineoplastic effect of silencing SERPINE1 may be associated with the induction of oxidative stress. CONCLUSION: In conclusion, this study introduces a new approach for the early diagnosis and treatment of CC, and further exploration of SERPINE1 could potentially lead to a significant advancement.

Zhang, L., et al. (2023). "Surgical management of tuberous sclerosis complex with big fat-poor bilateral renal angiomyolipomas: A case report." Int J Surg Case Rep **113**: 109060.

INTRODUCTION: Tuberous sclerosis complex (TSC) is an autosomal dominant disease that affects multiple organs. Medical therapy with the mTOR inhibitor everolimus has become the first option in patients with angiomyolipomas. But mTOR inhibitor treatment shows no effect in some patients, in the case, surgery is a suitable method for treatment. PRESENTATION OF CASE: A 30-year-old Chinese male patient received an ultrasound examination of the kidney, which showed bilateral hyperechogenic structures without stones or ureterohydronephrosis. A computed tomography (CT) scan of the kidneys showed multiple slightly high-density masses (largest size: left 6.5 cm, right 5.2 cm), and the masses lacking of lipids were obviously enhanced in the arterial phase. To clarify the components of the tumors, we performed retroperitoneal laparoscopic tumor enucleation to remove all visible masses in left kidney. The pathological results and genetic tests confirmed the diagnosis of TSC. For reducing the further spontaneously bleeding risk and the cost burden, the right renal tumors were also enucleated. Twelve months after the second operation, renal function remained normal, and no tumors were detected by CT. DISCUSSION: Large angiomyolipomas (>4 cm in diameter) may develop life-threatening hemorrhage or compress normal kidney tissue. Fat-poor renal angiomyolipomas are difficult for making a differential diagnosis from renal cancer or renal sarcomatoid carcinoma. When medication treatment does not work, surgery is a good option to diagnose and treat big bilateral renal angiomyolipomas. CONCLUSION: After 12 months of follow-up, retroperitoneal laparoscopic tumor enucleation may be a safe and effective method for treating big fat-poor renal angiomyolipomas in patients with TSC.

Zhang, X. and Z. H. Mi (2023). "Identification of potential diagnostic and prognostic biomarkers for breast cancer based on gene expression omnibus." World J Clin Cases **11**(27): 6344-6362.
BACKGROUND: Breast cancer is regarded as a highly malignant neoplasm in the female population, posing a significant risk to women's overall well-being. The prevalence of breast cancer has been observed to rise in China, accompanied by an earlier age of onset when compared to Western countries. Breast cancer continues to be a prominent contributor to cancer-related mortality and morbidity among women, primarily due to its limited responsiveness to conventional treatment modalities. The diagnostic process is challenging due to the presence of non-specific clinical manifestations and the suboptimal precision of conventional diagnostic tests. There is a prevailing uncertainty regarding the most effective screening method and target populations, as well as the specificities and execution of screening programs. AIM: To identify diagnostic and prognostic biomarkers for breast cancer. METHODS: Overlapping differentially expressed genes were screened based on Gene Expression Omnibus (GSE36765, GSE10810, and GSE20086) and The Cancer Genome Atlas datasets. A protein-protein interaction network was applied to excavate the hub genes among these differentially expressed genes. Gene Ontology and Kyoto Encyclopedia of Genes and Genomes pathway analyses, as well as gene set enrichment analyses, were conducted to examine the functions of these genes and their potential mechanisms in the development of breast cancer. For clarification of the diagnostic and prognostic roles of these genes, Kaplan-Meier and Cox proportional hazards analyses were conducted. RESULTS: This study demonstrated that calreticulin, heat shock protein family B member 1, insulin-like growth Factor 1, interleukin-1 receptor 1, Kruppel-like factor 4, suppressor of cytokine signaling 3, and triosephosphate isomerase 1 are potential diagnostic biomarkers of breast cancer as well as potential treatment targets with clinical implications. CONCLUSION: The screening of biomarkers is of guiding significance for the diagnosis and prognosis of the diseases.

Zhang, Z., et al. (2023). "Development and validation of a nomogram to predict cancer-specific survival in nonsurgically treated elderly patients with prostate cancer." Sci Rep **13**(1): 17719.
Prostate Cancer (PC) is the most common male nonskin tumour in the world, and most diagnosed patients are over 65 years old. The main treatment for PC includes surgical treatment and nonsurgical treatment. Currently, for nonsurgically treated elderly patients, few studies have evaluated their prognostic factors. Our aim was to construct a nomogram that could predict cancer-specific survival (CSS) in nonsurgically treated elderly PC patients to assess their prognosis-related independent risk factors. Patient information was obtained from the Surveillance, Epidemiology and End Results (SEER) database, and our target population was nonsurgically treated PC patients who were over 65 years old. Independent risk factors were determined using both univariate and multivariate Cox regression models. A nomogram was built using a multivariate Cox regression model. The accuracy and discrimination of the prediction model were tested using the consistency index (C-index), the area under the subject operating characteristic curve (AUC), and the calibration curve. Decision curve analysis (DCA) was used to examine the potential clinical value of this model. A total of 87,831 elderly PC patients with nonsurgical treatment in 2010-2018 were included in the study and were randomly assigned to the training set (N = 61,595) and the validation set (N = 26,236). Univariate and multivariate Cox regression model analyses showed that age, race, marital status, TNM stage, chemotherapy, radiotherapy

modality, PSA and GS were independent risk factors for predicting CSS in nonsurgically treated elderly PC patients. The C-index of the training set and the validation set was 0.894 (95% CI 0.888-0.900) and 0.897 (95% CI 0.887-0.907), respectively, indicating the good discrimination ability of the nomogram. The AUC and the calibration curves also show good accuracy and discriminability. We developed a new nomogram to predict CSS in elderly PC patients with nonsurgical treatment. The model is internally validated with good accuracy and reliability, as well as potential clinical value, and can be used for clinical aid in decision-making.

Zhao, J., et al. (2023). "MRI-based radiomics approach for the prediction of recurrence-free survival in triple-negative breast cancer after breast-conserving surgery or mastectomy." Medicine (Baltimore) **102**(42): e35646.
To explore the value of a radiomics signature and develop a nomogram combined with a radiomics signature and clinical factors for predicting recurrence-free survival in triple-negative breast cancer patients. We enrolled 151 patients from the cancer imaging archive who underwent preoperative contrast-enhanced magnetic resonance imaging. They were assigned to training, validation and external validation cohorts. Image features with coefficients not equal to zero in the 10-fold cross-validation were selected to generate a radiomics signature. Based on the optimal cutoff value of the radiomics signature determined by maximally selected log-rank statistics, patients were stratified into high- and low-risk groups in the training and validation cohorts. Kaplan-Meier survival analysis was performed for both groups. Kaplan-Meier survival distributions in these groups were compared using log-rank tests. Univariate and multivariate Cox regression analyses were used to construct clinical and combined models. Concordance index was used to assess the predictive performance of the 3 models. Calibration of the combined model was assessed using calibration curves. Four image features were selected to generate the radiomics signature. The Kaplan-Meier survival distributions of patients in the 2 groups were significantly different in the training ($P < .001$) and validation cohorts ($P = .001$). The C-indices of the radiomics model, clinical model, and combined model in the training and validation cohorts were 0.772, 0.700, 0.878, and 0.744, 0.574, 0.777, respectively. The C-indices of the radiomics model, clinical model, and combined model in the external validation cohort were 0.778, 0.733, 0.822, respectively. The calibration curves of the combined model showed good calibration. The radiomics signature can predict recurrence-free survival of patients with triple-negative breast cancer and improve the predictive performance of the clinical model.

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