Food-Frequency Questionnaire (FFQ) Based Estimates of Total Antioxidant Capacity and Risk of Non-Hodgkin Lymphoma (NHL)

Background: Dietary antioxidants have been hypothesized to protect against NHL. The Oxygen Radical Absorbance Capacity (ORAC) assay measures total antioxidant capacity, as estimated by the peroxy radical scavenging activity of individual foods. The ORAC assay also accounts for synergism between substances within a food. We tested the hypothesis that higher FFQ-based ORAC values are associated with a lower risk of NHL and the common subtypes of diffuse large B-cell, follicular, and chronic lymphocytic leukemia/small lymphocytic lymphomas.

Methods: We evaluated this hypothesis in a clinic-based study of 416 newly diagnosed NHL cases and 926 frequency-matched controls enrolled at the Mayo Clinic from 2002-2007. Usual diet two years before diagnosis/enrollment was assessed using a self-administered, 128-item FFQ, which was linked to the newly developed ORAC database for 275 foods (www.ars.usda.gov). Unconditional logistic regression was used to estimate odds ratios (ORs) and 95% confidence intervals (CI), adjusted for age, sex, residence, and total energy. All case pathology was centrally reviewed, and NHL subtype-specific risks were estimated using polychotomous logistic regression.

Results: The mean age at diagnosis was 60.8 years for cases and 57% were male; for controls, the mean age at enrollment was 60.8 years and 54% were men. NHL risk was inversely associated with total ORAC (OR for highest versus lowest quartile, 0.68; 95% CI 0.47-0.98; P-trend = 0.03). This inverse association was somewhat stronger for lipophilic-ORAC (OR = 0.48; 95% CI 0.32-0.72; P-trend < 0.001) compared with hydrophilic ORAC (OR = 0.67; 95% CI 0.46-0.98; P-trend = 0.01), although these two measures were correlated (r = 0.67). Further adjustment for education, family history of NHL, smoking, alcohol use, and BMI did not alter these results. There was little heterogeneity by NHL subtype.

Conclusions: This is the first study to show that diets high in antioxidants as measured by the FFQ/ORAC are inversely associated with risk of NHL.

A Multigenic Approach to Pain Severity in Lung Cancer Patients: Cox 2 and Interleukin 2.
Reyes-Gibby C, Spitz M, Wu X, Shete S.

While studies suggest that variants in inflammation genes explain individual variation in pain severity, these studies only assessed one or a few candidate genes. Given that pain is a complex trait, multiple genes with relatively small effects are likely to influence vulnerability to pain. In this study, we evaluated a comprehensive panel of 59 single nucleotide polymorphisms (SNP) in 37 inflammation genes in newly diagnosed non-Hispanic Caucasian lung cancer patients (n = 667) and assessed their association with pain severity. We also assessed the extent to which clinical and demographic factors explain pain severity in this population. Patients rated their pain “during the past week” on an 11-point numeric scale, (0 = ‘no pain’ and 10 = ‘pain as bad as you can imagine’) at presentation, prior to initiating cancer therapy. A score > 7/10 was considered to indicate severe pain. Results showed that 16% of the sample reported severe pain. As expected, severe pain was more prevalent among those with advanced stage of disease (OR = 2.34; 95% CI = 1.50-3.65), younger age (OR = 0.47; 95% CI = 0.30-0.75), depressed mood (OR = 3.68; 95% CI = 1.96-6.93) and fatigue (OR = 3.68; 95% CI = 1.96-6.93). Of the 59 SNPs, we initially found SNPs in 6 genes [IKB 3’-UTR/C/T, TNFA -308GA, TNFB Arg134Cys, IL2-330T/G, IL-8-251 T/A, COX2 3’-UTR/C/T] to be significantly associated with severe pain. Controlling for clinical and demographic variables, we found that carriers of CC alleles for COX2 3’-UTR T/C (OR = 3.24; 95% CI = 1.12, 9.39) and carriers of TT alleles for IL2-330T/G (OR = 1.68; 95% CI = 1.04, 2.73) persisted as significant correlates of severe pain. Because genetic polymorphisms are stable markers, understanding the extent to which genetic variability plays a role on cancer-related pain may prove useful in identifying patients at high-risk for pain development and importantly, could help in understanding patients who might benefit most from symptom intervention, and ultimately in developing personalized and more effective pain therapies.

Breast Cancer Incidence 50 + Years After Low Dose Chest Radiotherapy and Its Implication for Childhood Cancer Survivors

Purpose: Our aim is to estimate the lifetime breast cancer (BC) risk in young children treated with recent lower dose (<25 Gy) mediastinal radiotherapy (mRT) protocols by evaluating the cumulative BC incidence in a cohort treated with low dose chest RT for a benign condition over 50 years ago.

Methods: We reestablished a population-based, longitudinal cohort of subjects exposed to chest RT for an enlarged thymus during infancy from 1926 to 1957 and of their unexposed siblings. Previously followed between 1951 and 1987 for cancer incidence, we re-surveyed cohort members from 2004 to 2008. Self-reported BCs were confirmed by pathology report. We used the National Death Index to check vital status and cause of death for all non-respondents. Person-years at risk were calculated from birth because 95% of subjects were exposed by age 8 months; censoring occurred at date of BC diagnosis, death or last survey response.

Results: BC risk factors were similar in the two groups. During the 53,948 person-years (p-yrs) of follow-up in the 1101 females exposed to thymic irradiation (median breast dose = 0.69 Gy), 93 BCs occurred, resulting in a cumulative incidence rate of...
Increased Risk for Hereditary Breast and Ovarian Cancer

Preimplantation Genetic Diagnosis: Opinions of Women at Childhood with Reduced RT Doses. These women should remain a lifelong concern in female survivors treated during elimination of mRT, it does imply that increased BC risk will decrease BC risk, our results demonstrate that even at lower radiation doses have been shown to decrease BC risk, our results demonstrate that even at substantially lower doses than those used for children today (e.g. smoking, diabetes, family history) and suspected (e.g. BMI, cholecystectomy, diet, physical activity, and alcohol) risk factors. Population attributable risks (PARs) were computed and their impact on age-standardized death rates evaluated.

Results: Blacks had a 42% increased risk of pancreatic cancer mortality (HR = 1.42, 95% CI 1.28-1.58). Cigarette smoking increased risk by >60% in both races. Although Blacks smoked less intensely, risks were similar to Whites (Blacks: HR = 1.67, 95% CI 1.28-2.18; Whites: HR = 1.82, 95% CI 1.7-1.95), with a stronger impact in women than men. Obesity was significantly associated with increased risk in Black men (HR = 1.66, 95% CI 1.05-2.63), White men (HR = 1.42; 95% CI 1.25-1.60) and White women (HR = 1.37; 95% CI 1.22-1.54); results were null in Black women. The PAR due to smoking, family history, diabetes, cholecystectomy, and overweight/obesity was 24.3% in Whites and 21.8% in Blacks.

Conclusions: CPS-II includes the largest number of pancreatic cancer cases available for analysis to date. Smoking and overweight/obesity were strongly associated with pancreatic cancer in Whites and Blacks. The role of overweight/obesity is substantial, and variation in the impact of BMI and smoking underscores the need for studies on the race-sex level. The inability to attribute excess disease in Blacks to accepted risk factors, even when combined with suspected risks, points to yet undetermined factors that play a role in the disease process.

Case-control Study of Smoking and Non-melanoma Skin Cancer


Objective: Findings for an association between smoking and non-melanoma skin cancer (NMSC) have been inconsistent across previous studies, due in part to differences in participant selection and exposure assessment. The objective of the study was to further investigate smoking as a risk factor for NMSC in a well-characterized clinic-based population.

Methods: We conducted a case-control study of 348 histologically confirmed NMSC cases (212 BCC and 136 SCC) recruited from the dermatology clinic at the University of South Florida (USF). Controls were patients undergoing skin cancer screening exams who screened negative for NMSC and had no history of skin cancer (n = 336). Information on smoking and skin cancer risk factors was obtained from self-administered questionnaires. Associations between smoking and NMSC were estimated by odds ratios (OR) and 95% confidence intervals (CI) calculated using logistic regression, adjusting for age, race, ethnicity, education, history of sunburns, occupational sun exposure, eye, hair, and skin color, alcohol use, and protective sun behaviors.

Results: Overall, ever smoking was associated with an increased risk of NMSC (OR = 1.5, 95% CI = 1.0-2.2), including BCC (OR = 1.3, 95% CI = 0.9-2.0) and SCC (OR = 1.2, 95% CI = 1.2-3.8). As compared to never smoking, current smoking was more strongly associated with NMSC (OR = 6.1, 95% CI = 2.6-14.3) than former smoking (OR = 2.0, 95% CI = 1.3-3.2), particularly for SCC (current smoking: OR = 11.4, 95% CI = 3.8-34.5; former smoking: OR = 2.5, 95% CI = 1.3-4.7). Dose-response relationships were observed for both BCC and SCC, with trends for SCC being statistically significant. Specifically, smoking ≥20 years was associated with both BCC (OR = 1.9, 95% CI = 1.1-3.2; P for trend = 0.06) and SCC (OR = 2.7, 95% CI = 1.4-2.3; P for trend = 0.004), as was smoking ≥20 cigarettes per day (BCC: OR = 1.6, 95% CI = 0.9-2.7, P for trend = 0.08; SCC: OR = 2.4, 95% CI = 1.2-4.8; P for trend = 0.01) and ≥20 pack-years of smoking (BCC: OR = 1.7, 95% CI = 1.0-3.1, P for trend = 0.07; SCC: OR = 2.5, 95% CI = 1.2-5.1, P for trend = 0.01).

Conclusion: Smoking is an independent risk factor for NMSC, particularly SCC.

Cancer Epidemiology, Biomarkers & Prevention 2009;18(2). February 2009
Calorie Restriction Inhibits the Development of Pancreatic Cancer through an IGF-1-dependent Pathway

LM Lashinger, L Malone, EA Williams, SN Perkins, A Pavone, SM Fischer, SD Hursting

Recent epidemiologic evidence has established that obesity is an important risk factor for pancreatic cancer, although the underlying mechanisms have not been identified. Calorie restriction (CR), a strategy that prevents obesity, has potent anti-cancer effects in a variety of tumor types. We tested the effects of dietary modulation in BK5.COX-2 transgenic mice which display spontaneous pancreatic ductal lesions that lead to pancreatic ductal adenocarcinoma in response to cyclooxygenase (COX)-2 overexpression. We have found that calorie restriction (CR) significantly protects against these lesions, while control (CON) and high-fat (HF) diets do not. We hypothesized that the anti-tumorigenic effects of CR were due to reduced signaling through the Insulin-like Growth Factor (IGF)-1 pathway. Analyses were performed on tissues collected in this study, in which 6-to-8-week-old wild-type and BK5.COX-2 mice were placed on one of three diet regimens for 14 weeks (n = 12/group): CON (10 kcal% fat, ad libitum (AL); CR (30% of CON calorie intake); or HF (60 kcal% fat, AL). CR mice, relative to the CON and HF-fed mice, demonstrated a significant reduction in serum levels of IGF-1 irrespective of genotype. In addition, CR decreased protein expression of phosphorylated and total forms of IGF-1R, Akt, mTOR, and p70/S6K in the pancreas of BK5.COX-2 mice. The importance of IGF-1 was examined by injecting JC101 cells, a cell line derived from BK5.COX-2 ductal lesions, into 6-to-8-week-old liver-specific IGF-1-deficient (LID) (n = 15) transgenic mice or floxed IGF-1 littermate controls (LC) (n = 15). The LID mice displayed a 65% reduction in serum IGF-1 levels and reduced pancreatic tumor burden (0.23 ± 0.04 g/mouse) relative to LC mice (0.71 ± 0.10 g/mouse). In summary, either dietary or genetic reduction of circulating IGF-1 levels resulted in dramatic reductions in the development of pancreatic cancer. These findings provide the basis for future translational studies targeting the IGF-1 pathway, possibly through lifestyle or pharmacologic approaches, to prevent obesity-related pancreatic cancer.

Long-term Use of Beta-carotene, Retinol, Lycopene, and Lutein Supplements and Lung Cancer Risk

Satia J, Littman A, Slatore C, Galanko J, White E.

Aim: High-dose beta-carotene supplementation in high-risk persons increased lung cancer risk in two randomized clinical trials. It is unclear, however, whether use of supplemental beta-carotene and other carotenoids has similar effects in the general population. We examined associations of supplemental beta-carotene, retinol, vitamin A, lutein, and lycopene with lung cancer risk.

Methods: Eligible men and women, 50-76 y, in the VITamins And Lifestyle (VITAL) cohort Study (n = 77,126) completed a 24-page baseline questionnaire between 2000-2002, including detailed questions on supplement use (duration, frequency, dose) during the previous 10 years from multivitamins, individual supplements, and mixtures. Incident lung cancer cases as of Dec. 31, 2005 were identified by linkage to the SEER cancer registry. Hazard ratios (HR) were estimated via Cox regression, adjusting for smoking/other covariates.

Results: Lung cancer cases (n = 521) were older, male, and only 8% were never smokers. Longer duration of use of individual beta-carotene, retinol, and lutein supplements was associated with statistically significantly elevated risk for total lung cancer and histologic types (g, HR = 2.02, 95% CI: 1.28, 3.17) for individual supplemental lutein with total lung cancer, and for >4 years vs. no use, HR = 3.22, 95% CI: 1.29, 8.07 for individual beta-carotene with small cell lung cancer and HR = 1.80, 95% CI: 1.29, 2.52 for individual retinol with non-small cell lung cancer.

Ten-year average daily intake of supplemental beta-carotene >600 mcg and retinol >1200 mcg were each associated with a non-significant 25% elevated risk. There was little evidence for effect modification by gender or smoking status.

Conclusions: Overall, longer duration of carotenoid supplement use (except lycopene), but not 10-year average daily dose, was associated with significantly elevated lung cancer risk. Long-term use of individual beta-carotene, retinol, and lutein supplements should not be recommended for lung cancer prevention, particularly in smokers. Further studies examining the effects of supplement use on risk of lung and other cancers are needed.

Hispanic Women’s Knowledge and Attitudes towards Genetic Testing for HBOC

Quin G, McIntyre J, Vadaparampil S.

Purpose: This study sought to qualitatively explore knowledge and attitudes for genetic testing information among Mexican, Puerto Rican, and Cuban women at increased risk for hereditary breast and ovarian cancer.

Methods: Women aged 18-65 with a personal or family history of breast or ovarian cancer, were recruited from the Tampa Bay Area. Eligible women participated in a semi-structured interview. Data were analyzed using a combination of open-coding and a hermeneutical approach. Data were coded independently by at least two researchers and an inter-rater reliability rate of 90% was achieved.

Results: Fifty three women participated in the study. For the majority of content areas, there were no major differences between the sub-ethnicities. Women in all groups reported: having discussed cancer among family and friends; associating cancer risk with family history and lifestyle choices, never receiving physician recommendation for genetic testing; limited knowledge of genetic testing; and fear of test results. However, five key areas notably different between the three groups: Puerto Rican women said their primary source of health information is print (newspapers) whereas Cuban and Mexican women reported physicians as their primary source. Cuban and Puerto Rican women reported using the Internet routinely for health care information. Mexican women said they did not use computers. With respect to additional information about genetic testing, the majority of Cuban women wanted more information about what happens after the test (reporting) and how to handle positive results. However, Mexican women wanted to know more about the actual test procedures (pain) and Puerto Rican women wanted more data about the accuracy of the test and risk statistics.

Conclusions: While our data show there are similarities, such as low levels of knowledge and ambivalent attitudes, there are noteworthy differences between the groups on information preferences. In designing genetic education information for Hispanic audiences, it is important to consider varied channels for dissemination and preferences for specific types of information across sub-ethnicities.

Human Papillomavirus (HPV) Vaccine Availability, Recommendations, Cost, and Policies Among Health Departments in Seven Appalachian States

Katz ML, Reiter PL, Kennedy S, Schoenberg N, Johnson A, Ely G, Roberto KA, Lengerich E, Paskett E, Dignan M.

Purpose: To assess HPV vaccine availability, recommendations, cost, and educational materials in health departments in seven Appalachian states.

Methods: Telephone interviews of health department personnel in six states and a review of an immunization database from one state.
Results: There was variation within and among states for HPV vaccine availability, recommendations, costs, policies, and educational materials. Most health departments (230/233, 98.7%) serving the Appalachian counties reported receiving patient requests for the vaccine, and an estimation of the average monthly requests in health departments per state ranged from 10.3 to 21.5 requests. Only three (1%) health departments across the states reported that the HPV vaccine was not available for patients. Current HPV vaccine supply did not meet demand in some health departments due to costs and high demand (up to 48% of the health departments in Virginia). The HPV vaccine was available through the Vaccines For Children (VFC) program in all states, and some health departments in 6 of the 7 states limited the vaccine for only patients in the VFC program. Vaccine policy varied among states, cost per dose ranged from no cost to $170 for women who did not qualify for the VFC program, and most health departments provided patients with educational materials produced by the Center for Disease Control and Prevention and a pharmaceutical company.

Conclusion: Appalachian women suffer a disproportionate cervical cancer burden and future generations could potentially benefit from widespread dissemination of the HPV vaccine. This study documented variation of HPV vaccine availability, recommendations, cost, policies, and educational materials in health departments in Appalachia that could significantly affect vaccine distribution. Findings from this study highlight the need for more consistent policies that maximize accessibility of the HPV vaccine to women, especially those in underserved populations.

A Randomized Clinical Trial Evaluating Online Interventions to Improve Fruit and Vegetable Consumption


Purpose: Accumulating evidence has linked diet to a number of chronic diseases including cancer, prompting calls for innovative dietary interventions and increasing intake of fruits and vegetables (FV). Less than 25% of US adults eat five servings of FV per day, as previously recommended by the National Cancer Institute; far fewer meet current guidelines of 5-9 servings per day.

Methods: We assessed change in FV intake among a population-based sample, comparing an online untailedored program with a tailored behavioral intervention, with and without motivational interviewing-based counseling via email. This trial was conducted through the HMO Cancer Research Network, an NCI consortium of currently 14 research organizations affiliated with nonprofit integrated health care delivery systems, and in collaboration with the Center for Health Communications Research at the University of Michigan. A three arm randomized controlled intervention trial was conducted, enrolling members aged 21-65 years from five health plans in Seattle, Denver, Minneapolis, Detroit and Atlanta. Participants reported FV intake at baseline and at three, six and 12 month follow-ups. Mean change in FV servings per day was assessed at 12 months post baseline, using a validated self-report FV food frequency questionnaire.

Results: Of 2,540 trial participants, 80% were followed up at 12 months. Overall baseline mean FV intake was 4.4 servings per day. Average FV servings increased by >2 servings across all arms ($P < 0.001$), with the greatest increase (+2.8 servings) among participants receiving the tailored intervention plus email counseling ($P = 0.05$ compared to control). Overall program satisfaction was high.

Conclusions: This online nutritional intervention was well-received, convenient, easy to disseminate, cost effective and associated with sustained dietary change. Such programs have promise as population-based dietary interventions.

Vitamin D intake and Breast Cancer Risk among Women Living in the Southwestern U.S.

Rollison D, Giuliano A, Murtzaugh M, Risendal B, Baumgartner K, Byers T, Slattery M.

Objective: Higher vitamin D levels have been inversely associated with breast cancer in several studies, although similar associations have not been consistently observed for vitamin D intake. We investigated the association between vitamin D intake and breast cancer risk in a population-based case-control study of women living in Arizona, New Mexico, Colorado and Utah.

Methods: Breast cancer cases diagnosed in 1999-2004 were identified through state cancer registries ($n = 1,527$ non-Hispanic white (NHW); $n = 791$ Hispanics). Controls were frequency-matched on age and ethnicity, and selected from commercial mailing lists, driver’s licenses and social security records ($n = 1,599$ NHW; $n = 922$ Hispanics). Food consumption was assessed using a validated questionnaire, vitamin D intakes were estimated using the Nutrition Data System for Research, and quartiles were defined based on the controls. Associations with breast cancer were calculated using logistic regression, adjusting for age, study site, education, body mass index (BMI), smoking, age at menarche, age at first birth, parity, recent hormone exposure, height, physical activity, and total calories.

Results: Dietary vitamin D intake was associated with an increased risk of breast cancer (highest vs. lowest quartile (Q4 vs. Q1); odds ratio (OR) = 1.33, 95% confidence interval (CI) = 1.10-1.62, $P$ trend = 0.02), whereas vitamin D supplement use was inversely associated with breast cancer (10+ug/day vs. none: OR = 0.79, 95% CI = 0.65-0.96, $P$ trend = 0.01). Similar patterns in risk were observed by ethnicity, although risks were statistically significant only among Hispanic women (dietary vitamin D, Q4 vs. Q1: OR = 1.65, 95% CI = 1.16-2.33; vitamin D supplement use 10+ug/day vs. none: OR = 0.68, 95% CI = 0.47-0.97). Stratified analyses revealed no significant differences in vitamin D-associated breast cancer risks by menopausal status, BMI or high vs. low total fat consumption.

Conclusion: Breast cancer risks associated with vitamin D varied by source, with increased risks observed for dietary vitamin D and decreased risks observed for vitamin D supplement use.

Lean Mass and PSA Levels in NHANES 2001-2004

Richards C, Neugut A, Rundle A.

Background: Past studies indicate that body mass index (BMI) is inversely associated with PSA levels. It has been suggested that excess adipose tissue, particularly in the abdomen, causes hormonal disturbances that result in lower PSA levels. However, we previously showed in a clinical population that PSA was inversely associated with both lean mass and fat mass, and was positively associated with an abdominal distribution of body fat. Here we seek to replicate these findings in a nationally representative population.

Methods: We analyzed data collected from the National Health and Nutrition Examination Survey (NHANES) between the years 2001 to 2004, including waist circumference and body mass index (BMI) data on 2,107 men and body composition data measured by Bioelectrical Impedance Analysis on 596 men. We conducted cross-sectional multivariable linear regression analyses on both populations to predict PSA levels. SAS Proc SURVEY methods were used to account for the complex survey design and weighting methods used in NHANES.
**Results:** After control for age and race, a 5 pound difference in lean mass was associated with a -5.31% (P = 0.01) difference in PSA, while a 5 pound difference in fat mass was not (2.62%, P = 0.33). Waist circumference was significantly associated with PSA levels (P < 0.01), with a 1 cm increase in waist circumference being associated with a 0.34% decrease in PSA. However, waist circumference controlling for BMI, a measure of abdominal fat distribution, was not associated with PSA levels (P=0.14, P = 0.70).

**Conclusion:** These analyses confirm our prior work and provide further evidence that the hormonal effects of abdominal adipose tissue do not explain the inverse association between BMI and PSA levels. We suggest instead that the greater blood volume associated with both higher lean and fat mass effectively dilute PSA levels, yielding lower test scores.

**Association between BMI, Change in BMI over a Lifetime, and Upper Aerodigestive Tract (UADT) Cancers in the ARCADE Study**


Previous studies have reported a positive association between low body mass index (BMI <18 kg/m²) and upper aerodigestive tract (UADT) cancer risk; and an inverse association with high BMI (≥25 kg/m²). Examining change in BMI over a lifetime may clarify these previous observations. We used data from 2046 cases and 2173 controls from 10 European countries (ARCADE study) to investigate the relationship between BMI and adult change in BMI on UADT cancer risk. Odds ratios (OR) and 95% confidence intervals (CIs) were estimated for associations between BMI at 3 time intervals and BMI change on UADT cancer, adjusting for center, age, sex, education, fruit and vegetable intake, smoking, and alcohol consumption. We observed positive associations between BMI < 18 kg/m² and UADT cancer, inverse associations between BMI ≥ 25 kg/m² for BMI at interview-and 2 years prior and no association with BMI at 30 years of age. BMI decrease (BMI loss < 5%) vs. BMI stability (-5% ≤BMI change < 5%) between age 30 to 2 years prior to study entry showed no overall association with UADT cancer (OR = 1.12 95% CI = 0.84, 1.49). A BMI increase of >5% was inversely associated with UADT cancers (OR = 0.72; 95% CI = 0.59, 0.88). Suggestive associations between oral-oropharyngeal cancer and BMI change possibly indicate preclinical disease status. When stratified by smoking, and by drinking, association with BMI change was restricted to drinkers and smokers. In conclusion, BMI gain is inversely associated with UADT cancers and among current smokers and alcohol drinkers, weight change may serve as a proxy for cancer development and/or presence of UADT cancers.

**Racial Differences in Accuracy of Perceived Risk of Recurrence among Patients with Early-Stage Breast Cancer**

Liu Y, Perez M, Ah R, Schootman M, Gillanders W, Jette DB.

**Purpose:** To evaluate racial differences in accuracy of perceived risk of recurrence (PRR) among patients with early-stage breast cancer.

**Methods:** Patients’ PRR was measured 6 and 12 months after surgery. The 10-year risk of recurrence for ductal carcinoma in situ (DCIS) was estimated from the literature. The 10-year risk of recurrence for early-invasive breast cancer was a sum of risk estimates of three types of recurrence: local recurrence and contralateral breast cancer (both based on the literature) and distant recurrence calculated using Adjuvant! Online. The ‘actual’ risk estimates accounted for treatments received. We compared patients’ PRR with their ‘actual’ risk, creating four risk-perception categories: Accurate, Underestimated, Overestimated, and Uncertain. Three multinomial logit marginal effects models with repeated measures were fitted separately using Accurate as the reference and controlled for age, social support, cancer stage, and surgery type. Analyses were stratified by education and a family history of breast cancer (FHBC).

**Results:** Of 501 patients (90 African American, 411 white; mean age 58, range 40-89; 35% DCIS), 44% Underestimated, 21% Overestimated, and 18% were Uncertain about their actual risk 6 months after surgery; accuracy of PRR did not change significantly at 12 months. African American and white patients did not differ significantly by education or FHBC. African American patients with FHBC (OR = 2.02, 95% CI = 1.13, 3.60) and shigh school education (OR = 2.36; 95% CI = 1.17, 4.79) more likely Underestimated their risk compared with white patients with FHBC and shigh school, respectively. White patients with shigh school education were more likely than African American patients to Overestimate their risk (OR = 4.08; 95% CI = 1.44, 11.54). Racial differences were not found in patients without FHBC or with shigh school education.

**Conclusions:** Whether racial differences in accuracy of PRR observed in patients with FHBC and high school education are associated with subsequent disparities in adherance to recommended follow-up care requires further study.

**Colorectal Cancer Risk in Relation to Antidepressant Use**

Chubak J, Boudreau D, Rulyak S, Mandelson M.

**Purpose:** To determine whether the use of any antidepressants, selective serotonin reuptake inhibitors (SSRIs), or tricyclic antidepressants (TCAs) are associated with colorectal cancer risk.

**Methods:** We conducted a case-control study among enrollees of an integrated healthcare delivery system in Washington State. Cases (N = 641) were diagnosed with colorectal cancer between 2000 and 2003; controls (N = 641) were randomly selected from enrollees and matched to cases on age, sex, and length of enrollment. Controls were assigned a reference date corresponding to the diagnosis date of the matched case. We used conditional logistic regression to estimate the odds ratios (OR) and 95% confidence intervals (CI) for colorectal cancer in relation to the use of any antidepressant, SSRIs only, or TCAs only. In addition to matching variable, we adjusted for smoking status, NSAID/aspirin use, and diabetes. In a secondary, post-hoc analysis, we stratified results by body mass index (BMI) as measured 12-36 months before reference date.

**Results:** The use of any antidepressant was associated with a reduced risk of colorectal cancer (OR = 0.71, 95% CI = 0.53-0.94). Point estimates were similar for persons who used SSRIs exclusively (OR = 0.64, 95% CI = 0.34, 1.20) and TCAs exclusively (OR = 0.72, 95% CI = 0.44, 1.16) during the study period. Post-hoc analysis suggested that the association might be strongest in obese persons.

**Conclusions:** Our data support a previous epidemiologic study and several animal studies that antidepressants may reduce the risk of colorectal cancer. Previous studies have suggested a decreased risk with SSRI use, but results from studies of TCAs have been inconsistent; we did not have power to detect a reduced risk associate with use of either class of antidepressants individually. Future studies with larger sample sizes should be conducted to examine SSRIs and TCAs separately, individual drugs, and dose-response relationships.
Low Serum Levels of 25-Hydroxyvitamin D (25(OH)D) are Associated with Increased Risk of Clear Cell Renal Cell Carcinoma
Parker AS, McNeil RB, LeRoy TJ.

Introduction and Objective: Vitamin D deficiency has been linked with an increased risk of several human cancers; however, this hypothesis has not been adequately explored for clear cell renal cell carcinoma (ccRCC) specifically. This is noteworthy given that preclinical studies suggest that ccRCC cell lines are inhibited by the active form of vitamin D.

Methods: We analyzed 25(OH)D serum levels from 104 ccRCC cases and 71 non-cancer controls. Cases were prospectively collected as part of our Renal Mass Registry. As part of this registry, we collect detailed risk factor data (self-report questionnaire) as well as a pre-treatment, fasting blood sample. Tumor samples are reviewed by a pathologist to confirm histologic subtype and pathologic features. Controls were recruited through the Family Medicine Clinic as part of our Non-Cancer Control Registry. Each control completed the same risk factor questionnaire as the cases and provided a fasting blood sample. Controls were frequency matched to cases on age, gender and state of residence. We employed polychotomous logistic regression analyses to estimate the association of low serum 25(OH)D (<34 ng/mL) and ccRCC status, both overall and for aggressive ccRCC specifically.

Results: Overall, cases had approximately 2.2 times the odds of being vitamin D deficient as controls, regardless of aggressiveness level (95% confidence interval 1.1 to 4.4). The proportional odds assumption was not violated ($P = 0.27$), indicating that the odds of deficiency are consistent regardless of the reference category. Adjustment for BMI, smoking history and season of serum collection did not alter our results.

Conclusion: Our data suggest that low levels of serum 25(OH)D are associated with an increased risk of ccRCC development. Of note, our results are consistent with the findings of a previous Japanese investigation from 2000. Given the possible implications for prevention, future investigations that analyze a larger sample size and examine additional aspects of the vitamin D signaling pathway are warranted.