Cancer and Alcohol Research Literatures

Ma Hongbao [1], Margaret Ma [2], Yang Yan [1]

[1] Brookdale Hospital, Brooklyn, New York 11212, USA; [2] Cambridge, MA 02138, USA
ma8080@gmail.com

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

Ahmed, H. G. "Survey on knowledge and attitudes related to the relation between tobacco, alcohol abuse and cancer in the northern state of Sudan." Asian Pac J Cancer Prev. 2013;14(4):2483-6.
BACKGROUND: The aim of this study was to determine the epidemiology of tobacco smoking, toombak dipping and alcohol consumption as risk factors for cancer in the adult population of the northern state of Sudan. MATERIALS AND METHODS: A cross-sectional survey from March to April 2010, covering 963 adults, was performed. RESULT: Only 207 had responded, and the male female prevalence was 20.8% and 0.73%. Out of 207 respondents, 29.5% had smoked tobacco in their lifetime, 38% were toombak dippers, while 14% were consumers of alcoholic beverages. CONCLUSIONS: The prevalence of toombak dipping was higher than tobacco smoking among the adult population in the northern state of Sudan. Female participation in tobacco and alcohol related studies was found to suffer from major obstacles since these habits are considered as social stigma. Appreciation of the full impact of smoking on population health will definitely make a major contribution to improvement of the poor public health situation in Sudan.

Anantharaman, D., A. Chabrier, et al. "Genetic variants in nicotine addiction and alcohol metabolism genes, oral cancer risk and the propensity to smoke and drink alcohol: a replication study in India." PLoS One. 2014 Feb 5;9(2):e88240. doi: 10.1371/journal.pone.0088240. eCollection 2014.
BACKGROUND: Genetic variants in nicotinic acetylcholine receptor and alcohol metabolism genes have been associated with propensity to smoke tobacco and drink alcohol, respectively, and also implicated in genetic susceptibility to head and neck cancer. In addition to smoking and alcohol, tobacco chewing is an important oral cancer risk factor in India. It is not known if these genetic variants influence propensity or oral cancer susceptibility in the context of this distinct etiology. METHODS: We examined 639 oral and pharyngeal cancer cases and 791 controls from two case-control studies conducted in India. We investigated six variants known to influence nicotine addiction or alcohol metabolism, including rs16969968 (CHRNA5), rs578776 (CHRNA3), rs1229984 (ADH1B), rs698 (ADH1C), rs1573496 (ADH7), and rs4767364 (ALDH2). RESULTS: The CHRN variants were associated with the number of chewing events per day, including in those who chewed tobacco but never smoked (P = 0.003, P = 0.01 for rs16969968 and rs578776 respectively). Presence of the variant allele contributed to approximately 13% difference in chewing frequency compared to non-carriers. While no association was observed between rs16969968 and oral cancer risk (OR = 1.01, 95% CI = 0.83- 1.22), rs578776 was modestly associated with a 16% decreased risk of oral cancer (OR = 0.84, 95% CI =

0.72- 0.98). There was little evidence for association between polymorphisms in genes encoding alcohol metabolism and oral cancer in this population. CONCLUSION: The association between rs16969968 and number of chewing events implies that the effect on smoking propensity conferred by this gene variant extends to the use of smokeless tobacco.

Andrew, R., M. Tiggemann, et al. "Positive body image and young women's health: Implications for sun protection, cancer screening, weight loss and alcohol consumption behaviours." J Health Psychol. 2014 Feb 14.

This study examined the link between positive body image and a range of health behaviours. Participants were 256 women who completed an online questionnaire measuring body appreciation, body dissatisfaction, sun protection, cancer screening, seeking medical attention, weight-loss behaviour and alcohol and tobacco consumption. Results indicated that body appreciation was positively related to sun protection, skin screening and seeking medical attention and negatively related to weight-loss behaviour. Body appreciation explained unique variance, over and above body dissatisfaction, in sun protection, skin screening and weight-loss behaviour. These results have implications for interventions to improve adherence to health behaviours.

Badawy, A. A. and S. Bano "Elevation of Kynurenine Metabolites in Rat Liver and Serum: A Potential Additional Mechanism of the Alcohol Aversive and Anti-cancer Effects of Disulfiram?" Alcohol Alcohol. 2015 Jul 29. pii: agv085.

AIMS: The tryptophan metabolites 3-hydroxykynurenine (3-HK) and 3-hydroxyanthranilic acid (3-HAA) inhibit the liver mitochondrial low Km aldehyde dehydrogenase and possess alcohol-aversive and immunosuppressant properties. As the disulfiram (DS) metabolite carbon disulphide activates enzymes forming 3-HK and 3-HAA, we investigated if repeated disulfiram treatment increases the hepatic and serum levels of these 2 metabolites. METHODS: Livers and sera of male Wistar rats were analysed for tryptophan and kynurenine metabolites after repeated DS treatment for 7 days. RESULTS: DS increased liver and serum [3-HK] and [3-HAA] possibly by increasing the flux of tryptophan down the hepatic kynurenine pathway and activation of kynurenine hydroxylase and kynureninase. CONCLUSIONS: We provisionally suggest that elevation of some kynurenine metabolites may be an additional mechanism of the alcohol-aversive and anticancer effects of disulfiram.

Bagnardi, V., M. Rota, et al. "Alcohol consumption and site-specific cancer risk: a comprehensive dose-response meta-analysis." Br J Cancer. 2015 Feb 3;112(3):580-93. doi: 10.1038/bjc.2014.579. Epub 2014 Nov 25.

BACKGROUND: Alcohol is a risk factor for cancer of the oral cavity, pharynx, oesophagus, colorectum, liver, larynx and female breast, whereas its impact on other cancers remains controversial. METHODS: We investigated the effect of alcohol on 23 cancer types through a meta-analytic approach. We used dose-response meta-regression models and investigated potential sources of heterogeneity. RESULTS: A total of 572 studies, including 486 538 cancer cases, were identified. Relative risks (RRs) for heavy drinkers compared with nondrinkers and occasional drinkers were 5.13 for oral and pharyngeal cancer, 4.95 for oesophageal squamous cell carcinoma, 1.44 for colorectal, 2.65 for laryngeal and 1.61 for breast cancer; for those neoplasms there was a clear dose-risk relationship. Heavy drinkers also had a significantly higher risk of cancer of the stomach (RR 1.21), liver (2.07), gallbladder (2.64), pancreas (1.19) and lung (1.15). There was indication of a positive association between alcohol consumption and risk of melanoma and prostate cancer. Alcohol consumption and risk of Hodgkin's and Non-Hodgkin's lymphomas were inversely associated. CONCLUSIONS: Alcohol increases risk of cancer of oral cavity and pharynx, oesophagus, colorectum, liver, larynx and female breast. There is accumulating evidence that alcohol drinking is associated with some other cancers such as pancreas and prostate cancer and melanoma.

Bediaga, N. G., X. Marichalar-Mendia, et al. "Polymorphisms in alcohol and tobacco metabolism genes in head and neck cancer in the Basque Country." J Oral Pathol Med. 2015 Jan 31. doi: 10.1111/jop.12305.

BACKGROUND: The Basque Country has one of the highest rates of head and neck squamous cell carcinoma (HNSCC) in Europe, although tobacco and alcohol consumption are not high when compared to other European countries where HNSCC incidence is lower. Our aim was to determine the role of genetic variation with regard to the metabolism of alcohol and carcinogens from tobacco smoke in the Basque Country. METHODS: Fourteen polymorphisms in alcohol or tobacco metabolism genes were genotyped in 84 HNSCC patients and 242 healthy individuals from the Basque Country. RESULTS: ADH1B histidine allele (rs1229984), CYP2E1 rs3813867 heterozygous genotype, and GSTT1 deletion conferred protection against HNSCC (OR: 0.318 [0.04-0.75], OR: 0.13 [0.02-0.94], and OR: 0.12 [0.02-0.60], respectively) while GSTP1 (rs1695) Val/Val

genotype was related to an increased risk (OR: 4.12 [1.11-15.31]). Regarding alcohol and tobacco habits, GSTT1 deletion was associated with tobacco usage, while the 3 polymorphisms tested in ALDH2 were associated with alcohol consumption. However, genotypic distributions of these 7 SNPs did not differ from those observed for other Caucasian populations where HNSCC incidence is lower. CONCLUSIONS: The identified genotypic variations in alcohol and tobacco metabolizing genes only by themselves do not seem to be responsible for the higher incidence of HNSCC observed in the Basque Country.

Bergmann, M. M., J. Rehm, et al. "The association of pattern of lifetime alcohol use and cause of death in the European prospective investigation into cancer and nutrition (EPIC) study." Int J Epidemiol. 2013 Dec;42(6):1772-90. doi: 10.1093/ije/dyt154.
     BACKGROUND: There is limited evidence for an association between the pattern of lifetime alcohol use and cause-specific risk of death. METHODS: Multivariable hazard ratios were estimated for different causes of death according to patterns of lifetime alcohol consumption using a competing risks approach: 111 953 men and 268 442 women from eight countries participating in the European Prospective Investigation into Cancer and Nutrition (EPIC) study were included. Self-reported alcohol consumption at ages 20, 30, 40 or 50 years and at enrollment were used for the analysis; 26 411 deaths were observed during an average of 12.6 years of follow-up. RESULTS: The association between lifetime alcohol use and death from cardiovascular diseases was different from the association seen for alcohol-related cancers, digestive, respiratory, external and other causes. Heavy users (>5 drinks/day for men and >2.5 drinks/day for women), regardless of time of cessation, had a 2- to 5-times higher risk of dying due to alcohol-related cancers, compared with subjects with lifetime light use (</=1 and </=0.5 drink/week for men and women, respectively). Compared with lifetime light users, men who used <5 drinks/day throughout their lifetime had a 24% lower cardiovascular disease mortality (95% confidence interval 2-41). The risk of death from coronary heart disease was also found to be 34-46% lower among women who were moderate to occasionally heavy alcohol users compared with light users. However, this relationship was only evident among men and women who had no chronic disease at enrollment. CONCLUSIONS: Limiting alcohol use throughout life is associated with a lower risk of death, largely due to cardiovascular disease but also other causes. However, the potential health benefits of alcohol use are difficult to establish due to the possibility of selection bias and competing risks related to diseases occurring later in life.

Bowden, J. A., P. Delfabbro, et al. "Alcohol consumption and NHMRC guidelines: has the message got out, are people conforming and are they aware that alcohol causes cancer?" Aust N Z J Public Health. 2014 Feb;38(1):66-72. doi: 10.1111/1753-6405.12159.
     OBJECTIVE: To examine self-reported alcohol consumption and relationships between consumption, awareness of the 2009 NHMRC guidelines of no more than two standard drinks per day, drinking in excess of the guideline threshold and perceptions of alcohol as a risk factor for cancer. METHODS: Questions were included in annual, cross-sectional surveys of approximately 2,700 South Australians aged 18 years and over from 2004 to 2012. Consumption data for 2011 and 2012 were merged for the majority of analyses. RESULTS: In 2011 and 2012, 21.6% of adults drank in excess of the guideline threshold (33.0% males; 10.7% females). While 53.5% correctly identified the NHMRC consumption threshold for women, only 20.3% did so for men (39.0% nominated a higher amount). A large minority said they did not know the consumption threshold for women (39.2%) or men (40.4%). In 2012, only 36.6% saw alcohol as an important risk factor for cancer. Important predictors of excess consumption for men were: higher household income; and not perceiving alcohol as an important risk factor for cancer. Predictors for women were similar but the role of household income was even more prominent. CONCLUSIONS: Men were nearly three times as likely to drink in excess of the guidelines as women. The majority of the population did not see an important link between alcohol and cancer. Awareness of the latest NHMRC guidelines consumption threshold is still low, particularly for men. IMPLICATIONS: A strategy to raise awareness of the NHMRC guidelines and the link between alcohol and cancer is warranted.

Boyle, T., L. Fritschi, et al. "Smoking, alcohol, diabetes, obesity, socioeconomic status, and the risk of colorectal cancer in a population-based case-control study." Cancer Causes Control. 2014 Dec;25(12):1659-68. doi: 10.1007/s10552-014-0470-7. Epub 2014 Oct 10.
     PURPOSE: Although previous research has identified factors that may determine willingness to participate in research, relatively few studies have attempted to quantify the impact non-participation may have on exposure-disease associations. The aims of this study were to (a) investigate the associations between smoking, alcohol, diabetes, obesity, and

socioeconomic status and the risk of colorectal cancer in a case-control study (59.7 and 47.2 % response fractions among cases and controls, respectively); and (b) perform sensitivity analyses to examine the possible influence of non-participation. METHODS: Logistic regression was used to estimate the exposure-disease associations. We then investigated the associations between various demographic and health factors and the likelihood that an individual would participate in the case-control study and then performed two sensitivity analyses (sampling weights and multiple imputation) to examine whether non-participation bias may have influenced the exposure-disease associations. RESULTS: The exposures alcohol, smoking, and diabetes were associated with an increased risk of colorectal cancer. We found some differences between cases and controls when examining the factors associated with the participation in the study, and in the sensitivity analyses, the exposure-disease associations were slightly attenuated when compared with those from the original analysis. CONCLUSION: Non-participation may have biased the risk estimates away from the null, but generally not enough to change the conclusions of the study.

Breitenbach, K., M. Epstein-Reeves, et al. "Alcohol use assessment in young adult cancer survivors." Oncol Nurs Forum. 2014 Sep;41(5):517-22. doi: 10.1188/14.ONF.41-05AP.
PURPOSE/OBJECTIVES: To determine whether oncology practitioners assess for alcohol consumption rates and usage patterns among young adult cancer survivors, and to determine drinking patterns and frequency of alcoholic beverage consumption among young adult cancer survivors. DESIGN: Retrospective chart review. SETTING: Two outpatient cancer clinics. SAMPLE: 77 young adult survivors of childhood cancer aged 18-30 years. METHODS: Charts were selected from June to December 2009 and data were extracted using a structured questionnaire. MAIN RESEARCH VARIABLES: Oncology practitioner assessment of alcohol use and alcohol consumption of young adult cancer survivors. FINDINGS: Alcohol screening was conducted for 48 participants. No significant differences were noted in most variables between those not screened for alcohol use and those screened for alcohol use. Of the 48 screened for alcohol use, 30 reported "no use." For the 18 who reported alcohol use, the terms used to describe the frequency varied and were vague. CONCLUSIONS: The key finding of the study was that screening and documentation of alcohol consumption was poorly and inconsistently performed in the authors' sample of young adult cancer survivors. IMPLICATIONS FOR NURSING: Similar to healthy young adults aged 18-30 years,

young adult cancer survivors are at a developmental age where it is likely they will engage in unhealthy drinking; therefore, they should be screened for alcohol use and binge drinking. Practitioners can incorporate simple, short questions into health assessment visits that allow them to screen for unhealthy alcohol use.

Buykx, P., C. Gilligan, et al. "Public support for alcohol policies associated with knowledge of cancer risk." Int J Drug Policy. 2015 Apr;26(4):371-9. doi: 10.1016/j.drugpo.2014.08.006. Epub 2014 Aug 21.
BACKGROUND: Several options are advocated by policy experts to mitigate alcohol-related harms, although the most effective strategies often have the least public support. While knowledge of tobacco-related health risks predicts support for relevant public health measures, it is not known whether knowledge of alcohol health risks is similarly associated with the acceptability of policies intended to reduce alcohol consumption and related harms. This study aims to gauge public support for a range of alcohol policies and to determine whether or not support is associated with knowledge of a long-term health risk of alcohol consumption, specifically cancer. METHODS: 2482 adults in New South Wales (NSW), Australia, participated in an online survey. Logistic regression analysis was used to examine the association between demographic data, alcohol consumption, smoking status, knowledge of alcohol as a risk factor for cancer and support for alcohol-related policies. RESULTS: Most participants were supportive of health warnings, restricting access to internet alcohol advertising to young people, and requiring information on national drinking guidelines on alcohol containers. Almost half of participants supported a ban on sport sponsorship, while less than 41% supported price increases, volumetric taxation, or reducing the number of retail outlets. Only 47% of participants identified drinking too much alcohol as a risk factor for cancer. Knowledge of alcohol as a risk factor for cancer was a significant predictor of support for all policies, while level of alcohol consumption had a significant inverse relationship with policy support. CONCLUSION: The finding that support for alcohol management policies is associated with awareness that drinking too much alcohol may contribute to cancer could assist in the planning of future public health interventions. Improving awareness of the long term health risks of alcohol consumption may be one avenue to increasing public support for effective alcohol harm-reduction policies.

Camargo, M. C., C. Koriyama, et al. "Case-case comparison of smoking and alcohol risk associations with Epstein-Barr virus-positive gastric cancer." Int J

Helicobacter pylori is the primary cause of gastric cancer. However, monoclonal Epstein-Barr virus (EBV) nucleic acid is also present in up to 10% of these tumors worldwide. EBV prevalence is increased with male sex, nonantral localization and surgically disrupted anatomy. To further examine associations between EBV and gastric cancer, we organized an international consortium of 11 studies with tumor EBV status assessed by in situ hybridization. We pooled individual-level data on 2,648 gastric cancer patients, including 184 (7%) with EBV-positive cancers; all studies had information on cigarette use (64% smokers) and nine had data on alcohol (57% drinkers). We compared patients with EBV-positive and EBV-negative tumors to evaluate smoking and alcohol interactions with EBV status. To account for within-population clustering, multilevel logistic regression models were used to estimate interaction odds ratios (OR) adjusted for distributions of sex (72% male), age (mean 59 years), tumor histology (56% Lauren intestinal-type), anatomic subsite (61% noncardia) and year of diagnosis (1983-2012). In unadjusted analyses, the OR of EBV positivity with smoking was 2.2 [95% confidence interval (CI) 1.6-3.2]. The OR was attenuated to 1.5 (95% CI 1.01-2.3) by adjustment for the possible confounders. There was no significant interaction of EBV status with alcohol drinking (crude OR 1.4; adjusted OR 1.0). Our data indicate the smoking association with gastric cancer is stronger for EBV-positive than EBV-negative tumors. Conversely, the null association with alcohol does not vary by EBV status. Distinct epidemiologic characteristics of EBV-positive cancer further implicate the virus as a cofactor in gastric carcinogenesis.

Castro, G. D. and J. A. Castro "Alcohol drinking and mammary cancer: Pathogenesis and potential dietary preventive alternatives." World J Clin Oncol. 2014 Oct 10;5(4):713-29. doi: 10.5306/wjco.v5.i4.713.

Alcohol consumption is associated with an increased risk of breast cancer, increasing linearly even with a moderate consumption and irrespectively of the type of alcoholic beverage. It shows no dependency from other risk factors like menopausal status, oral contraceptives, hormone replacement therapy, or genetic history of breast cancer. The precise mechanism for the effect of drinking alcohol in mammary cancer promotion is still far from being established. Studies by our laboratory suggest that acetaldehyde produced in situ and accumulated in mammary tissue because of poor detoxicating mechanisms might play a role in mutational and promotional events. Additional studies indicated the production of reactive oxygen species accompanied of decreases in vitamin E and GSH contents and of glutathione transferase activity. The resulting oxidative stress might also play a relevant role in several stages of the carcinogenic process. There are reported in literature studies showing that plasmatic levels of estrogens significantly increased after alcohol drinking and that the breast cancer risk is higher in receptor ER-positive individuals. Estrogens are known that they may produce breast cancer by actions on ER and also as chemical carcinogens, as a consequence of their oxidation leading to reactive metabolites. In this review we introduce our working hypothesis integrating the acetaldehyde and the oxidative stress effects with those involving increased estrogen levels. We also analyze potential preventive actions that might be accessible. There remains the fact that alcohol drinking is just one of the avoidable causes of breast cancer and that, at present, the suggested acceptable dose for prevention of this risk is of one drink per day.

Chandran, U., G. Zirpoli, et al. "Does alcohol increase breast cancer risk in African-American women? Findings from a case-control study." Br J Cancer. 2013 Oct 1;109(7):1945-53. doi: 10.1038/bjc.2013.513. Epub 2013 Sep 5.

BACKGROUND: Alcohol is an important risk factor for breast cancer in Caucasian women, but the evidence in African-American (AA) women is limited and results are inconclusive. METHODS: Associations between recent and lifetime drinking and breast cancer risk were evaluated in a large sample of AA women from a case-control study in New York and New Jersey. Multivariable logistic regression models provided odds ratios (ORs) and 95% confidence intervals (CIs). RESULTS: There was no association between recent drinking and breast cancer risk, even when stratified by menopausal status or by hormone receptor status. A borderline decreased risk with increased lifetime consumption was found (OR=0.77; 95% CI: 0.58-1.03), which was stronger among women who drank when under 20 years of age (OR=0.65; 95% CI: 0.47-0.89), regardless of menopausal or hormone receptor status. CONCLUSION: Breast cancer risk associated with recent alcohol consumption was not apparent in AA women, while early age drinking seemed to decrease risk. This is the first investigation on recent and lifetime drinking in subgroups and drinking during different age periods in AA women. If findings are replicated, racial differences in biological pathways involving alcohol and its metabolites should be explored.

Cook, M. B., P. Guenel, et al. "Tobacco and alcohol in relation to male breast cancer: an analysis of the male breast cancer pooling project consortium." Cancer Epidemiol Biomarkers Prev. 2015 Mar;24(3):520-31. doi: 10.1158/1055-9965.EPI-14-1009. Epub 2014 Dec 16.

BACKGROUND: The etiology of male breast cancer is poorly understood, partly due to its relative rarity. Although tobacco and alcohol exposures are known carcinogens, their association with male breast cancer risk remains ill-defined. METHODS: The Male Breast Cancer Pooling Project consortium provided 2,378 cases and 51,959 controls for analysis from 10 case-control and 10 cohort studies. Individual participant data were harmonized and pooled. Unconditional logistic regression was used to estimate study design-specific (case-control/cohort) ORs and 95% confidence intervals (CI), which were then combined using fixed-effects meta-analysis. RESULTS: Cigarette smoking status, smoking pack-years, duration, intensity, and age at initiation were not associated with male breast cancer risk. Relations with cigar and pipe smoking, tobacco chewing, and snuff use were also null. Recent alcohol consumption and average grams of alcohol consumed per day were also not associated with risk; only one subanalysis of very high recent alcohol consumption (>60 g/day) was tentatively associated with male breast cancer (OR$_{unexposed\ referent}$ = 1.29; 95% CI, 0.97-1.71; OR$_{>0-<7\ g/day\ referent}$ = 1.36; 95% CI, 1.04-1.77). Specific alcoholic beverage types were not associated with male breast cancer. Relations were not altered when stratified by age or body mass index. CONCLUSIONS: In this analysis of the Male Breast Cancer Pooling Project, we found little evidence that tobacco and alcohol exposures were associated with risk of male breast cancer. IMPACT: Tobacco and alcohol do not appear to be carcinogenic for male breast cancer. Future studies should aim to assess these exposures in relation to subtypes of male breast cancer.

Cotter, T., D. Perez, et al. "Knowledge and beliefs about alcohol consumption, longer-term health risks, and the link with cancer in a sample of Australian adults." N S W Public Health Bull. 2013 Nov;24(2):81-6. doi: 10.1071/NB12089.

AIM: This study explores knowledge and beliefs about longer-term health risks related to alcohol consumption among Australian adults. METHODS: Data were drawn from the 2009 Cancer Institute NSW Lifestyle and Cancer Survey, a telephone survey of adults in NSW. Participants (n=1255) were asked about their alcohol consumption, knowledge of the Australian guidelines (revised in 2009), and personal perceptions and beliefs about longer-term health risks from alcohol consumption. RESULTS: Seventy-eight percent of the sample drank alcohol either occasionally or weekly, with 37% of drinkers drinking above the current Australian guidelines (two standard drinks on any day). Two-thirds (67%) correctly nominated the maximum number of standard drinks per day that met the current Australian guidelines, and a similar proportion (64%) agreed that regular moderate alcohol consumption can have serious health consequences in the longer term. Knowledge of the guidelines and longer-term health consequences was lower for drinkers, especially those drinking above the guidelines. Less than half (48%) of the participants were aware that drinking alcohol could cause cancer and 51% were aware that limiting alcohol intake helps prevent cancer. CONCLUSION: The current Australian guidelines, the longer-term health risks and the link with cancer are not well understood, especially by those who drink frequently and above the guidelines.

Crous-Bou, M., G. Rennert, et al. "Polymorphisms in alcohol metabolism genes ADH1B and ALDH2, alcohol consumption and colorectal cancer." PLoS One. 2013 Nov 25;8(11):e80158. doi: 10.1371/journal.pone.0080158. eCollection 2013.

BACKGROUND: Colorectal cancer (CRC) is a leading cause of cancer death worldwide. Epidemiological risk factors for CRC included alcohol intake, which is mainly metabolized to acetaldehyde by alcohol dehydrogenase and further oxidized to acetate by aldehyde dehydrogenase; consequently, the role of genes in the alcohol metabolism pathways is of particular interest. The aim of this study is to analyze the association between SNPs in ADH1B and ALDH2 genes and CRC risk, and also the main effect of alcohol consumption on CRC risk in the study population. METHODOLOGY/PRINCIPAL FINDINGS: SNPs from ADH1B and ALDH2 genes, included in alcohol metabolism pathway, were genotyped in 1694 CRC cases and 1851 matched controls from the Molecular Epidemiology of Colorectal Cancer study. Information on clinicopathological characteristics, lifestyle and dietary habits were also obtained. Logistic regression and association analysis were conducted. A positive association between alcohol consumption and CRC risk was observed in male participants from the Molecular Epidemiology of Colorectal Cancer study (MECC) study (OR = 1.47; 95%CI = 1.18-1.81). Moreover, the SNPs rs1229984 in ADH1B gene was found to be associated with CRC risk: under the recessive model, the OR was 1.75 for A/A genotype (95%CI = 1.21-2.52; p-value = 0.0025). A path analysis based on structural equation modeling showed a direct effect of ADH1B gene

polymorphisms on colorectal carcinogenesis and also an indirect effect mediated through alcohol consumption. CONCLUSIONS/SIGNIFICANCE: Genetic polymorphisms in the alcohol metabolism pathways have a potential role in colorectal carcinogenesis, probably due to the differences in the ethanol metabolism and acetaldehyde oxidation of these enzyme variants.

Cybulski, C., J. Lubinski, et al. "Prospective evaluation of alcohol consumption and the risk of breast cancer in BRCA1 and BRCA2 mutation carriers." Breast Cancer Res Treat. 2015 Jun;151(2):435-41. doi: 10.1007/s10549-015-3393-4. Epub 2015 May 3.

Given the adverse effect of alcohol in the development of breast cancer among women in the general population, we evaluated whether a similar association exists among women with a BRCA1 or BRCA2 mutation. Information regarding baseline daily alcohol consumption was abstracted from a research questionnaire for 3067 BRCA mutation carriers enrolled in a prospective cohort study. Women were followed biennially until the date of the last follow-up questionnaire, date of breast cancer diagnosis, date of prophylactic bilateral mastectomy, or date of death. Cox proportional hazards models were used to estimate relative risks (RRs) and 95 % confidence intervals (CIs) for invasive breast cancer associated with alcohol consumed at or prior to completion of the baseline questionnaire. After a mean of 5.4 years of follow-up, we observed 259 incident cases of primary invasive breast cancer. Compared with non-users, the adjusted RRs were 1.06 (95 % CI 0.78-1.44) for ever use and 1.08 (0.79-1.47) for current alcohol use. For women in the highest versus lowest quintile of cumulative alcohol consumption, the RR was 0.94 (95 % CI 0.63-1.40; P trend = 0.65). Our findings suggest that alcohol consumption is not a risk factor for breast cancer among women with a BRCA1 or BRCA2 mutation.

Davis, S. R., X. Tao, et al. "Evaluation of a bladder cancer cluster in a population of criminal investigators with the Bureau of Alcohol, Tobacco, Firearms and Explosives--part 2: the association of cancer risk and fire scene investigation." J Environ Public Health. 2013;2013:986023. doi: 10.1155/2013/986023. Epub 2013 Apr 13.

This study evaluated the association of bladder cancer risk and fire scene investigation within a cohort of white male criminal investigators with the United States Bureau of Alcohol, Tobacco, Firearms and Explosives that was found to be at increased risk for bladder cancer. Medical surveillance data were used in a nested case-control study to determine odds ratios (ORs) estimating the relative risk of the cancer associated with post-fire investigation. The study comprised seven bladder cancer cases and 1525 controls. Six of the cases reported holding assignments associated with post-fire investigation. The OR for bladder cancer was 19.01 (95% confidence interval = 1.94-186.39) for those holding any one or more of these assignments for one to four years versus zero years and 12.56 (1.14-138.58) for those holding any one or more of these assignments for five or more years versus zero years. The risk for bladder cancer is significantly elevated for those holding post-fire investigation assignments compared to those not holding these assignments.

de Menezes, R. F., A. Bergmann, et al. "Alcohol consumption and risk of cancer: a systematic literature review." Asian Pac J Cancer Prev. 2013;14(9):4965-72.

This study aimed to discuss the consumption of alcohol as a risk factor for major cancers. We performed a search in the PubMed database, using the following inclusion criteria: meta-analysis published in English in the last 10 years that addressed the relationship between alcohol and the risk of developing cancer. The results indicate that moderate to heavy consumption of alcohol increases the risk of developing cancer of the oral cavity and pharynx, esophagus, stomach, larynx, colorectum, central nervous system, pancreas, breast and prostate. This review did not find any association between alcohol consumption and an increased risk of cancers of the lung, bladder, endometrium and ovary. It was also observed that alcohol consumption may be inversely related to thyroid cancer. Our systematic review has confirmed consumption of alcohol as a risk factor for the development of several types of cancer.

Dixon, H. G., I. S. Pratt, et al. "Using a mass media campaign to raise women's awareness of the link between alcohol and cancer: cross-sectional pre-intervention and post-intervention evaluation surveys." BMJ Open. 2015 Mar 11;5(3):e006511. doi: 10.1136/bmjopen-2014-006511.

OBJECTIVES: To evaluate the effectiveness of a population-based, statewide public health intervention designed to improve women's awareness and knowledge of the link between alcohol and cancer. DESIGN: Cross-sectional tracking surveys conducted pre-intervention and post-intervention (waves I and III of campaign). SETTING: Western Australia. PARTICIPANTS: Cross-sectional samples of Western Australian women aged 25-54 years before the campaign (n=136) and immediately after wave I (n=206) and wave III (n=155) of the campaign. INTERVENTION: The 'Alcohol and Cancer' mass

media campaign ran from May 2010 to May 2011 and consisted of three waves of paid television advertising with supporting print advertisements. MAIN OUTCOME MEASURES: Campaign awareness; knowledge of drinking guidelines and the link between alcohol and cancer; intentions towards drinking. RESULTS: Prompted recognition of the campaign increased from 67% following wave I to 81% following wave III (adjusted OR (adj OR)=2.31, 95% CI 1.33 to 4.00, p=0.003). Improvements in women's knowledge that drinking alcohol on a regular basis increases cancer risk were found following wave I (adj OR=2.60, 95% CI 1.57 to 4.30, p<0.001) and wave III (adj OR=4.88, 95% CI 2.55 to 9.36, p<0.001) compared with baseline. Knowledge of the recommended number of standard drinks for low risk in the long term increased between baseline and wave I (adj OR=1.68, 95% CI 1.02 to 2.76, p=0.041), but not baseline and wave III (adj OR=1.42, 95% CI 0.84 to 2.39, p=0.191). Among women who drink alcohol, the proportion expressing intentions to reduce alcohol consumption increased significantly between baseline and wave III (adj OR=2.38, 95% CI 1.11 to 5.12, p=0.026). However, no significant reductions in recent drinking behaviour were found following the campaign. CONCLUSIONS: Results indicate a population-based mass media campaign can reach the target audience and raise awareness of links between alcohol and cancer, and knowledge of drinking guidelines. However, a single campaign may be insufficient to measurably curb drinking behaviour in a culture where pro-alcohol social norms and product marketing are pervasive.

Druesne-Pecollo, N., Y. Keita, et al. "Alcohol drinking and second primary cancer risk in patients with upper aerodigestive tract cancers: a systematic review and meta-analysis of observational studies." Cancer Epidemiol Biomarkers Prev. 2014 Feb;23(2):324-31. doi: 10.1158/1055-9965.EPI-13-0779. Epub 2013 Dec 4.
BACKGROUND: We conducted a systematic review and meta-analysis of existing data from observational studies to assess the strength of the association of alcohol drinking with second primary cancer risk in patients with upper aerodigestive tract (UADT; oral cavity, pharynx, larynx, and esophagus) cancer. METHODS: PubMed and Embase were searched up to July 2012 and the reference lists of studies included in the analysis were examined. Random-effects models were used to estimate summary relative risks (RR) and 95% confidence interval (CI). RESULTS: Nineteen studies, 8 cohort and 11 case-control studies, were included. In highest versus lowest meta-analyses, alcohol drinking was associated with significantly increased risk of UADT

second primary cancers (RR, 2.97; 95% CI, 1.96-4.50). Significantly increased risks were also observed for UADT and lung combined (RR, 1.90; 95% CI, 1.16-3.11) and all sites (RR, 1.60; 95% CI, 1.22-2.10) second primary cancers. For an increase in the alcohol intake of 10 grams per day, dose-response meta-analysis resulted in a significantly increased RR of 1.09 (95% CI, 1.04-1.14) for UADT second primary cancers. CONCLUSIONS: Alcohol drinking in patients with UADT cancer is associated with an increased risk of second primary cancers. Studies conducted in alcohol drinking patients with UADT cancer and evaluating the effect of alcohol cessation on second primary cancer and other outcomes are needed. IMPACT: Our results emphasize the importance of prevention policies aiming to reduce alcohol drinking. Health-care professionals should encourage alcohol drinking patients with UADT cancer to reduce their consumption and reinforce the surveillance of this at-risk subpopulation.

Fagherazzi, G., A. Vilier, et al. "Alcohol consumption and breast cancer risk subtypes in the E3N-EPIC cohort." Eur J Cancer Prev. 2015 May;24(3):209-14. doi: 10.1097/CEJ.0000000000000031.
The aim of this study was to obtain an overview of the associations between alcohol consumption and breast cancer risk at adulthood, by type of alcohol and subtype of breast cancer. Between 1993 and 2008, 66,481 women from the French E3N-EPIC cohort were followed up and asked to report their alcohol consumption, by type of alcohol, through a 208-item diet-history questionnaire. A total of 2812 breast cancer cases were validated during the follow-up session. No association was found between high alcohol consumption, whatever its type, and increase in breast cancer risk in the premenopausal period. During the postmenopausal period, a linear association between total alcohol consumption and breast cancer risk was found (P<0.0001), mainly driven by the associations with wine and beer [hazard ratio=1.33 (1.11-1.58) and 1.85 (1.19-2.89)] for more than two glasses per day of wine and beer, respectively, compared with nondrinkers] and with ER+/PR+ breast cancer subtypes. In the postmenopausal period, we observed interactions between total alcohol and folate intake levels (P=0.1192) and BMI (P=0.0367), with higher increased risks observed for high alcohol intake among women with low folate intake or who were overweight or obese. Our results make precise the current body of knowledge on the relationship between alcohol and breast cancer subtypes. Interactions between alcohol and other factors should further be taken into account in public health nutrition programs.

Falk, R. T., P. Maas, et al. "Alcohol and risk of breast cancer in postmenopausal women: an analysis of etiological heterogeneity by multiple tumor characteristics." Am J Epidemiol. 2014 Oct 1;180(7):705-17. doi: 10.1093/aje/kwu189. Epub 2014 Aug 22.

Alcohol consumption is an established risk factor for breast cancer. Whether associations vary by specific tumor characteristics independent of other characteristics is unclear. We evaluated the association between alcohol consumption and breast cancer risk in the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial cohort (54,562 women aged 55-74 years recruited at 10 US screening centers between 1993 and 2001; median follow-up, 8.9 years; 1,905 invasive breast cancer cases). Hazard ratios and 95% confidence intervals for subtypes defined by histological type and estrogen receptor (ER)/progesterone receptor (PR) status were calculated with standard Cox models. A novel 2-stage Cox model assessed heterogeneity in risk for individual tumor characteristics while adjusting for others. Significant trends across categories of alcohol consumption were observed, with hazard ratios for those consuming 7 or more drinks per week versus never drinkers as follows: for estrogen receptor-positive (ER+) cancer, 1.48 (95% confidence interval (CI): 1.19, 1.83); for progesterone receptor-positive (PR+) cancer, 1.64 (95% CI: 1.31, 2.06); for ER+/PR+ cancer, 1.63 (95% CI: 1.30, 2.05); and for mixed ductal/lobular cancer, 2.51 (95% CI: 1.20, 5.24). For ER+ and PR+ cancers, trends were significant for ductal and mixed ductal/lobular types. PR status explained the positive association with ER status (for ER status, Pheterogeneity=0.70 after adjustment for PR status). Alcohol consumption was not associated with all breast cancer subtypes. Future work should emphasize large collaborative studies, precise definition of subtypes, and adjustment for correlated tumor characteristics.

Ferreira Antunes, J. L., T. N. Toporcov, et al. "Joint and independent effects of alcohol drinking and tobacco smoking on oral cancer: a large case-control study." PLoS One. 2013 Jul 10;8(7):e68132. doi: 10.1371/journal.pone.0068132. Print 2013.

Alcohol drinking and tobacco smoking are assumed to have significant independent and joint effects on oral cancer (OC) development. This assumption is based on consistent reports from observational studies, which, however, overestimated the independent effects of smoking and drinking, because they did not account for the interaction effect in multivariable analyses. This case-control study sought to investigate the independent and the joint effects of smoking and drinking on OC in a homogeneous sample of adults. Case patients (N = 1,144) were affected by invasive oral/oropharyngeal squamous cell carcinoma confirmed histologically, diagnosed between 1998 and 2008 in four hospitals of Sao Paulo (Brazil). Control patients (N = 1,661) were not affected by drinking-, smoking-associated diseases, cancers, upper aero-digestive tract diseases. Cumulative tobacco and alcohol consumptions were assessed anamnestically. Patients were categorized into never/ever users and never/level-1/level-2 users, according to the median consumption level in controls. The effects of smoking and drinking on OC adjusted for age, gender, schooling level were assessed using logistic regression analysis; Model-1 did not account for the smoking-drinking interaction; Model-2 accounted for this interaction and included the resultant interaction terms. The models were compared using the likelihood ratio test. According to Model-1, the adjusted odds ratios (ORs) for smoking, drinking, smoking-drinking were 3.50 (95% confidence interval -95CI, 2.76-4.44), 3.60 (95CI, 2.86-4.53), 12.60 (95CI, 7.89-20.13), respectively. According to Model-2 these figures were 1.41 (95CI, 1.02-1.96), 0.78 (95CI, 0.48-1.27), 8.16 (95CI, 2.09-31.78). Analogous results were obtained using three levels of exposure to smoking and drinking. Model-2 showed statistically significant better goodness-of-fit statistics than Model-1. Drinking was not independently associated with OC, while the independent effect of smoking was lower than expected, suggesting that observational studies should be revised adequately accounting for the smoking-drinking interaction. OC control policies should focus on addictive behaviours rather than on single lifestyle risk factors.

Fowke, J. H., L. Howard, et al. "Alcohol intake increases high-grade prostate cancer risk among men taking dutasteride in the REDUCE trial." Eur Urol. 2014 Dec;66(6):1133-8. doi: 10.1016/j.eururo.2014.01.037. Epub 2014 Feb 9.

BACKGROUND: Although most studies found no association between alcohol intake and prostate cancer (PCa) risk, an analysis of the Prostate Cancer Prevention Trial found that high alcohol intake significantly increased PCa risk among men randomized to the 5alpha-reductase inhibitor (5-ARI) finasteride. OBJECTIVE: Determine whether alcohol affects PCa risk among men taking the 5-ARI dutasteride. DESIGN, SETTINGS, AND PARTICIPANTS: Reduction by Dutasteride of Prostate Cancer Events was a 4-yr, multicenter, randomized, double-blind, placebo-controlled trial to compare PCa after dutasteride administration

(0.5mg/d) with placebo. Participants had a baseline prostate-specific antigen between 2.5 and 10.0 ng/ml and a recent negative prostate biopsy. Alcohol intake was determined by baseline questionnaire, and participants underwent a prostate biopsy to determine PCa status at 2 yr and 4 yr of follow-up. OUTCOME MEASUREMENTS AND STATISTICAL ANALYSIS: Multivariable logistic regression was used to calculate odds ratios (ORs) and 95% confidence intervals (CIs) for the associations between alcohol intake and low-grade (Gleason <7) and high-grade (Gleason >7) PCa. RESULTS AND LIMITATIONS: Of 6374 participants in our analysis, approximately 25% reported no alcohol consumption, 49% were moderate drinkers (one to seven drinks per week), and 26% were heavy drinkers (more than seven drinks per week). Alcohol intake was not associated with low- or high-grade PCa in the placebo arm and was not associated with low-grade PCa among men taking dutasteride. In contrast, men randomized to dutasteride and reporting more than seven drinks per week were 86% more likely to be diagnosed with high-grade PCa (p=0.01). Among alcohol abstainers, dutasteride was associated with significantly reduced risk of high-grade PCa (OR: 0.59; 95% CI, 0.38-0.90), but dutasteride was no longer associated with reduced high-grade PCa among men reporting high alcohol intake (OR: 0.99; 95% CI, 0.67-1.45). CONCLUSIONS: Alcohol consumption negated a protective association between dutasteride and high-grade PCa. PATIENT SUMMARY: We confirmed a prior study that alcohol affects PCa prevention in patients taking 5-ARIs. Patients taking 5-ARIs may wish to eliminate alcohol intake if they are concerned about PCa.

Glasdam, S. and C. Oye "Alcohol abuse in cancer patients: a shadow side in the oncological field and research." Med Health Care Philos. 2014 Aug;17(3):437-46. doi: 10.1007/s11019-013-9541-x.
        This article aims to foreground alcohol abuse by cancer patients and explore how alcohol abuse functions as a biographic master motive and at the same time is a shadow side in the oncological field and research. The research is based on a single case study which draws on empirical material from interviews, field notes and staff policy, with analysis using Bourdieu's concepts of trajectory of life and habitus. The findings show that the cancer patient's alcohol abuse is an important part of the trajectory of his private life and spare time. In social life with family and friends alcohol is given and normal and acts as a socialisator. Alcohol abuse provides both stability and instability in the cancer patient's life. When cancer results in work breaks and retirement, and spare time often is used as drinking time, then all

daily life becomes drinking time for the cancer patient. Alcohol is often a hidden abuse at the working place and in the oncological field. In meetings with healthcare professionals, the patient chooses not to speak about his alcohol abuse to avoid further medicalisation. The challenge for the healthcare professionals is to see and accept alcohol abusers with cancer and their social lives without always trying to change their 'unhealthy' lifestyles.

Hackshaw-McGeagh, L. E., C. M. Penfold, et al. "Physical activity, alcohol consumption, BMI and smoking status before and after prostate cancer diagnosis in the ProtecT trial: opportunities for lifestyle modification." Int J Cancer. 2015 Sep 15;137(6):1509-15. doi: 10.1002/ijc.29514. Epub 2015 Apr 1.
        Associations between certain lifestyle characteristics and prostate cancer risk have been reported, and continuation post-diagnosis can adversely affect prognosis. We explored whether men make spontaneous changes to their physical activity and alcohol intake, body mass index (BMI) and smoking status, following a diagnosis of localised prostate cancer. A detailed diet, health and lifestyle questionnaire was completed by 511 participants within the Prostate Testing for Cancer and Treatment (ProtecT) randomised controlled trial, both before and 9 months after a diagnosis of prostate cancer. Of 177 men who were insufficiently active before their diagnosis (median 0 activity units/week; IQR 0-9), 40.7% had increased their activity by a median of 22 U week(-1) (IQR 15-35) 9 months later, and there was weak evidence that men were more active after diagnosis than before (p = 0.07). Men categorised as "working" occupational social class and who were insufficiently active before diagnosis were 2.03 (95%, CI = 1.03-3.99, p = 0.04) times more likely to have increased their physical activity levels compared to men classified as "managerial or professional." Similarly, men who were insufficiently active pre-diagnosis and with T-stage 2 compared with T-stage 1 prostate cancer were 2.47 (95%, CI = 1.29-4.71, p = 0.006) times more likely to be sufficiently active post-diagnosis. Following diagnosis, there was an overall reduction in alcohol intake (p = 0.03) and the proportion of current smokers (p = 0.09), but no overall change in BMI. We conclude that some men spontaneously change certain lifestyle behaviours on receiving a diagnosis of prostate cancer. For many men, however, additional support through lifestyle interventions is probably required to facilitate and maintain these changes.

Hakenewerth, A. M., R. C. Millikan, et al. "Effects of polymorphisms in alcohol metabolism and oxidative

stress genes on survival from head and neck cancer." Cancer Epidemiol. 2013 Aug;37(4):479-91. doi: 10.1016/j.canep.2013.03.010. Epub 2013 Apr 28.

BACKGROUND: Heavy alcohol consumption increases risk of developing squamous cell carcinoma of the head and neck (SCCHN). Alcohol metabolism to cytotoxic and mutagenic intermediates acetaldehyde and reactive oxygen species is critical for alcohol-drinking-associated carcinogenesis. We hypothesized that polymorphisms in alcohol metabolism-related and antioxidant genes influence SCCHN survival. METHODS: Interview and genotyping data (64 polymorphisms in 12 genes) were obtained from 1227 white and African-American cases from the Carolina Head and Neck Cancer Epidemiology study, a population-based case-control study of SCCHN conducted in North Carolina from 2002 to 2006. Vital status, date and cause of death through 2009 were obtained from the National Death Index. Kaplan-Meier log-rank tests and adjusted hazard ratios were calculated to identify alleles associated with survival. RESULTS: Most tested SNPs were not associated with survival, with the exception of the minor alleles of rs3813865 and rs8192772 in CYP2E1. These were associated with poorer cancer-specific survival (HRrs3813865, 95% CI=2.00, 1.33-3.01; HRrs8192772, 95% CI=1.62, 1.17-2.23). Hazard ratios for 8 additional SNPs in CYP2E1, GPx2, SOD1, and SOD2, though not statistically significant, were suggestive of differences in allele hazards for all-cause and/or cancer death. No consistent associations with survival were found for SNPs in ADH1B, ADH1C, ADH4, ADH7, ALDH2, GPx2, GPx4, and CAT. CONCLUSIONS: We identified some polymorphisms in alcohol and oxidative stress metabolism genes that influence survival in subjects with SCCHN. Previously unreported associations of SNPs in CYP2E1 warrant further investigation.

Haugvik, S. P., P. Hedenstrom, et al. "Diabetes, smoking, alcohol use, and family history of cancer as risk factors for pancreatic neuroendocrine tumors: a systematic review and meta-analysis." Neuroendocrinology. 2015;101(2):133-42. doi: 10.1159/000375164. Epub 2015 Jan 22.

BACKGROUND AND AIMS: Risk factors for pancreatic neuroendocrine tumors (PNETs) are not well understood. The aim of this systematic review was to assess if diabetes mellitus, smoking, alcohol use, and family history of cancer are risk factors for PNETs. METHODS: MEDLINE and abstracts from the European and North American Neuroendocrine Tumor Societies (ENETS and NANETS) were searched for studies published until October 2013. Eligible studies were selected according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement. RESULTS: Five studies evaluating 4 individual populations were included (study accrual period 2000-2011) into the meta-analysis, involving 827 cases (range 160-309 per study) and 2,407 controls (range 233-924 per study). All studies had a case-control design and described regional series. The pooled adjusted odds ratio was 2.74 (95% CI: 1.63-4.62; $p < 0.01$; $I(2) = 60.4\%$) for history of diabetes, 1.21 (95% CI: 0.92-1.58; $p = 0.18$; $I(2) = 45.8\%$) for ever smoking, 1.37 (95% CI: 0.99-1.91; $p = 0.06$; $I(2) = 0.0\%$) for heavy smoking, 1.09 (95% CI: 0.64-1.85; $p = 0.75$; $I(2) = 85.2\%$) for ever alcohol use, 2.72 (95% CI: 1.25-5.91; $p = 0.01$; $I(2) = 57.8\%$) for heavy alcohol use, and 2.16 (95% CI: 1.64-2.85; $p < 0.01$; $I(2) = 0.0\%$) for first-degree family history of cancer. CONCLUSIONS: Diabetes mellitus and first-degree family history of cancer are associated with an increased risk of sporadic PNET. There was also a trend for diagnosis of sporadic PNET associated with heavy smoking. Alcohol use may be a risk factor for PNET, but there was considerable heterogeneity in the meta-analysis. These results suggest the need for a larger, homogeneous, international study for the clarification of risk factors for the occurrence of PNET.

Hidaka, A., S. Sasazuki, et al. "Genetic polymorphisms of ADH1B, ADH1C and ALDH2, alcohol consumption, and the risk of gastric cancer: the Japan Public Health Center-based prospective study." Carcinogenesis. 2015 Feb;36(2):223-31. doi: 10.1093/carcin/bgu244. Epub 2014 Dec 18.

The association between alcohol consumption, genetic polymorphisms of alcohol dehydrogenase (ADH) and aldehyde dehydrogenase (ALDH) and gastric cancer risk is not completely understood. We investigated the association between ADH1B (rs1229984), ADH1C (rs698) and ALDH2 (rs671) polymorphisms, alcohol consumption and the risk of gastric cancer among Japanese subjects in a population-based, nested, case-control study (1990-2004). Among 36 745 subjects who answered the baseline questionnaire and provided blood samples, 457 new gastric cancer cases matched to 457 controls were used in the analysis. The odds ratios (OR) and corresponding 95% confidence intervals (CI) were calculated using logistic regression models. No association was observed between alcohol consumption, ADH1B (rs1229984), ADH1C (rs698) and ALDH2 (rs671) polymorphisms and gastric cancer risk. However, considering gene-environmental interaction, ADH1C G allele carriers who drink >/=150 g/week of ethanol had a 2.5-fold increased risk of gastric cancer (OR = 2.54, 95% CI = 1.05-6.17) relative to AA genotype carriers who drink 0 to <150

g/week (P for interaction = 0.02). ALDH2 A allele carriers who drink >/=150 g/week also had an increased risk (OR = 2.08, 95% CI = 1.05-4.12) relative to GG genotype carriers who drink 0 to < 150 g/week (P for interaction = 0.08). To find the relation between alcohol consumption and gastric cancer risk, it is important to consider both alcohol consumption level and ADH1C and ALDH2 polymorphisms.

Hirko, K. A., W. Y. Chen, et al. "Alcohol consumption and risk of breast cancer by molecular subtype: Prospective analysis of the nurses' health study after 26 years of follow-up." Int J Cancer. 2015 Sep 18. doi: 10.1002/ijc.29861.

Alcohol consumption is a consistent risk factor for breast cancer, although it is unclear whether the association varies by breast cancer molecular subtype. We investigated associations between cumulative average alcohol intake and risk of breast cancer by molecular subtype among 105,972 women in the prospective Nurses' Health Study cohort, followed from 1980 to 2006. Breast cancer molecular subtypes were defined according to estrogen receptor (ER), progesterone receptor, human epidermal growth factor 2 (HER2), cytokeratin 5/6, and epidermal growth factor status from immunostained tumor microarrays in combination with histologic grade. Multivariable Cox proportional hazards models were used to estimate hazard ratios (HR) and 95% confidence intervals (CI). Competing risk analyses were used to assess heterogeneity by subtype. We observed suggestive heterogeneity in associations between alcohol and breast cancer by subtype (phet = 0.06). Alcohol consumers had an increased risk of luminal A breast cancers [n = 1,628 cases, per 10 g/day increment HR (95%CI) = 1.10(1.05-1.15)], and an increased risk that was suggestively stronger for HER2-type breast cancer [n = 160 cases, HR (95%CI) = 1.16(1.02-1.33)]. We did not observe statistically significant associations between alcohol and risk of luminal B [n = 631 cases, HR (95%CI) = 1.08(0.99-1.16)], basal-like [n = 254 cases, HR (95%CI) = 0.90(0.77-1.04)], or unclassified [n = 87 cases, HR (95%CI) = 0.90(0.71-1.14)] breast cancer. Alcohol consumption was associated with increased risk of luminal A and HER2-type breast cancer, but not significantly associated with other subtypes. Given that ERs are expressed in luminal A but not in HER2-type tumors, our findings suggest that other mechanisms may play a role in the association between alcohol and breast cancer.

Hvidtfeldt, U. A., A. Tjonneland, et al. "Risk of breast cancer in relation to combined effects of hormone therapy, body mass index, and alcohol use, by hormone-receptor status." Epidemiology. 2015 May;26(3):353-61. doi: 10.1097/EDE.0000000000000261.

BACKGROUND: Alcohol consumption, increased body mass index (BMI), and hormone therapy are risk factors for postmenopausal breast cancer, but their combined effects are not well understood. Because hormone therapy is effective for the relief of menopausal symptoms, the identification of "high-risk" users is important for therapeutic reasons. We investigated interactions between hormone therapy use and alcohol-use/high BMI status in relation to invasive breast cancer risk, both overall and according to estrogen receptor (ER) status. METHODS: Two Danish prospective cohorts were pooled, including 30,789 women ages 50+ years (study period 1981 to 2009). Information on risk factors was obtained in baseline questionnaires. We performed analyses using the Aalen additive hazards model. Serum estradiol and testosterone measurements were obtained in a subsample of approximately 1000 women. RESULTS: During 392,938 person-years of follow-up, 1579 women developed invasive breast cancer. Among nonusers of hormone therapy, the risk of breast cancer was slightly increased with overweight/obesity and increasing alcohol consumption. Compared with normal-weight nonusers, the risk of breast cancer was higher in hormone therapy users across all BMI strata (P for interaction = 0.003). A markedly higher risk of breast cancer was also observed for alcohol combined with hormone therapy use compared with abstinent nonusers (P for interaction = 0.02). These effects were primarily restricted to ER-positive cases. Combined effects of hormone therapy/high BMI and hormone therapy/alcohol on serum estradiol and testosterone supported the hypothesis of a hormonal pathway linking these exposures to breast cancer. CONCLUSION: These analyses suggest an increased risk of breast cancer associated with hormone therapy use-a risk that may be particularly strong among women consuming alcohol.

Jayasekara, H., R. J. MacInnis, et al. "Lifetime alcohol consumption and upper aero-digestive tract cancer risk in the Melbourne Collaborative Cohort Study." Cancer Causes Control. 2015 Feb;26(2):297-301. doi: 10.1007/s10552-014-0495-y. Epub 2014 Nov 18.

PURPOSE: Cohort studies have rarely examined the association between upper aero-digestive tract (UADT) cancer risk and lifetime alcohol intake. We examined the associations between incident squamous cell carcinoma of the UADT (oral cavity, pharynx, larynx, and esophagus) and alcohol intake for different periods in life using data from the Melbourne Collaborative Cohort Study. METHODS: Usual alcohol intake for 10-year periods from age 20

was calculated using recalled frequency and quantity of beverage-specific consumption. Cox regression with age as the time axis was performed to estimate hazard ratios (HR) and 95 % confidence intervals (CI) for the associations of UADT cancer with alcohol intake for different periods in life compared with abstention. RESULTS: During a mean follow-up of 16.2 person-years, 98 incident cases of UADT cancer were identified. We observed a dose-dependent association between lifetime alcohol intake and the risk of UADT cancer (multivariable-adjusted HR 2.67, 95 % CI 1.27-5.60 for an intake of >/=40 g/day and multivariable-adjusted HR 1.16, 95 % CI 1.06-1.28 for a 10 g/day increment in intake). A positive association with baseline alcohol intake (multivariable-adjusted HR 1.12, 95 % CI 1.02-1.24 for a 10 g/day increment in intake) was found to be a slightly weaker predictor of risk than lifetime intake. CONCLUSIONS: Limiting alcohol intake from early adulthood may reduce UADT cancer risk.

Jelski, W., M. Laniewska-Dunaj, et al. "The activity of alcohol dehydrogenase (ADH) isoenzymes and aldehyde dehydrogenase (ALDH) in the sera of patients with brain cancer." Neurochem Res. 2014 Dec;39(12):2313-8. doi: 10.1007/s11064-014-1402-3. Epub 2014 Oct 10.

Human brain tissue contains various alcohol dehydrogenase (ADH) isoenzymes and possess also aldehyde dehydrogenase (ALDH) activity. In our last experiments we have shown that ADH and ALDH are present also in the brain tumour cells. Moreover the activities of total ADH and class I isoenzymes were significantly higher in cancer tissue than healthy cells. It can suggests that these changes may be reflected by enzyme activity in the serum of patients with brain cancer. Serum samples were taken for routine biochemical investigation from 62 patients suffering from brain cancer (36 glioblastoma, 26 meningioma). For the measurement of the activity of class I and II ADH isoenzymes and ALDH activity, the fluorometric methods were used. The total ADH activity and activity of class III and IV isoenzymes were measured by the photometric method. A statistically significant increase of class I alcohol dehydrogenase isoenzymes was found in the sera of patients with brain cancer. The median activity of this class isoenzyme in the patients group increased about 24 % in the comparison to the control level. The total alcohol dehydrogenase activity was also significantly higher (26 %) among patients with brain tumour than healthy ones. The activities of other tested ADH isoenzymes and total ALDH were unchanged. The increase of the activity of total ADH and class I alcohol dehydrogenase isoenzyme in the sera of patients with brain cancer seems to be caused by the release of this isoenzyme from tumour's cells.

Jeong, J. B., J. Choi, et al. "Patchouli alcohol, an essential oil of Pogostemon cablin, exhibits anti-tumorigenic activity in human colorectal cancer cells." Int Immunopharmacol. 2013 Jun;16(2):184-90. doi: 10.1016/j.intimp.2013.04.006. Epub 2013 Apr 17.

Patchouli alcohol (PA) is one of the important compounds isolated from the essential oil of Pogostemon cablin (patchouli). PA has neuroprotective, anti-influenza and anti-inflammatory activities. However, anti-cancer activity of PA has not been studied so far. We performed in vitro study to investigate whether PA affects proliferation and apoptosis of human colorectal cancer cells, and to define potential molecular mechanisms. PA suppressed cell growth and induced apoptosis in a dose-dependent manner in human colorectal cancer cells (HCT116, SW480). In addition, PA decreased cell growth in MCF7, BxPC3, PC3, and HUVEC cells. Exposure of PA to HCT116 and SW480 cells activated p21 expression and suppressed the expressions of cyclin D1 and cyclin-dependent kinase 4 (CDK4) in a dose-dependent manner. In addition, PA attenuated the expressions of HDAC2 (histone deacetylase 2) and c-myc, and HDAC enzyme activity. We also observed that PA induced the transcriptional activity of NF-kappaB through an increase of nuclear translocation of p65. These findings suggest that PA exerts an anti-cancer activity by decreasing cell growth and increasing apoptosis in human colorectal cancer cells. The proposed mechanisms include the inhibition of HDAC2 expression and HDAC enzyme activity, and subsequent downregulation of c-myc and activation of NF-kappaB pathway.

Klarich, D. S., S. M. Brasser, et al. "Moderate Alcohol Consumption and Colorectal Cancer Risk." Alcohol Clin Exp Res. 2015 Aug;39(8):1280-91. doi: 10.1111/acer.12778. Epub 2015 Jun 25.

BACKGROUND: Heavy alcohol drinking is a risk factor for colorectal cancer (CRC); previous studies have shown a linear dose-dependent association between alcohol intake and CRC. However, some studies suggest that moderate alcohol consumption may have a protective effect, similar to that seen in cardiovascular disease. Other factors may interact with alcohol and contribute additional risk for CRC. We aimed to determine the association between moderate alcohol consumption, limited to 30 g of alcohol per day, by beverage type on CRC risk and to assess the effects of other factors that interact with alcohol to influence CRC risk. METHODS: The PubMed database was used to find articles published

between 2008 and 2014 related to alcohol and CRC. Twenty-one relevant articles were evaluated and summarized, including 11 articles reporting on CRC risk associated with moderate intake and 10 articles focusing on genetic interactions associated with alcohol and CRC risk. RESULTS: The association between alcohol and increased risk for CRC was found when intakes exceeded 30 g/d alcohol. Nonsignificant results were consistently reported for intakes <30 g/d. Additional risks for CRC were found to be related to obesity and folate status for regular alcohol consumers. Some significant results suggest that the development of CRC is dependent on the interaction of gene and environment. CONCLUSIONS: The association between the amount of alcohol consumed and the incidence of CRC was not significant at moderate intake levels. Moderate alcohol consumption was associated with a reduced CRC risk in study populations with greater adherence to a Mediterranean diet, where wine contributed substantially to the alcoholic beverage consumed. Other factors such as obesity, folate deficiency, and genetic susceptibility may contribute additional CRC risk for those consuming alcohol. To minimize CRC risk, appropriate recommendations should encourage intakes below 30 g of alcohol each day.

Laffoy, M., T. McCarthy, et al. "Cancer incidence and mortality due to alcohol: an analysis of 10-year data." Ir Med J. 2013 Nov-Dec;106(10):294-7.

Alcohol consumption is causally related to cancer of the upper aero-digestive tract, liver, colon, rectum, female breast and pancreas. The dose response relationship varies for each site. We calculated Ireland's cancer incidence and mortality attributable to alcohol over a 10-year period. Between 2001 and 2010, 4,585 (4.7%) male and 4,593 (4.2%) female invasive cancer diagnoses were attributable to alcohol. The greatest risk was for the upper aero-digestive tract where 2,961 (52.9%) of these cancers in males and 866 (35.2%) in females were attributable to alcohol. Between 2001 and 2010, 2,823 (6.7%) of male cancer deaths and 1,700 (4.6%) of female cancer deaths were attributable to alcohol. Every year approximately 900 new cancers and 500 cancer deaths are attributable to alcohol. Alcohol is a major cause of cancer after smoking, obesity and physical inactivity. Public awareness of risk must improve. Over half of alcohol related cancers are preventable by adhering to Department of Health alcohol consumption guidelines.

Land, S. R., Q. Liu, et al. "Cigarette smoking, physical activity, and alcohol consumption as predictors of cancer incidence among women at high risk of breast cancer in the NSABP P-1 trial." Cancer Epidemiol Biomarkers Prev. 2014 May;23(5):823-32. doi: 10.1158/1055-9965.EPI-13-1105-T. Epub 2014 Feb 25.

BACKGROUND: NSABP P-1 provides an opportunity to examine the association of behavioral factors with prospectively monitored cancer incidence and interactions with tamoxifen. METHODS: From 1992 to 1997, 13,388 women with estimated 5-year breast cancer risk greater than 1.66% or a history of lobular carcinoma in situ (87% younger than age 65; 67% postmenopausal) were randomly assigned to tamoxifen versus placebo. Invasive breast cancer, lung cancer, colon cancer, and endometrial cancer were analyzed with Cox regression. Predictors were baseline cigarette smoking, leisure-time physical activity, alcohol consumption, and established risk factors. RESULTS: At median 7 years follow-up, we observed 395, 66, 35, and 74 breast cancer, lung cancer, colon cancer, and endometrial cancer, respectively. Women who had smoked were at increased risk of breast cancer (P = 0.007; HR = 1.3 for 15-35 years smoking, HR = 1.6 for >/= 35 years), lung cancer (P < 0.001; HR = 3.9 for 15-35 years, HR = 18.4 for >/= 35 years), and colon cancer (P < 0.001; HR = 5.1 for >/= 35 years) versus never-smokers. Low activity predicted increased breast cancer risk only among women assigned to placebo (P = 0.021 activity main effect, P = 0.013 activity-treatment interaction; HR = 1.4 for the placebo group) and endometrial cancer among all women (P = 0.026, HR = 1.7). Moderate alcohol (>0-1 drink/day) was associated with decreased risk of colon cancer (P = 0.019; HR = 0.35) versus no alcohol. There were no other significant associations between these behaviors and cancer risk. CONCLUSION: Among women with elevated risk of breast cancer, smoking has an even greater impact on breast cancer risk than observed in past studies in the general population. IMPACT: Women who smoke or are inactive should be informed of the increased risk of multiple types of cancer.

Laniewska-Dunaj, M., W. Jelski, et al. "The activity of class I, II, III and IV of alcohol dehydrogenase (ADH) isoenzymes and aldehyde dehydrogenase (ALDH) in brain cancer." Neurochem Res. 2013 Jul;38(7):1517-21. doi: 10.1007/s11064-013-1053-9. Epub 2013 Apr 27.

The brain being highly sensitive to the action of alcohol is potentially susceptible to its carcinogenic effects. Alcohol dehydrogenase (ADH) and aldehyde dehydrogenase (ALDH) are the main enzymes involved in ethanol metabolism, which leads to the generation of carcinogenic acetaldehyde. Human brain tissue contains various ADH isoenzymes and possess also ALDH activity. The purpose of this study was to

compare the capacity for ethanol metabolism measured by ADH isoenzymes and ALDH activity in cancer tissues and healthy brain cells. The samples were taken from 62 brain cancer patients (36 glioblastoma, 26 meningioma). For the measurement of the activity of class I and II ADH isoenzymes and ALDH activity, the fluorometric methods were used. The total ADH activity and activity of class III and IV isoenzymes were measured by the photometric method. The total activity of ADH, and activity of class I ADH were significantly higher in cancer cells than in healthy tissues. The other tested classes of ADH and ALDH did not show statistically significant differences of activity in cancer and in normal cells. Analysis of the enzymes activity did not show significant differences depending on the location of the tumor. The differences in the activity of total alcohol dehydrogenase, and class I isoenzyme between cancer tissues and healthy brain cells might be a factor for metabolic changes and disturbances in low mature cancer cells and additionally might be a reason for higher level of acetaldehyde which can intensify the carcinogenesis.

Lochhead, P., R. Nishihara, et al. "Postdiagnostic intake of one-carbon nutrients and alcohol in relation to colorectal cancer survival." Am J Clin Nutr. 2015 Sep 30. pii: ajcn115162.
        BACKGROUND: Observational data have suggested that intakes of nutrients involved in one-carbon metabolism are inversely associated with risk of colorectal carcinoma and adenomas. In contrast, results from some preclinical studies and cardiovascular and chemoprevention trials have raised concerns that high folate intake may promote carcinogenesis by facilitating the progression of established neoplasia. OBJECTIVE: We tested the hypothesis that higher total folate intake (including food folate and folic acid from fortified foods and supplements) or other one-carbon nutrient intakes might be associated with poorer survival after a diagnosis of colorectal cancer. DESIGN: We used rectal and colon cancer cases within the following 2 US prospective cohort studies: the Nurses' Health Study and the Health Professionals Follow-Up Study. Biennial questionnaires were used to gather information on medical history and lifestyle factors, including smoking and alcohol consumption. B-vitamin and methionine intakes were derived from food-frequency questionnaires. Data on tumor molecular characteristics (including microsatellite instability, CpG island methylator phenotype, KRAS, BRAF, and PIK3CA mutations, and long interspersed nucleotide element 1 methylation level) were available for a subset of cases. We assessed colorectal cancer-specific mortality according to postdiagnostic intakes

of one-carbon nutrients with the use of multivariable Cox proportional hazards regression models. RESULTS: In 1550 stage I-III colorectal cancer cases with a median follow-up of 14.9 y, we documented 641 deaths including 176 colorectal cancer-specific deaths. No statistically significant associations were observed between postdiagnostic intakes of folate or other one-carbon nutrients and colorectal cancer-specific mortality (multivariate P-trend >/= 0.21). In an exploratory molecular pathologic epidemiology survival analysis, there was no significant interaction between one-carbon nutrients or alcohol and any of the tumor molecular biomarkers examined. CONCLUSIONS: Higher postdiagnostic intakes of one-carbon nutrients are not associated with the prognosis in stage I-III colorectal cancer. Our findings do not support the hypothesis that higher folate intake after colorectal cancer diagnosis might increase risk of cancer-related death.

Maasland, D. H., P. A. van den Brandt, et al. "Alcohol consumption, cigarette smoking and the risk of subtypes of head-neck cancer: results from the Netherlands Cohort Study." BMC Cancer. 2014 Mar 14;14:187. doi: 10.1186/1471-2407-14-187.
        BACKGROUND: Prospective data on alcohol consumption, cigarette smoking and risk of head-neck cancer (HNC) subtypes, i.e. oral cavity cancer (OCC), oro-/hypopharyngeal cancer (OHPC), and laryngeal cancer (LC), are limited. We investigated these associations within the second largest prospective study on this topic so far, the Netherlands Cohort Study. METHODS: 120,852 participants completed a questionnaire on diet and other cancer risk factors in 1986. After 17.3 years of follow-up, 395 HNC (110 OCC, 83 OHPC, and 199 LC) cases and 4288 subcohort members were available for case-cohort analysis using Cox proportional hazards models. RESULTS: For total HNC, the multivariable adjusted incidence rate ratio (RR) was 2.74 (95% confidence interval (CI) 1.85-4.06) for those drinking >/=30 g ethanol/day compared with abstainers; in subtypes, RRs were 6.39 for OCC, 3.52 for OHPC, and 1.54 for LC. Compared with never cigarette smokers, current cigarette smokers had a RR of 4.49 (95%CI 3.11-6.48) for HNC overall, and 2.11 for OCC, 8.53 for OHPC, and 8.07 for LC. A significant, positive, multiplicative interaction between categories of alcohol consumption and cigarette smoking was found for HNC overall (P interaction 0.03). CONCLUSIONS: Alcohol consumption and cigarette smoking were independently associated with risk of HNC overall, with a positive, multiplicative interaction. The strength of these associations differed among HNC-subtypes: OCC was most strongly associated with

alcohol consumption but most weakly with cigarette smoking, whereas LC was not statistically significantly associated with alcohol consumption.

Marnerides, A., E. Zagelidou, et al. "An unusual case of multiple-gunshot suicide of an alcohol-intoxicated cancer sufferer with prolonged physical activity." J Forensic Sci. 2013 Mar;58(2):537-9. doi: 10.1111/1556-4029.12073. Epub 2013 Mar 4.

Multishot firearm suicides are relatively rare and suggest the possibility of homicide. Physical activity following gunshots to the head, the neck, and the thorax does occur, and immediate incapacitation does not occur in every fatal gunshot wound that penetrates the head or perforates the heart. Cancer patients appear to be at increased suicide risk, but alcohol intoxication is less common in such cases. We present-to the best of our knowledge for the first time-a case of a 54-year old, male, liver cancer sufferer, who under the influence of alcohol, discharged his revolver three times, suffered, among other wounds, a heart-perforating wound, and died after c. 1.5 h, being able to talk until just before he died. Our case underlines the importance of keeping an open critical mind when dealing with multiple-gunshot fatalities, especially when posttraumatic physical activity might be crucial in differentiating homicide from suicide.

Matsuo, K., I. Oze, et al. "The aldehyde dehydrogenase 2 (ALDH2) Glu504Lys polymorphism interacts with alcohol drinking in the risk of stomach cancer." Carcinogenesis. 2013 Jul;34(7):1510-5. doi: 10.1093/carcin/bgt080. Epub 2013 Mar 1.

The impact of alcohol on the risk of stomach cancer is controversial. Although aldehyde dehydrogenase 2 (ALDH2) Glu504Lys (rs671) polymorphism has a strong effect on acetaldehyde metabolism, little is known about its impact on stomach cancer risk when combined with alcohol drinking. This case-control study included a total of 697 incident stomach cancer case subjects and 1372 non-cancer control subjects who visited Aichi Cancer Center between 2001 and 2005. We estimated odds ratios (OR) and 95% confidence intervals (CI) for ALDH2 genotypes and alcohol consumption using logistic regression models after adjustment for potential confounders, including Helicobacter pylori infection. The ALDH2 504Lys allele was associated with the risk of stomach cancer, with adjusted ORs of 1.40 (95% CI, 1.11-1.76) for Glu/Lys and 1.73 (1.12-2.68) for Lys/Lys compared with Glu/Glu. Heavy drinking was associated with risk (OR 1.72, 1.17-2.52) after adjustment for ALDH2 genotype and other confounders. Moreover, ORs for heavy drinking were 1.28 (0.77-2.12) for those with ALDH2 Glu/Glu and 3.93 (1.99-5.79) for those with the ALDH2 Lys allele

relative to non-drinkers with the Glu/Glu genotype (P for interaction = 0.0054). In conclusion, ALDH2 and alcohol drinking showed interaction for risk factors of stomach cancer, indicating that acetaldehyde plays a role in stomach carcinogenesis.

Mayadev, J., C. S. Li, et al. "Alcohol Abuse Decreases Pelvic Control and Survival in Cervical Cancer: An Opportunity of Lifestyle Intervention for Outcome Improvement." Am J Clin Oncol. 2015 Mar 13.

PURPOSE: We examined the incidence and the effect of alcohol abuse on pelvic control (PC), disease-free survival (DFS), and overall survival (OS) in locally advanced cervical cancer patients undergoing definitive radiation therapy (RT). METHODS: Between 2007 and 2013, 95 patients treated with RT were reviewed, and the tumor characteristics, the RT dose, the treatment time, chemotherapy, and the number of cycles were recorded. The association between alcohol abuse and DFS, OS, and the duration of PC was analyzed using multivariable Cox proportional hazards models. RESULTS: Of the 95 patients with an average age of 54.8 years (range, 27 to 91 y), 30% were FIGO stage 1B1, 1B2, 2A, 52% stage 2B, 3A; and 18% stage 3B; 86% of the patients were treated with weekly cisplatin chemotherapy. Alcohol history showed that 10 (10.5%) patients met the CDC criteria for heavy alcohol use. With a mean follow-up time of 2 years, 85 patients (88.5%) achieved PC and 86 patients (90.5%) were free of distant metastasis. A total of 82 patients (86.3%) were alive at the last follow-up. When controlling for the total treatment time, excessive alcohol abuse was significantly associated with a decrease in DFS (P=0.005; hazard ratio [HR], 6.19; 95% confidence interval [CI]: 1.73, 22.18), OS (P=0.001; HR, 6.68; 95% CI: 2.10, 21.26), and PC (P=0.029; HR, 3.10; 95% CI: 1.13, 8.56) on univariable analysis. On multivariable analysis, excessive alcohol abuse was significantly associated with a decrease in DFS (P=0.005; HR, 10.57; 95% CI: 2.07, 53.93) and OS (P=0.001; HR, 10.80; 95% CI: 2.57, 45.40). CONCLUSIONS: In this small hypothesis-generating series of patients with heavy alcohol use, the data support the association that heavy alcohol use increases the risk of cancer recurrence and mortality. Additional research is required to better define the patient- and treatment-related factors that may be targeted for intervention.

McDonald, J. A., A. Goyal, et al. "Alcohol Intake and Breast Cancer Risk: Weighing the Overall Evidence." Curr Breast Cancer Rep. 2013 Sep;5(3). doi: 10.1007/s12609-013-0114-z.

Moderate alcohol consumption has been linked to an approximate 30-50% increased risk in

breast cancer. Case-control and cohort studies have consistently observed this modest increase. We highlight recent evidence from molecular epidemiologic studies and studies of intermediate markers like mammographic density that provide additional evidence that this association is real and not solely explained by factors/correlates of the exposure and outcome present in non-randomized studies. We also review evidence from studies of higher risk women including BRCA1 and BRCA2 mutation carriers. Given the incidence of heart disease is higher than breast cancer and modest alcohol consumption is associated with reduced risk of heart disease, we examine the latest evidence to evaluate if alcohol reduction should be targeted to women at high risk for breast cancer. We also review the most recent evidence on the effect of alcohol use on tumor recurrence and survival for those diagnosed with breast cancer.

Moyses, R. A., R. V. Lopez, et al. "Significant differences in demographic, clinical, and pathological features in relation to smoking and alcohol consumption among 1,633 head and neck cancer patients." Clinics (Sao Paulo). 2013 Jun;68(6):738-44. doi: 10.6061/clinics/2013(06)03.

OBJECTIVE: As a lifestyle-related disease, social and cultural disparities may influence the features of squamous cell carcinoma of the head and neck in different geographic regions. We describe demographic, clinical, and pathological aspects of squamous cell carcinoma of the head and neck according to the smoking and alcohol consumption habits of patients in a Brazilian cohort. METHODS: We prospectively analyzed the smoking and alcohol consumption habits of 1,633 patients enrolled in five Sao Paulo hospitals that participated in the Brazilian Head and Neck Genome Project - Gencapo. RESULTS: The patients who smoked and drank were younger, and those who smoked were leaner than the other patients, regardless of alcohol consumption. The non-smokers/non-drinkers were typically elderly white females who had more differentiated oral cavity cancers and fewer first-degree relatives who smoked. The patients who drank presented significantly more frequent nodal metastasis, and those who smoked presented less-differentiated tumors. CONCLUSIONS: The patients with squamous cell carcinoma of the head and neck demonstrated demographic, clinical, and pathological features that were markedly different according to their smoking and drinking habits. A subset of elderly females who had oral cavity cancer and had never smoked or consumed alcohol was notable. Alcohol consumption seemed to be related to nodal metastasis, whereas smoking correlated with the degree of differentiation.

Nelson, D. E., D. W. Jarman, et al. "Alcohol-attributable cancer deaths and years of potential life lost in the United States." Am J Public Health. 2013 Apr;103(4):641-8. doi: 10.2105/AJPH.2012.301199. Epub 2013 Feb 14.

OBJECTIVES: Our goal was to provide current estimates of alcohol-attributable cancer mortality and years of potential life lost (YPLL) in the United States. METHODS: We used 2 methods to calculate population-attributable fractions. We based relative risks on meta-analyses published since 2000, and adult alcohol consumption on data from the 2009 Alcohol Epidemiologic Data System, 2009 Behavioral Risk Factor Surveillance System, and 2009-2010 National Alcohol Survey. RESULTS: Alcohol consumption resulted in an estimated 18,200 to 21,300 cancer deaths, or 3.2% to 3.7% of all US cancer deaths. The majority of alcohol-attributable female cancer deaths were from breast cancer (56% to 66%), whereas upper airway and esophageal cancer deaths were more common among men (53% to 71%). Alcohol-attributable cancers resulted in 17.0 to 19.1 YPLL for each death. Daily consumption of up to 20 grams of alcohol (</= 1.5 drinks) accounted for 26% to 35% of alcohol-attributable cancer deaths. CONCLUSIONS: Alcohol remains a major contributor to cancer mortality and YPLL. Higher consumption increases risk but there is no safe threshold for alcohol and cancer risk. Reducing alcohol consumption is an important and underemphasized cancer prevention strategy.

Newcomb, P. A., E. Kampman, et al. "Alcohol consumption before and after breast cancer diagnosis: associations with survival from breast cancer, cardiovascular disease, and other causes." J Clin Oncol. 2013 Jun 1;31(16):1939-46. doi: 10.1200/JCO.2012.46.5765. Epub 2013 Apr 8.

PURPOSE: Alcohol intake is associated with increased risk of breast cancer. In contrast, the relation between alcohol consumption and breast cancer survival is less clear. PATIENTS AND METHODS: We assessed pre- and postdiagnostic alcohol intake in a cohort of 22,890 women with incident invasive breast cancer who were residents of Wisconsin, Massachusetts, or New Hampshire and diagnosed from 198 to 200 at ages 20 to 79 years. All women reported on prediagnostic intake; a subsample of 4,881 reported on postdiagnostic intake. RESULTS: During a median follow-up of 11.3 years from diagnosis, 7,780 deaths occurred, including 3,484 resulting from breast cancer. Hazard ratios (HR) and 95% CIs were estimated. Based on a quadratic analysis, moderate alcohol consumption before diagnosis was modestly associated with disease-specific survival (compared

with nondrinkers, HR = 0.93 [95% CI, 0.85 to 1.02], 0.85 [95% CI, 0.75 to 0.95], 0.88 [95% CI, 0.75 to 1.02], and 0.89 [95% CI, 0.77 to 1.04] for two or more, three to six, seven to nine, and >/= 10 drinks/wk, respectively). Alcohol consumption after diagnosis was not associated with disease-specific survival (compared with nondrinkers, HR = 0.88 [95% CI, 0.61 to 1.27], 0.80 [95% CI, 0.49 to 1.32], 1.01 [95% CI, 0.55 to 1.87], and 0.83 [95% CI, 0.45 to 1.54] for two or more, three to six, seven to nine, and >/= 10 drinks/wk, respectively). Results did not vary by beverage type. Women consuming moderate levels of alcohol, either before or after diagnosis, experienced better cardiovascular and overall survival than nondrinkers. CONCLUSION: Overall alcohol consumption before diagnosis was not associated with disease-specific survival, but we found a suggestion favoring moderate consumption. There was no evidence for an association with postdiagnosis alcohol intake and breast cancer survival. This study, however, does provide support for a benefit of limited alcohol intake for cardiovascular and overall survival in women with breast cancer.

Nishihara, R., M. Wang, et al. "Alcohol, one-carbon nutrient intake, and risk of colorectal cancer according to tumor methylation level of IGF2 differentially methylated region." Am J Clin Nutr. 2014 Dec;100(6):1479-88. doi: 10.3945/ajcn.114.095539. Epub 2014 Oct 8.
BACKGROUND: Although a higher consumption of alcohol, which is a methyl-group antagonist, was previously associated with colorectal cancer risk, mechanisms remain poorly understood. OBJECTIVE: We hypothesized that excess alcohol consumption might increase risk of colorectal carcinoma with hypomethylation of insulin-like growth factor 2 (IGF2) differentially methylated region-0 (DMR0), which was previously associated with a worse prognosis. DESIGN: With the use of a molecular pathologic epidemiology database in 2 prospective cohort studies, the Nurses' Health Study and Health Professionals Follow-up Study, we examined the association between alcohol intake and incident colorectal cancer according to the tumor methylation level of IGF2 DMR0. Duplication-method Cox proportional cause-specific hazards regression for competing risk data were used to compute HRs and 95% CIs. In addition, we investigated intakes of vitamin B-6, vitamin B-12, methionine, and folate as exposures. RESULTS: During 3,206,985 person-years of follow-up, we identified 993 rectal and colon cancer cases with an available tumor DNA methylation status. Compared with no alcohol consumption, the consumption of >/=15 g alcohol/d was associated with elevated risk of

colorectal cancer with lower levels of IGF2 DMR0 methylation [within the first and second quartiles: HRs of 1.55 (95% CI: 1.08, 2.24) and 2.11 (95% CI: 1.44, 3.07), respectively]. By contrast, alcohol consumption was not associated with cancer with higher levels of IGF2 DMR0 methylation. The association between alcohol and cancer risk differed significantly by IGF2 DMR0 methylation level (P-heterogeneity = 0.006). The association of vitamin B-6, vitamin B-12, and folate intakes with cancer risk did not significantly differ according to IGF2 DMR0 methylation level (P-heterogeneity > 0.2). CONCLUSIONS: Higher alcohol consumption was associated with risk of colorectal cancer with IGF2 DMR0 hypomethylation but not risk of cancer with high-level IGF2 DMR0 methylation. The association between alcohol intake and colorectal cancer risk may differ by tumor epigenetic features.

Owusu, D., M. Quinn, et al. "Alcohol Consumption, Depression, Insomnia and Colorectal Cancer Screening: Racial Differences." Int J High Risk Behav Addict. 2015 Jun 20;4(2):e23424. doi: 10.5812/ijhrba.4(2)2015.23424. eCollection 2015 Jun.
BACKGROUND: Mortality from colorectal cancer (CRC) can be reduced drastically by early detection and early treatment. However, uptake of CRC screening is relatively low, about 50% for those whom the test is highly recommended. OBJECTIVES: We examined the influence of and racial differences in depression, insomnia, alcohol use, and tobacco use on CRC screening uptake in the US. PATIENTS AND METHODS: Analysis of the 2012 National Health Information Survey data was conducted. Both weighted univariate and multiple logistic regression analyses were performed in SAS to estimate the odds ratios (ORs) and their 95% confidence intervals (CIs). A total of 21511 participants were included in the analysis. RESULTS: Prevalence of CRC screening in the participants was 19%. Adjusting for all factors, insomnia (OR = 1.18, 95%CI = 1.06 - 1.32), moderate alcohol drinking (OR = 1.16, 95%CI = 1.01 - 1.30), past smoking (OR = 1.17, 95%CI = 1.04 - 1.32), depression (OR = 1.37, 95%CI = 1.18 - 1.58), African American (AA) race, and cancer history were positively associated with CRC screening. Females and Single were inversely associated with CRC screening prevalence. In stratified analysis by races (White and AA), depression was associated with CRC screening in both races. Marital status, smoking, cancer history and insomnia were associated with CRC screening in Whites only; while alcohol use was associated with CRC screening in AAs only. CONCLUSIONS: We have found significant associations between lifestyle factors (alcohol consumption and smoking) and mental health

problems (depression and insomnia) and CRC screening uptake. To improve overall CRC screening uptake in the US, it is important to consider racial differences in predictors and tailor appropriate interventions to each racial/ethnic group.

Park, B., S. Y. Kong, et al. "Health Behaviors of Cancer Survivors in Nationwide Cross-Sectional Survey in Korea: Higher Alcohol Drinking, Lower Smoking, and Physical Inactivity Pattern in Survivors with Higher Household Income." Medicine (Baltimore). 2015 Aug;94(31):e1214. doi: 10.1097/MD.0000000000001214.

This study investigated the prevalence of smoking, alcohol consumption, and physical activity in cancer survivors and examined the sociodemographic factors affecting these health-related behaviors.We used data from the 4th and 5th Korean National Health and Nutrition Examination Survey conducted between 2007 and 2012, which identified 1153 cancer cases and 36,451 people without a history of cancer $\geq$/=20 years of age. We used a structured questionnaire to obtain information concerning cancer diagnosis, health-related behaviors, and sociodemographic characteristics.The proportion of cancer survivors who were current drinkers, heavy drinkers, current smokers, or engaged in physical activity were 49.1, 9.0, 9.2, or 50.7%, respectively. Compared with people with no history of cancer, cancer survivors were less likely to be current drinkers (odds ratio [OR] = 0.45; 95% confidence interval [CI] 0.36-0.56), heavy drinkers (OR = 0.53; 95% CI 0.36-0.78), current smokers (OR = 0.37; 95% CI 0.24-0.55), or physically inactive (OR = 0.77; 95% CI 0.63-0.95). Cancer survivors with higher household incomes had higher odds of current drinking and heavy drinking (P trend = 0.039 and 0.033, respectively) and were less likely to be current smokers or physically inactive (P trend = 0.016 and 0.046, respectively). Age, sex, sites of cancer, and the time since diagnosis affected the health behaviors in cancer survivors. Furthermore, we confirmed that these unhealthy behaviors are interrelated.We found that household income had a bidirectional effect on health behaviors and confirmed an aggregation of unhealthy lifestyles. Identification of survivors vulnerable to unhealthy lifestyles, focusing on household income level would allow intervention programs to be more effective.

Petti, S., M. Masood, et al. "Alcohol is not a risk factor for oral cancer in nonsmoking, betel quid non-chewing individuals. A meta-analysis update." Ann Ig. 2013 Jan-Feb;25(1):3-14. doi: 10.7416/ai.2013.1901.

BACKGROUND: Alcohol drinking is associated with high oral cancer (OC) risk. This association is particularly evident in tobacco smoking/betel quid (BQ) chewing subjects. In a previous stratified meta-analysis (Petti S et al., Cancer Epidemiol 2012) we reported that drinking was inversely associated with OC in non-smoking BQ non-chewing individuals, while this association was reversed in smoking individuals. However, the previous study could be excessively influenced by a large primary study, which yielded more than 50% of the weight of all the primary studies. Therefore, we updated this analysis using only recent studies. METHODS: Case-control studies published between 2010 and 2012 were searched. In each study, non-smoking/ BQ non-chewing exposed (ever routine drinkers) and unexposed (never drinkers) subjects with (cases)/without (controls) OC were extracted and odds ratio (OR) calculated. Between-study heterogeneity was assessed with Cochran's Q. Publication bias was formally assessed with trim and fill method. Sensitivity analysis to inclusion criteria was made. The pooled OR was assessed with the fixed- and random-effect methods and corrected for publication bias. RESULTS: Seven of these studies met the inclusion criteria: they were not heterogeneous enough. Correction for publication bias was not necessary and provided only one missing study. The OR estimates were 0.70 (95% confidence interval -95CI, 0.51-0.98), 0.70 (95CI, 0.51-0.96), 0.75 (95CI, 0.54-1.03) with the three methods. Sensitivity analysis did not change the OR estimates considerably. CONCLUSIONS: This analysis corroborated the results of the previous analysis, confirming that drinking was inversely associated with OC in non-smoking, BQ non-chewing subjects.

Rahman, F., M. Cotterchio, et al. "Association between alcohol consumption and pancreatic cancer risk: a case-control study." PLoS One. 2015 Apr 9;10(4):e0124489. doi: 10.1371/journal.pone.0124489. eCollection 2015.

PURPOSE: Evidence is inconsistent regarding alcohol and pancreatic cancer risk, although heavy drinking may increase risk. METHODS: A population-based case-control study was conducted using 345 pancreas cancer cases diagnosed 2011-2012 and 1,285 frequency-matched controls from Ontario, Canada. Logistic regression was used to evaluate alcohol consumption and pancreatic cancer risk; data was also stratified by sex and smoking status to assess interaction. RESULTS: Alcohol consumption was not associated with pancreatic cancer risk (age-adjusted odds ratio=0.78, 95% CI: 0.58, 1.05 for 1 - 3 drinks/week; age-adjusted odds ratio=0.86, 95% CI: 0.63, 1.17 for 4 - 20 drinks/week), however there was a non-significant increased risk for heavy drinkers consuming $\geq$/= 21 drinks/week (age-adjusted odds

ratio=1.35, 95% CI: 0.81, 2.27). Cigarette smoking modified the alcohol-cancer relationship; among current smokers, heavy alcohol consumption was associated with a significantly increased pancreatic cancer risk (age-adjusted odds ratio=4.04, 95% CI: 1.58, 10.37), whereas this significant association with heavy drinking was not observed among non-smokers (age-adjusted odds ratio=2.01, 95% CI: 0.50, 8.18). Furthermore, light - moderate alcohol intake was associated with increased pancreas cancer risk among current smokers. CONCLUSIONS: While alcohol was not significantly associated with pancreatic cancer risk, smoking status modified this relationship such that among current smokers, alcohol intake was associated with a greater than two-fold increased risk of pancreatic cancer. The results should be interpreted with caution due to small sample sizes within subgroups and correction for multiple comparisons should be considered. These findings should be replicated in larger studies where more precise estimates of risk can be obtained.

Roerecke, M., K. D. Shield, et al. "Estimates of alcohol-related oesophageal cancer burden in Japan: systematic review and meta-analyses." <u>Bull World Health Organ. 2015 May 1;93(5):329-338C. doi: 10.2471/BLT.14.142141. Epub 2015 Feb 24.</u>
    OBJECTIVE: To refine estimates of the burden of alcohol-related oesophageal cancer in Japan. METHODS: We searched PubMed for published reviews and original studies on alcohol intake, aldehyde dehydrogenase polymorphisms, and risk for oesophageal cancer in Japan, published before 2014. We conducted random-effects meta-analyses, including subgroup analyses by aldehyde dehydrogenase variants. We estimated deaths and loss of disability-adjusted life years (DALYs) from oesophageal cancer using exposure distributions for alcohol based on age, sex and relative risks per unit of exposure. FINDINGS: We identified 14 relevant studies. Three cohort studies and four case-control studies had dose-response data. Evidence from cohort studies showed that people who consumed the equivalent of 100 g/day of pure alcohol had an 11.71 fold, (95% confidence interval, CI: 2.67-51.32) risk of oesophageal cancer compared to those who never consumed alcohol. Evidence from case-control studies showed that the increase in risk was 33.11 fold (95% CI: 8.15-134.43) in the population at large. The difference by study design is explained by the 159 fold (95% CI: 27.2-938.2) risk among those with an inactive aldehyde dehydrogenase enzyme variant. Applying these dose-response estimates to the national profile of alcohol intake yielded 5279 oesophageal cancer deaths and 102 988 DALYs lost - almost double the estimates produced by the most recent global burden of disease exercise. CONCLUSION: Use of global dose-response data results in an underestimate of the burden of disease from oesophageal cancer in Japan. Where possible, national burden of disease studies should use results from the population concerned.

Rosario, M., H. L. Corliss, et al. "Mediation by peer violence victimization of sexual orientation disparities in cancer-related tobacco, alcohol, and sexual risk behaviors: pooled youth risk behavior surveys." <u>Am J Public Health. 2014 Jun;104(6):1113-23. doi: 10.2105/AJPH.2013.301764. Epub 2014 Apr 17.</u>
    OBJECTIVES: We examined the role of adolescent peer violence victimization (PVV) in sexual orientation disparities in cancer-related tobacco, alcohol, and sexual risk behaviors. METHODS: We pooled data from the 2005 and 2007 Youth Risk Behavior Surveys. We classified youths with any same-sex sexual attraction, partners, or identity as sexual minority and the remainder as heterosexual. We had 4 indicators of tobacco and alcohol use and 4 of sexual risk and 2 PVV factors: victimization at school and carrying weapons. We stratified associations by gender and race/ethnicity. RESULTS: PVV was related to disparities in cancer-related risk behaviors of substance use and sexual risk, with odds ratios (ORs) of 1.3 (95% confidence interval [CI] = 1.03, 1.6) to 11.3 (95% CI = 6.2, 20.8), and to being a sexual minority, with ORs of 1.4 (95% CI = 1.1, 1.9) to 5.6 (95% CI = 3.5, 8.9). PVV mediated sexual orientation disparities in substance use and sexual risk behaviors. Findings were pronounced for adolescent girls and Asian/Pacific Islanders. CONCLUSIONS: Interventions are needed to reduce PVV in schools as a way to reduce sexual orientation disparities in cancer risk across the life span.

Roswall, N. and E. Weiderpass "Alcohol as a risk factor for cancer: existing evidence in a global perspective." <u>J Prev Med Public Health. 2015 Jan;48(1):1-9. doi: 10.3961/jpmph.14.052. Epub 2015 Jan 27.</u>
    The purpose of the present review is to give an overview of the association between alcohol intake and the risk of developing cancer. Two large-scale expert reports; the World Cancer Research Fund (WCRF)/American Institute of Cancer Research (AICR) report from 2007, including its continuous update project, and the International Agency for Research of Cancer (IARC) monograph from 2012 have extensively reviewed this association in the last decade. We summarize and compare their findings, as well as relate these to the public health impact, with a particular focus on region-specific drinking patterns

and disease tendencies. Our findings show that alcohol intake is strongly linked to the risk of developing cancers of the oral cavity, pharynx, larynx, oesophagus, colorectum (in men), and female breast. The two expert reports diverge on the evidence for an association with liver cancer and colorectal cancer in women, which the IARC grades as convincing, but the WCRF/AICR as probable. Despite these discrepancies, there does, however, not seem to be any doubt, that the Population Attributable Fraction of alcohol in relation to cancer is large. As alcohol intake varies largely worldwide, so does, however, also the Population Attributable Fractions, ranging from 10% in Europe to almost 0% in countries where alcohol use is banned. Given the World Health Organization's prediction, that alcohol intake is increasing, especially in low- and middle-income countries, and steadily high in high-income countries, the need for preventive efforts to curb the number of alcohol-related cancers seems growing, as well as the need for taking a region- and gender-specific approach in both future campaigns as well as future research. The review acknowledges the potential beneficial effects of small doses of alcohol in relation to ischaemic heart disease, but a discussion of this lies without the scope of the present study.

Schootman, M., A. D. Deshpande, et al. "Alcohol outlet availability and excessive alcohol consumption in breast cancer survivors." J Prim Care Community Health. 2013 Jan;4(1):50-8. doi: 10.1177/2150131912443133. Epub 2012 Apr 18.

BACKGROUND: Breast cancer survivors who consume alcohol excessively are at increased risk of recurrence and have worse prognosis. Because the environments in which people live shape many health behaviors, there has been increased attention to how neighborhood environments (eg, alcohol outlet availability) may influence alcohol consumption. The authors hypothesized that proximity to alcohol outlets increases the likelihood of excessive consumption (ie, more than 1 drink/day) among breast cancer survivors independent of their personal or neighborhood characteristics. METHODS: With the Missouri Cancer Registry, the authors conducted a cross-sectional study of 1047 female breast cancer survivors (aged 27-96 years) 1 year after diagnosis. Using telephone interviews, the authors obtained data regarding survivors' alcohol consumption during the past 30 days and several covariates of alcohol use. They also obtained street addresses of all licensed alcohol outlets in Missouri and calculated the road network distance between a participant's address of residence and the nearest alcohol outlet, using a geographic information system. Logistic regression was used to determine if distance was independently associated with excessive

alcohol consumption. RESULTS: Eighteen percent of participants reported consuming more than 1 drink on average per day. Women who lived within 3 miles of the nearest outlet were more likely to report excessive alcohol consumption (odds ratio: 2.09; 95% confidence interval: 1.08, 4.05) than women who lived at least 3 miles from the nearest outlet in adjusted analysis. DISCUSSION: Opportunities exist to reduce excessive alcohol use among breast cancer survivors through policy (eg, restricting number of alcohol outlets) and behavioral (eg, counseling) interventions.

Scoccianti, C., M. Cecchini, et al. "European Code against Cancer 4th Edition: Alcohol drinking and cancer." Cancer Epidemiol. 2015 Jun 24. pii: S1877-7821(15)00023-5. doi: 10.1016/j.canep.2015.01.007.

Alcohol consumption is the third leading risk factor for disease and mortality in Europe. The International Agency for Research on Cancer (IARC) Monographs provide strengthened evidence that the consumption of alcoholic beverages is causally associated with cancers of the oral cavity, pharynx, larynx, oesophagus, liver, colorectum and female breast, even for low and moderate alcohol intakes. The risk of cancer increases in a dose-dependent manner, and the higher the amount of alcohol consumed, the higher the risk of developing cancer. Several biological mechanisms explain the carcinogenicity of alcohol; among them, ethanol and its genotoxic metabolite acetaldehyde play a major role. Taking all this evidence into account, a recommendation of the 4th edition of the European Code against Cancer (ECAC) is: "If you drink alcohol of any type, limit your intake. Not drinking alcohol is better for cancer prevention."

Scoccianti, C., B. Lauby-Secretan, et al. "Female breast cancer and alcohol consumption: a review of the literature." Am J Prev Med. 2014 Mar;46(3 Suppl 1):S16-25. doi: 10.1016/j.amepre.2013.10.031.

CONTEXT: Consumption of alcoholic beverages is one of the single most important known and modifiable risk factor for human cancer. Among women, breast cancer is the most common cancer worldwide and the leading cause of cancer-related mortality. Consumption of alcoholic beverages is causally associated with female breast cancer and the association shows a linear dose-response relationship. The role of heavy drinking has been long recognized and even a moderate intake is associated with an increased risk for breast cancer. The present review is an update of the current evidence on the association between alcohol consumption and breast cancer risk. The aim is to gain further insight into this association and to improve our current understanding of the effects of the major modifying factors. EVIDENCE

ACQUISITION: Epidemiologic and experimental studies published since the most recent International Agency for Research on Cancer (IARC) Monograph on alcoholic beverages were identified in PubMed using a combination of keywords such as alcohol, breast cancer, polymorphisms, menopausal status. EVIDENCE SYNTHESIS: Cumulative lifetime consumption, drinking frequency, drinking patterns and timing of exposure each modulate the association between alcohol consumption and breast cancer. Hormonal status, genetic polymorphisms, and nutritional factors may interact with ethanol metabolism and further influence breast cancer risk. CONCLUSIONS: Better standardization among experimental and epidemiologic designs in assessing alcohol intake and timing of exposure may improve our understanding of the heterogeneity observed across studies, possibly allowing the quantification of the effects of occasional heavy drinking and the identification of a window of higher susceptibility to breast cancer development.

Seitz, H. K. and S. Mueller "Alcohol and cancer: an overview with special emphasis on the role of acetaldehyde and cytochrome P450 2E1." Adv Exp Med Biol. 2015;815:59-70. doi: 10.1007/978-3-319-09614-8_4.

The mechanisms by which chronic alcohol consumption enhances carcinogenesis include acetaldehyde (AA) generated by alcohol dehydrogenase and reactive oxygen species (ROS) generated predominantly by cytochrome P450 2E1 (CYP2E1), but also by other factors during inflammation. In addition, ethanol also alters epigenetics by changing DNA and histone methylation and acetylation. A loss of retinoic acid due to a CYP2E1-related enhanced degradation results in enhanced cellular proliferation and decreased cell differentiation. Changes in cancer genes and in signaling pathways (MAPK, RAS, Rb, TGFbeta, p53, PTEN, ECM, osteopontin, Wnt) may also contribute to ethanol-mediated mechanisms in carcinogenesis. Finally, immunosuppression may facilitate tumor spread. In the present review major emphasis is led on AA and ROS. While AA binds to proteins and DNA generating carcinogenic DNA adducts and inhibiting DNA repair and DNA methylation, ROS results in lipid peroxidation with the generation of lipid peroxidation products such as 4-hydoxynonenal which binds to DNA-forming highly carcinogenic exocyclic DNA adducts. ROS production correlates significantly with CYP2E1 in the liver but also in the esophagus, and its generation can be significantly reduced by the specific CYP2E1 inhibitor clomethiazole. Finally, CMZ also inhibits alcohol-mediated nitrosamine-induced hepatocarcinogenesis.

Simonsson, M., A. Markkula, et al. "Pre- and postoperative alcohol consumption in breast cancer patients: impact on early events." Springerplus. 2014 May 22;3:261. doi: 10.1186/2193-1801-3-261. eCollection 2014.

PURPOSE: To investigate the association between pre- and postoperative alcohol consumption and risk for early breast cancer events, since the association between alcohol consumption and prognosis in breast cancer patients is unclear. METHODS: Alcohol consumption was recorded for 934 primary breast cancer patients who underwent breast cancer surgery in Lund, Sweden, between 2002 and 2011 and were followed until December 31(st) 2012. Clinical data were obtained from medical records and population registries. Pre- and postoperative alcohol consumption was analyzed in relation to risk for early events. RESULTS: Median follow-up time was 3.03 years and 100 breast cancer events, 65 distant metastases, and 76 deaths occurred. Compared to no consumption, any preoperative alcohol consumption was weakly associated with lower risk for early events, adjusted HR 0.69 (0.45-1.04), distant metastases, 0.60 (0.36-1.00) and death, 0.62 (0.38-1.01). In the 572 patients without axillary lymph node involvement, any alcohol consumption was not associated with risk for early events. However, in the 360 patients with axillary lymph node involvement, preoperative alcohol consumption was associated with lower risk for early events (adjusted HR 0.43 0.24-0.77; P interaction = 0.01). CONCLUSION: Pre- and postoperative alcohol consumption was weakly associated with lower risk for early breast cancer events. The data does not support recommending that all breast cancer patients abstain from low to moderate alcohol consumption.

Smyth, A., K. K. Teo, et al. "Alcohol consumption and cardiovascular disease, cancer, injury, admission to hospital, and mortality: a prospective cohort study." Lancet. 2015 Sep 17. pii: S0140-6736(15)00235-4. doi: 10.1016/S0140-6736(15)00235-4.

BACKGROUND: Alcohol consumption is proposed to be the third most important modifiable risk factor for death and disability. However, alcohol consumption has been associated with both benefits and harms, and previous studies were mostly done in high-income countries. We investigated associations between alcohol consumption and outcomes in a prospective cohort of countries at different economic levels in five continents. METHODS: We included information from 12 countries participating in the Prospective Urban Rural Epidemiological (PURE) study, a prospective cohort study of individuals aged 35-70 years. We used Cox proportional hazards

regression to study associations with mortality (n=2723), cardiovascular disease (n=2742), myocardial infarction (n=979), stroke (n=817), alcohol-related cancer (n=764), injury (n=824), admission to hospital (n=8786), and for a composite of these outcomes (n=11 963). FINDINGS: We included 114 970 adults, of whom 12 904 (11%) were from high-income countries (HICs), 24 408 (21%) were from upper-middle-income countries (UMICs), 48 845 (43%) were from lower-middle-income countries (LMICs), and 28 813 (25%) were from low-income countries (LICs). Median follow-up was 4.3 years (IQR 3.0-6.0). Current drinking was reported by 36 030 (31%) individuals, and was associated with reduced myocardial infarction (hazard ratio [HR] 0.76 [95% CI 0.63-0.93]), but increased alcohol-related cancers (HR 1.51 [1.22-1.89]) and injury (HR 1.29 [1.04-1.61]). High intake was associated with increased mortality (HR 1.31 [1.04-1.66]). Compared with never drinkers, we identified significantly reduced hazards for the composite outcome for current drinkers in HICs and UMICs (HR 0.84 [0.77-0.92]), but not in LMICs and LICs, for which we identified no reductions in this outcome (HR 1.07 [0.95-1.21]; pinteraction<0.0001). INTERPRETATION: Current alcohol consumption had differing associations by clinical outcome, and differing associations by income region. However, we identified sufficient commonalities to support global health strategies and national initiatives to reduce harmful alcohol use. FUNDING: Population Health Research Institute, the Canadian Institutes of Health Research, Heart and Stroke Foundation of Ontario, AstraZeneca (Canada), Sanofi-Aventis (France and Canada), Boehringer Ingelheim (Germany and Canada), Servier, GlaxoSmithKline, Novartis, King Pharma, and national or local organisations in participating countries.

Szabo, G., B. Saha, et al. "Alcohol and HCV: implications for liver cancer." Adv Exp Med Biol. 2015;815:197-216. doi: 10.1007/978-3-319-09614-8_12.

Liver cancers are one of the deadliest known malignancies which are increasingly becoming a major public health problem in both developed and developing countries. Overwhelming evidence suggests a strong role of infection with hepatitis B and C virus (HBV and HCV), alcohol abuse, as well as metabolic diseases such as obesity and diabetes either individually or synergistically to cause or exacerbate the development of liver cancers. Although numerous etiologic mechanisms for liver cancer development have been advanced and well characterized, the lack of definite curative treatments means that gaps in knowledge still exist in identifying key molecular mechanisms and pathways in the pathophysiology of liver cancers. Given the limited success with current therapies and preventive strategies against liver cancer, there is an urgent need to identify new therapeutic options for patients. Targeting HCV and or alcohol-induced signal transduction, or virus-host protein interactions may offer novel therapies for liver cancer. This review summarizes current knowledge on the mechanistic development of liver cancer associated with HCV infection and alcohol abuse as well as highlights potential novel therapeutic strategies.

Touvier, M., N. Druesne-Pecollo, et al. "Demographic, socioeconomic, disease history, dietary and lifestyle cancer risk factors associated with alcohol consumption." Int J Cancer. 2014 Jan 15;134(2):445-59. doi: 10.1002/ijc.28365. Epub 2013 Aug 5.

Data are lacking regarding the association of alcohol consumption with a broad range of other cancer risk factors. OBJECTIVES: (i) to assess which sociodemographic, lifestyle and dietary factors were associated with alcohol consumption; (ii) to identify profiles of alcohol consumers by beverage type; (iii) to estimate the number of cancer risk factors accumulated on the individual level according to alcohol consumption. Alcohol and dietary intakes were assessed by six 24 hr records among 29,566 adults of the NutriNet-Sante cohort. Factors associated with alcohol consumption (nondrinkers (reference)/< 10 g/day/>/= 10 g/day) were assessed by polytomic multivariate logistic regression stratified by gender. Among alcohol consumers, percentages of alcohol brought by each beverage type were compared across sociodemographic and lifestyle characteristics using Kruskal-Wallis rank tests. Several factors were associated with alcohol consumption >/= 10 g/day in both genders: older age (p(men)=0.02, p(women)<0.0001), smoking (p(men&women) < 0.0001), higher socioprofessional category (p(men&women)<0.0001), higher income (p(men)=0.003, p(women)<0.0001) and less healthy dietary intakes. Profiles of subjects varied across alcoholic beverage types. Men with history of cardiovascular disease (p=0.0002) or depression (p=0.03) and women with history of cirrhosis (p<0.0001) consumed less alcohol. In women, personal history of cancer was associated with a lower proportion of moderate alcohol users only (< 10 g/day, p=0.04). In both genders, higher alcohol drinkers clustered more cancer risk factors (median=5, apart from alcohol) than nondrinkers (median=4), p< .0001. The multiplicity of deleterious lifestyle behaviors combined with alcohol drinking must be taken into account in cancer prevention efforts. Gender-specific

medical advice for people with personal or family history of alcohol-related diseases, including cancer, should be strengthened.

Trinh, T., S. E. Christensen, et al. "Background risk of breast cancer influences the association between alcohol consumption and mammographic density." Br J Cancer. 2015 Jun 30;113(1):159-65. doi: 10.1038/bjc.2015.185. Epub 2015 Jun 2.

BACKGROUND: Alcohol consumption has been suggested to increase risk of breast cancer through a mechanism that also increases mammographic density. Whether the association between alcohol consumption and mammographic density is modified by background breast cancer risk has, however, not been studied. METHODS: We conducted a population-based cross-sectional study of 53 060 Swedish women aged 40-74 years. Alcohol consumption was assessed using a web-based self-administered questionnaire. Mammographic density was measured using the fully-automated volumetric Volpara method. The Tyrer-Cuzick prediction model was used to estimate risk of developing breast cancer in the next 10 years. Linear regression models were used to evaluate the association between alcohol consumption and volumetric mammographic density and the potential influence of Tyrer-Cuzick breast cancer risk. RESULTS: Overall, increasing alcohol consumption was associated with higher absolute dense volume (cm(3)) and per cent dense volume (%). The association between alcohol consumption and absolute dense volume was most pronounced among women with the highest (5%) Tyrer-Cuzick 10-year risk. Among high-risk women, women consuming 5.0-9.9, 10.0-19.9, 20.0-29.9, and 30.0-40.0 g of alcohol per day had 2.6 cm(3) (95% confidence interval (CI), 0.2-4.9), 2.9 cm(3) (95% CI, -0.6 to 6.3), 4.6 cm(3) (95% CI, 1.5-7.7), and 10.8 cm(3) (95% CI, 4.8-17.0) higher absolute dense volume, respectively, as compared with women abstaining from alcohol. A trend of increasing alcohol consumption and higher absolute dense volume was seen in women at low (3%) risk, but not in women at moderate (3.0-4.9%) risk. CONCLUSION: Alcohol consumption may increase breast cancer risk through increasing mammographic density, particularly in women at high background risk of breast cancer.

Tsai, S. T., T. Y. Wong, et al. "The interplay between alcohol consumption, oral hygiene, ALDH2 and ADH1B in the risk of head and neck cancer." Int J Cancer. 2014 Nov 15;135(10):2424-36. doi: 10.1002/ijc.28885. Epub 2014 Apr 19.

Alcohol consumption is an established risk factor for head and neck cancer (HNC). The major carcinogen from alcohol is acetaldehyde, which may be produced by humans or by oral microorganisms through the metabolism of ethanol. To account for the different sources of acetaldehyde production, the current study examined the interplay between alcohol consumption, oral hygiene (as a proxy measure for the growth of oral microorganisms), and alcohol-metabolizing genes (ADH1B and ALDH2) in the risk of HNC. We found that both the fast (*2/*2) and the slow (*1/*1+ *1/*2) ADH1B genotypes increased the risk of HNC due to alcohol consumption, and this association differed according to the slow/non-functional ALDH2 genotypes (*1/*2+ *2/*2) or poor oral hygiene. In persons with the fast ADH1B genotype, the HNC risk associated with alcohol drinking was increased for those with the slow/non-functional ALDH2 genotypes. For those with the slow ADH1B genotypes, oral hygiene appeared to play an important role; the highest magnitude of an increased HNC risk in alcohol drinkers occurred among those with the worst oral hygiene. This is the first study to show that the association between alcohol drinking and HNC risk may be modified by the interplay between genetic polymorphisms of ADH1B and ALDH2 and oral hygiene. Although it is important to promote abstinence from or reduction of alcohol drinking to decrease the occurrence of HNC, improving oral hygiene practices may provide additional benefit.

Tsukamoto, H., L. Mishra, et al. "Alcohol, TLR4-TGF-beta antagonism, and liver cancer." Hepatol Int. 2014 Sep;8 Suppl 2:408-12. doi: 10.1007/s12072-013-9489-1. Epub 2013 Dec 27.

Alcohol abuse and obesity are two known risk factors for hepatocellular carcinoma (HCC) that also synergistically promote HBV/HCV-related carcinogenesis. TLR4, the receptor for endotoxin, participates in inflammatory processes such as M1 activation of hepatic macrophages in alcoholic liver disease. However, its role in liver carcinogenesis via ectopic expression and activation has only recently been revealed in alcohol/HCV-associated HCC models. Alcohol feeding to mice expressing the HCV Ns5a in a hepatocyte specific manner aggravates liver inflammation via activation of overexpressed TLR4 in the parenchymal cells. Long-term alcohol feeding produces liver tumors in these transgenic mice in a manner dependent on TLR4. From these mice, CD133+/CD49f+ tumor-initiating stem cell-like cells (TICs) have been isolated. These TICs exhibit self-renewal and tumorigenic activities driven by TLR4-dependent upregulation of the stem cell factor NANOG. A defective TGF-beta tumor suppressor pathway is identified in the TICs and mediated by NANOG target genes Igf2bp3 and Yap1. This TGF-beta pathway antagonism is responsible in part for the

TICs' tumorigenic activity and chemoresistance. Conversely, mice with an attenuated TGF-beta pathway due to haploinsufficiency of beta2-Spectrin, spontaneously develop liver tumors and alcohol feeding increases tumor incidence in a TLR4-dependent manner. This reciprocal antagonism between TLR4 and TGF-beta pathways may serve as a novel therapeutic target for HCC.

Weaver, A. M., S. E. McCann, et al. "Alcohol intake over the life course and breast cancer survival in Western New York exposures and breast cancer (WEB) study: quantity and intensity of intake." Breast Cancer Res Treat. 2013 May;139(1):245-53. doi: 10.1007/s10549-013-2533-y. Epub 2013 Apr 19.

Alcohol intake is a risk factor for breast cancer, but the association between alcohol and mortality among breast cancer survivors is poorly understood. We examined the association between alcohol intake from all sources, assessed by cognitive lifetime drinking history, and all-cause and breast cancer mortality among women with breast cancer (N = 1,097) who participated in a population-based case-control study. Vital status was ascertained through 2006 using the National Death Index. Using Cox proportional hazards models, we computed hazard ratios for all-cause and breast cancer mortality in association with alcohol intake. We examined lifetime volume and intensity (drinks per drinking day) of alcohol consumption as well as drinking status during various life periods. Analyses were stratified by menopausal status. After adjustment for total intake, postmenopausal women with consumption of four or more drinks per drinking day over their lifetimes were nearly three times more likely to die from any cause compared to abstainers (HR 2.94, 95 % CI 1.31, 6.62). There was a similar but non-significant association with breast cancer mortality (HR 2.68, 95 % CI 0.94, 7.67). Postmenopausal women who drank one drink or fewer per drinking day between menarche and first birth had a significantly decreased hazard of all-cause (HR 0.54, 95 % CI 0.31, 0.95) and breast cancer mortality (HR 0.27, 95 % CI 0.09, 0.77). Premenopausal breast cancer survival was not associated with drinking intensity. We observed no associations between drinking status or total volume of alcohol intake and breast cancer or all-cause mortality. High-intensity alcohol consumption may be associated with decreased survival in postmenopausal women with breast cancer. Low-intensity alcohol consumption between menarche and first birth may be inversely associated with all-cause and breast cancer mortality; this period may be critical for development of and survival from breast cancer. Intensity of alcohol intake may be a more important factor than absolute volume of intake on survival in women with breast cancer.

Zakhari, S. "Chronic alcohol drinking: Liver and pancreatic cancer?" Clin Res Hepatol Gastroenterol. 2015 Sep;39 Suppl 1:S86-91. doi: 10.1016/j.clinre.2015.05.006. Epub 2015 Jul 17.

Cancer is a multifactorial disease that results from complex interactions of numerous risk factors - genetic and environmental - over time, eventually leading to the diseased phenotypes. Thus, while epidemiological studies can point to risk factors, they cannot determine cause and effect relationships, and are unable to give biological and clinical insights into carcinogenesis. The link between any risk factor and carcinogenesis needs to be validated in experimental models. This is particularly true in epidemiological studies on alcohol consumption and its consequences. While there is no doubt that heavy alcohol consumption has devastating health effects, the inconsistencies in alcohol-related epidemiological studies and cancer suffer from possible sources of the variability in outcomes, ranging from inaccuracy of self-report of consumption to the problem of correlating cancer that started decades earlier to current or recent alcohol consumption. To further study the interactions between alcohol and cancer, the use of "Molecular Pathological Epidemiology" (MPE) advocated by Ogino et al. for dissecting the interplay between etiological factors, cellular and molecular characteristics, and disease progression in cancer is appropriate. MPE does not consider cancer as a single entity, rather it integrates analyses of epidemiological studies with the macroenvironment and molecular and microenvironment. This approach allows investigating the relationships between potential etiological agents and cancer based on molecular signatures. More research is needed to fully elucidate the link between heavy alcohol consumption and pancreatic cancer, and to further investigate the roles of acetaldehyde and FAEEs in pancreatic carcinogenesis.

The above contents are the collected information from Internet and public resources to offer to the people for the convenient reading and information disseminating and sharing.

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