

**ABSTRACTS • 36th Annual Meeting • American Society
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The following are the 20 highest scoring abstracts of those submitted for presentation at the 36th Annual ASPO meeting held March 4–6, 2012, in Washington, DC.

The Role of Polymorphisms in DNA Repair Genes and HPV 18 Integration Status in Cervical Dysplasia

Amirian ES, Marquez-Do D, Adler-Storh K, Follen M, Scheurer ME

Despite the fact that cervical cancer is one of the leading causes of death in women worldwide, research has yet to elucidate why some HPV-infected women develop cancerous lesions while others are able to clear the infection. Previous studies have shown that HPV integration status may be associated with cervical cancer development, and yet, host genetic factors that may be involved in the viral integration process have not yet been identified. The purpose of this study was to examine the association between both HPV 18 viral integration status and single nucleotide polymorphisms (SNPs) in non-homologous end-joining (NHEJ) DNA repair pathway genes on cervical dysplasia. Specifically, we sought to compare women with no dysplasia to those with low-grade or high-grade squamous intraepithelial lesions. **METHODS:** A total of 765 women were selected from two large trials designed to evaluate optical technologies for cervical cancer. Genotyping was performed using the Illumina Golden Gate platform. HPV 18 integration status was determined using a previously established protocol. Chi-square tests were conducted to determine which SNPs were associated with normal cytology, low-grade, or high-grade lesions. Among participants with cervical dysplasia, polytomous logistic regression models were used to evaluate the effect of each polymorphism on viral integration status. An additive genetic model was used for all tests. P-values were adjusted using the false discovery rate method. **RESULTS:** Women with high-grade lesions were significantly younger than women with low-grade or no lesions. Tag-SNPs in 13 DNA repair genes, including MRE11A, ATM, and XRCC4, were significantly associated with cervical dysplasia. Most participants had a mix of both episomal and integrated HPV 18. Tag-SNPs in the XRCC4, PRKCH, and MRE11A genes were found to be significantly associated with HPV 18 integration

status. **CONCLUSION:** Our study indicates that host genetic variation in NHEJ DNA repair pathway genes, including MRE11A and XRCC4, are significantly associated with HPV 18 integration, and that these genes may play a key role in determining cervical cancer development and progression. This is the first study to examine host genetic variation in association with the viral integration event.

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Predictors of Cancer Survivors' Receptivity to Lifestyle Behavior Change Interventions

Basen-Engquist K, Carmack C, Blalock J, Baum G, Rahming W, Demark-Wahnefried W

Purpose: To assess cancer survivors' interest in lifestyle behavior change interventions, and to identify predictors of interest.

Methods: Mailed surveys were sent to a stratified random sample of breast, colorectal, and prostate cancer survivors ascertained from the MD Anderson tumor registry and departmental databases. Surveys queried survivors about their diet, exercise, and smoking behaviors; symptoms; and their interest in interventions.

Results: Surveys were received from 1053 cancer survivors. Roughly half of the sample were very/extremely interested in programs to help them get in shape (45%), eat a healthy diet (54%), and control weight (49%), and 20% had no interest at all. Because they were highly intercorrelated we combined interest in diet/exercise/weight control into a single interest index. Interest was related to race/ethnicity (AA and Hispanics more interested than whites), age ($p = .000$, younger more interested), marital status ($p = .000$, divorced most interested, widowed least interested), education ($p = .008$, college-educated less interested than those with HS degree or some college/vocational training), and gender ($p = .000$; women more interested). Interest was not related to time from diagnosis, and there were no differences by cancer site after controlling for gender. BMI had a small but significant correlation with interest in programs ($r = .19$, $p = .000$; the correlation was higher in women [$r = .24$] than men [$r = .18$]). Symptom severity and interference, and feelings of distress

and sadness, were positively correlated to interest ($r = .07-.12$, $p = .000-.034$); relationships were stronger among men than women. Among the 78 smokers, 51% were very/extremely interested in smoking cessation, while 20% were not at all interested. Demographic and disease-related predictors were not significantly related to interest in smoking cessation, but symptom severity and interference, and feelings of sadness were positively related to interest.

Conclusion: Survivors' interest in lifestyle behavior change interventions varies with demographic variables, but also with symptom distress. Experiencing symptoms after cancer diagnosis is related to higher receptivity to intervention opportunities.

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Ruminant Fatty Acids and Prostate Cancer Risk in the Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study

Wright M, Albanes D, Moser A, Snyder K, Virtamo J, Gann P

Consumption of high fat animal products is a characteristic feature of Western diets, which have been consistently linked with elevated risks of prostate cancer. In order to elucidate which specific fatty acids may contribute to this association, we measured circulating concentrations of myristic (C14:0), pentadecanoic (C15:0), palmitic (C16:0), heptadecanoic (C17:0), vaccenic (C18:1n-7), and alpha-linolenic (C18:3n-3) acids - all of which are present in ruminant meat and/or dairy products - in a nested case-control study within the Alpha-Tocopherol, Beta-Carotene Cancer Prevention (ATBC) Study. Prediagnostic blood samples from 300 prostate cancer cases and 300 controls matched on age and date of serum blood draw were analyzed for the aforementioned fatty acids by gas chromatography-mass spectrometry. There was a positive association between serum alpha-linolenic acid and overall prostate cancer risk, with a notable threshold effect (for increasing quartiles, odds ratios and 95% confidence intervals = 1.0 (referent), 1.65 (1.02-2.67), 1.96 (1.22-3.14), and 1.57 (0.97-2.54); p trend = 0.15). This association was stronger among men with low baseline levels of beta-carotene and vitamin E. The other fatty acids were unrelated to prostate cancer risk. Our findings indicate that higher blood levels of alpha-linolenic acid - the predominant omega-3 fatty acid in Western diets - is associated with elevated risks of prostate cancer, particularly within subgroups of men with low antioxidant levels.

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Prospective Cohort Studies of Vitamin B6 Intake and Colorectal Cancer Incidence: Modification by Time?

Zhang X, Lee JE, Ma J, Je Y, Wu K, Willett WC, Fuchs CS, Giovannucci EL

Background: Vitamin B6 may influence colorectal carcinogenesis through its role in one-carbon metabolism related DNA synthesis and methylation. However, observational studies have been inconclusive and no studies have investigated when in the natural history vitamin B6 intake may prevent colorectal cancer.

Method: We followed 86,440 women in the Nurses' Health Study and 44,410 men in the Health Professionals Follow-up Study for up to 28 years. We assessed vitamin B6 intake every 4 years using validated food frequency questionnaires. We evaluated whether higher vitamin B6 intake in the remote past is strongly associated with a lower risk of colorectal cancer than intake in the recent past. Cox proportional hazards regression models were used to estimate multivariable relative risks (MV RRs, 95% CIs).

Results: Comparing top with bottom quintiles of total vitamin B6 intake, the mean plasma pyridoxal 5-phosphate (PLP, the active form of vitamin B6) levels were 98.3 pmol/mL and 38.9 pmol/mL in women and were 183.2 pmol/mL and 66.0 pmol/mL in men. Total vitamin B6 intake was significantly associated with an approximately 20-30% lower risk of colorectal cancer in age-adjusted results but these significant associations became attenuated and non-significant after adjustment for other colorectal cancer risk factors. Compared extreme quintiles of cumulative intake of total vitamin B6, the MV RRs (95% CIs) for colorectal cancer were 0.98 (0.80, 1.22; P trend = 0.79) in women and 0.98 (0.76, 1.26; P trend = 0.60) in men. For the same comparison, the MV RRs were 0.92 (0.73, 1.16) for total vitamin B6 intake 0-4 year before diagnosis, 0.99 (0.78, 1.26) for intake 4-8 year before diagnosis, 0.93 (0.71, 1.21) for intake 8-12 year before diagnosis, and 0.93 (0.69, 1.26) for intake 12-16 years before diagnosis. The corresponding MV RRs for men were 0.85 (0.63, 1.16), 0.98 (0.70, 1.37), 0.90 (0.63, 1.28), and 1.19 (0.78, 1.83), respectively. Additionally, results did not differ by cancer sub-site, sources of vitamin B6 (food or supplement), or intake of alcohol and folate.

Conclusion: Although a small effect cannot be excluded, our results do not support a strong role of vitamin B6 intake in adulthood in colorectal carcinogenesis among middle-aged U.S. health professionals.

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Tobacco Addiction and The Risk of Upper Aerodigestive Tract Cancer in A Multicenter Case-Control Study

Lee YC, Marron M, Benhamou S, Bouchardy C, Ahrens W, Pohlman H, Laggiou P, Trichopoulos D, Agudo A,

Castellsague X, Bencko V, Holcatova I, Kjaerheim K, Merletti F, Richiardi L, Macfarlane GJ, Macfarlane TV, Talamini R, Barzan L, Canova C, Simonato L, Conway DI, McKinney PA, Thomson P, Znaor A, Healy CM, McCartan BE, Boffetta P, Brennan P, Hashibe M

Background: While previous studies on tobacco and alcohol and the risk of upper aerodigestive tract (UADT) cancers have clearly shown dose-response relations with the frequency and duration of tobacco and/or alcohol, studies on addiction to tobacco itself as a risk factor for UADT cancer have not been published, to our knowledge. The aim of this report is to assess whether smoking addiction is a risk factor for UADT SCC risk in the multicenter case-control study (ARCAGE) in Western Europe independent of tobacco smoking or alcohol drinking intensity or duration. **Methods:** The analyses included 1,905 ever smoking UADT SCC cases (871 oral cavity/oropharynx, 814 hypopharynx/larynx, 127 esophagus, and 93 overlapping oral cavity/pharynx) and 1,489 ever smoking controls. The addiction variables included first cigarette after waking up, difficulty refraining from smoking in places where it is forbidden, and cigarettes per day. Odds ratios (OR) and 95% confidence intervals (95% CI) for UADT cancers with addiction variables were estimated with unconditional logistic regression, adjusting for center, age, sex, education level, alcohol consumption, and tobacco smoking. **Results:** Among current smokers, 76.47% of cases were categorized in the highest addiction level, whereas 54.69% of controls were in that category. The participants who smoked their first cigarette within 5 minutes of waking up were two times more likely to develop UADT SCC (OR = 2.22, 95% CI 1.57–3.15) than those who smoked 60 minutes after waking up. A higher modified Fagerstram score, reflecting greater tobacco addiction, was associated with an increased risk of UADT SCC among current smokers, but not among former smokers. **Conclusion:** We observed that time to first cigarette after waking up was associated with UADT SCC risk, regardless of heavy smoking or alcohol drinking behaviors. These results are consistent with residual effect of smoking that was not captured by the questionnaire responses alone.

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Perceived Risk and Worry for One's Partner and Self Correlate With Desire to Quit in Dual-Smoker Couples

Ranby KW, Lewis MA, Toll BA, Rohrbaugh MJ, Lipkus IM

Among smokers, the desire to quit smoking is often related to one's health concerns. However, much less is known about how perceptions of health concerns are

related in couples in which both partners smoke (i.e., dual smoker couples) and their associations with desire to quit for self. We explored these issues using baseline survey data collected from 63 dual smoker couples recruited from the community in central North Carolina. Participants were aged 21 to 67 (M = 43.0, SD = 11.3) and had been smoking for 4 to 51 years (M = 22.9, SD = 11.3) with an average of 17 (SD = 8.8) cigarettes per day. Within couples, partners exhibited similar beliefs about worry about physical harm of smoking for oneself ($r = .30, p < .05$) and partner ($r = .30, p < .05$), perceived risk of disease for self ($r = .26, p < .05$) and partner ($r = .24, p < .05$), and desire that their partner quit ($r = .34, p < .01$). Individuals' desire to quit was related to their own perceived risk of disease ($r = .34, p < .05$) and worry about harm ($r = .47, p < .001$). Further, own desire to quit was related to worry about partner's health ($r = .29, p < .01$), perceived risk of partner getting a disease if they continued to smoke ($r = .39, p < .001$), and belief that their smoking has caused partner physical harm ($r = .38, p < .001$). Participants had an extremely strong desire (78% = 7 on 1–7 scale) for their partner's help if they were to quit smoking. These data show 1) there is significant concordance in partners' rating of risk of disease and worry; and 2) an individual's desire to quit is related to both one's perceptions of risk and worry of harm for self but also importantly perceptions of risk, and worry of harm for the partner. Interventions that highlight how smoking harms a couple may be a fruitful, yet currently under-utilized, method to increase cessation in dual smoker couples, a high risk group with lower cessation rates and higher relapse rates.

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Phenol Xenoestrogens and Mammographic Breast Density

Trentham-Dietz A, Sprague BL, Wang J, Hampton JM, Buist DSM, Aiello Bowles E, Sisney G, Burnside E, Hemming J, Hedman C

Concerns have been raised, largely on the basis of laboratory studies, regarding exposure to phenols, particularly bisphenol-A (BPA), in relation to hormone-related cancers. BPA is present in plastic consumer products including canned food linings and #7 polycarbonate plastics. According to recent NHANES data, human exposure as measured in urine is widespread (about 93% of people aged >5) and more common in females than males (Calafat EHP 2008). Concern regarding BPA in relation to breast cancer risk is based on in vivo and in vitro studies that suggest BPA may have a role in estrogen metabolism and mammary gland development. We examined the cross-sectional association of circulating serum levels of 3 phenols with mammographic breast density - a strong marker for breast cancer risk. A total of

264 postmenopausal women ages 55–70 years with no history of postmenopausal hormone use were recruited from mammography clinics in Madison, Wisconsin. Subjects completed a questionnaire regarding known breast cancer risk factors and provided a blood sample that was analyzed for octylphenol, nonylphenol, and BPA. Percent breast density (mean 15.3%, range 0.4–71.2%) was measured from subjects' mammograms using a computer-assisted thresholding method (Cumulus software). Since phenol levels are higher in the urine than in the serum, as expected many women had undetectable levels of the phenols in their serum: 86.7% octylphenol, 58.7% nonylphenol, and 73.1% BPA. After adjusting for age and body mass index in analysis of variance models, women with detectable serum BPA levels above the median (>0.56 ng/mL; $N = 35$) had higher percent breast density than women with BPA levels below the median (0.01 – 0.56 ng/mL; $N = 36$) and women with no detectable BPA ($N = 193$) in their serum (17.8% vs. 13.3% vs 12.7%, respectively; $P = 0.01$). Breast density was not associated with serum levels of either octylphenol or nonylphenol ($P = 0.77$, $P = 0.36$, respectively). Given that this study suggests that higher levels of BPA were associated with a clinically-relevant 5% greater breast density, further investigation into the potential influence of BPA on breast cancer risk using human populations is warranted. Supported by DOD BC062649, Komen FAS0703857, and NIH R03 CA139548.

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Reduction in Breast Cancer Risk Associated with Meeting the WCRF/AICR Cancer Prevention Recommendations

Hastert T, White E

In 2007 the World Cancer Research Fund (WCRF) and the American Institute for Cancer Research (AICR) published eight recommendations related to body weight, physical activity and dietary behaviors aimed at reducing cancer incidence worldwide. These were based on a comprehensive review of the literature on these topics in relation to each of the common cancers. An expert panel operationalized seven of those recommendations (maintaining normal body weight, participating in moderate physical activity for at least 30 minutes per day, avoiding energy-dense foods, eating 5 or more servings of non-starchy fruits and vegetables per day, limiting consumption of red meat to no more than 18 oz per week, limiting alcohol consumption to one drink per day for women and two drinks per day for men, and limiting sodium consumption to 2400 mg per day), and we examined their association with breast cancer incidence over eight years of follow-up in the VITamins And Lifestyle (VITAL) Study cohort. Participants included 24,916 women aged 50–76 years at baseline in 2000–2002 who had no history of cancer and who had complete data for

the recommendations evaluated. Incident cancers ($n = 694$) were tracked through the Western Washington Surveillance, Epidemiology and End Results (SEER) database. The median number of recommendations followed was 3 (0–7). After adjusting for age, education, race/ethnicity, mammogram in previous two years, history of breast cancer in a first-degree relative, years of combined estrogen plus progestin hormone therapy use, age at menarche, age at first birth, and age at menopause, the hazard ratios and 95% confidence intervals associated with meeting 1, 2, 3, 4, 5, and 6–7 recommendations compared with meeting none of the recommendations were: 0.57 (0.35, 0.95), 0.63 (0.39, 1.02), 0.55 (0.34, 0.88), 0.46 (0.28, 0.74), 0.44 (0.26, 0.75), and 0.31 (0.15, 0.65). These results suggest that meeting the WCRF/AICR recommendations could substantially decrease breast cancer risk.

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An Affective Booster Moderates the Relationship Between Message Frame and Behavioral Intentions

Ferrer RA, Klein WMP, Zajac LE, Land SR, Ling BS

This study examined whether emotion moderates the degree to which framed messages influences colorectal cancer (CRC) screening intentions and self-efficacy for screening. Previous research has demonstrated that loss-framed messages are more effective than gain-framed messages in motivating detection behaviors such as screening. However, overall effects of framing in the context of health messages have been small and heterogeneous, highlighting the pressing need to identify moderators of framed message effectiveness. We paired a standard framing manipulation with an "affective booster" to increase anticipated and anticipatory emotions associated with the framed messages in a 2×2 (gain-loss by affective booster-no booster). The loss-framed message was paired with a complementary affective booster intended to facilitate worry and regret; the gain-framed message was paired with a complementary booster intended to facilitate relief. Consistent with previous research, we found that loss-framed messages were more effective in increasing intentions to screen for CRC ($\hat{\beta}^2 = .38$, $t = -2.19$, $p = .03$, $d = 0.55$). The inclusion of the affective booster had no overall effect on intentions to screen ($\hat{\beta}^2 = -.06$, $t = -0.39$, $p = .70$, $d = 0.10$). However, we found a significant interaction ($\hat{\beta}^2 = .48$, $t = 2.13$, $p = .04$, $d = 0.53$), such that among individuals who received gain-framed messages (but not loss-framed messages), the affective booster increased message persuasiveness. A similar pattern of results was uncovered with respect to self-efficacy for screening, where an affective booster increased self-efficacy among the gain-frame message recipients, bringing their self-efficacy in line with those who had received the loss-framed message. This study indicates that in the presence of affective boosters,

loss-framed messages may lose their advantage over gain-framed messages in motivating detection behaviors.

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Lifestyle and Dietary Risk Factors for Colorectal Hyperplastic and Adenomatous Polyps

Michal S, Li L, Chen Z

Background: Increasing evidence suggests that colon hyperplastic polyps (HP) increases predisposition to the development of colon cancer, albeit to a lesser degree than colon adenoma. Data on behavioral and lifestyle risk factors for HP are limited.

Methods: We compared the risk factor profiles for colon adenoma and colon HP in 1,826 patients without known history of colorectal cancer or polyps who are undergoing screening colonoscopy at our institution. Five hundred and eight patients were diagnosed with one or more colon adenomas, 215 with HP, 140 patients with both adenoma and HP, and 963 with negative colonoscopic examination. Information on behavioral and lifestyle risk factors and dietary habits were collected by computer-assisted personal interview (CAPI) and Food Frequency Questionnaire prior to colonoscopy. We used multivariate unconditional logistic regressions to assess risk associations.

Results: Positive association were found between adenomatous polyps and male gender (OR 1.702, 95% CI 1.210–2.394, p 0.002), current smoker (OR 1.598, 95% CI 1.091–2.340, p 0.016) and family history (OR 1.409, 95% CI 1.034–1.920, p 0.030). For hyperplastic polyps, positive associations were found between current smoker (OR 2.038, 95% CI 1.207–3.441, p 0.008) and regular alcohol drinker (OR 1.661, 95% CI 1.057–2.610, p 0.028). For both types of polyps positive associations were found between male gender (OR 2.282, 95% CI 1.233–4.222, p 0.009), current smoker (OR 2.692, 95% CI 1.475–4.912, p 0.001) and family history (OR 2.472, 95% CI 1.506–4.057, p 0.00). In a subgroup analysis by gender, regular alcohol consumption (OR 1.780, 95% CI 1.008–3.143, p 0.047) was associated with increased risk and HRT (OR 0.450, 95% CI 0.225–0.903, p 0.025) was associated with a decreased risk of hyperplastic polyps in females. Whereas in males, ever smokers (OR 3.074, 95% CI 1.357–6.965, p 0.007) and current smokers (OR 3.311, 95% CI 1.307–8.389, p 0.012) were associated with an increase risk of hyperplastic polyps.

Conclusion: Our data indicate that there are several lifestyle and dietary risk factors that are associated with both colorectal adenomatous and hyperplastic polyps. These risk factors vary not only by type of polyp but also gender.

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Deficits in Health-Promoting Behaviors Among Veteran and Non-Veteran Male Cancer Survivors in Texas

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Objectives: Cancer survivors may have increased risk for additional malignancies and illnesses. Veterans comprise a significant proportion of Texas male cancer survivors and may differ in their health status and needs from non-veterans. It is unknown whether they differ in general health-promotion strategies. This study sought to identify deficits in health-promoting behaviors among Texas male cancer survivors and to determine whether veteran-status predicts differences along these behaviors.

Methods: Using the Behavioral Risk Factor Surveillance System 2009 survey, we conducted secondary analysis of 280 veteran and 250 non-veteran Texas male cancer survivors. Data were analyzed using Fisher's exact test and logistic-regression models.

Results: Survivors averaged 68 years (SD = 11.4) and were primarily white (93%), married (71.5%), college graduates (51%), and non-smokers (91%). Respondents reported several different cancer diagnoses; most commonly prostate (28%). More non-veterans than veterans were obese (31.6% vs. 22.5%; p = 0.03). Veteran-status was not associated with other co-morbidities, current smoking, binge drinking, or fruit/vegetable consumption. However, only 22% met recommendations for daily fruits/vegetables. In multivariate regression, veterans were less likely to meet moderate (OR = 0.54, 95% CI = 0.30–0.95) and vigorous (OR = 0.67, 95% CI = 0.45–0.99) physical-activity recommendations, but were more likely to have had health examinations within the previous year (OR = 1.77, 95% CI = 1.11–2.83).

Conclusion: Texas male cancer survivors reported deficits across important health behaviors, including dietary and physical-activity recommendations. Veterans reported low compliance with physical-activity guidelines, in spite of evidence-based veterans health-promotion programs, e.g., MOVE! ®. Our results suggest veterans' adherence to routine care may offer a point of intervention to implement health-promotion guidelines among cancer survivors. Further research is needed to understand how to use the growing focus on cancer survivorship within the VA healthcare system to encourage greater adoption of health promotion practices among veteran cancer survivors.

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Observed Social Support Behaviors and Cancer-Related Cognitive Processing in Couples Coping with Head and Neck Cancer (HNC)

Milbury K, Badr H

Given the disfiguring and debilitating nature of HNC and its treatment, patients and their spouses are at risk of

experiencing trauma symptoms including cognitive intrusion and avoidance which may exacerbate psychological distress. Even though the Social Cognitive Processing Model (SCPM) posits that social support facilitates adaptive cognitive processing, recent literature has pointed to harmful effects of received support. Most studies use self-report measures of perceived as opposed to actual received support focusing on the patient as the recipient of support. In reality, the support process is reciprocal and interdependent involving both receiving and providing support in both patients and spouses. Further, self-reports of cognitive processing are susceptible to self-presentation and defensive biases. The purpose of this research was to examine the association between actual observed support behaviors and cognitive intrusion and avoidance in 60 newly diagnosed HNC patients (87% male) and their spouses using a multi-method approach. As part of an ongoing longitudinal study, couples completed baseline questionnaires including an explicit measure of cognitive intrusion and avoidance (IES), completed a problem-solving discussion task in the laboratory immediately followed by an implicit assessment of cognitive intrusion (cancer Stroop task (CST)). We used the Social Support Interaction Coding System (SSICS) to code the video-recorded discussions. Dyadic analyses using multi-level modeling revealed that when patients and spouses received more (compared to less) positive support behaviors, they demonstrated slower reaction times (RT) on the CST ($p < .01$) indicating greater cognitive intrusion. The results were similar using the self-report method (IES; $p < .05$). No role differences (patients vs. spouses) were found. The current findings map on to recent literature suggesting that receiving support may be initially distressing in the acute phase of the traumatic event as it may elicit negative emotional responses, which are yet necessary to facilitate successful long-term adjustment. Thus, our next step in this ongoing longitudinal study is to examine long-term consequences of these findings as they will reveal clinical implications.

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Epidemiological Risk Factors Associated with Inflammatory Breast Cancer Triple Negative Subtype

Atkinson RL, Sexton K, Ueno NT, Krishnamurthy S, Woodward W, El-Zein R, Brewster AM

Background: Inflammatory breast cancer (IBC) is rare and accounts for ~1% of all invasive breast cancers. The 5-year survival rates are significantly lower than for other types of breast cancer, highlighting the significance of cancer prevention in IBC. A disproportionately higher percentage of IBC patients have triple-negative breast cancer (TNBC; ER⁻, PR⁻ and Her2⁻) than patients with non-IBC. TNBCs are thought to arise from normal breast stem cells. Our preliminary data indicates that normal

breast stem cells are enriched in adjacent normal tissues of patients with TN IBC. We hypothesize that parity and breastfeeding, risk factors that influence the normal stem cell compartment in the breast, will differ between TN IBC and non-TN IBC subtypes.

Methods: We identified 144 patients diagnosed with IBC in 1991–2011 at MD Anderson. Breast cancer risk factors including parity and breast-feeding were compared between patients with TN and non-TN IBC with chi square or Wilcoxon rank sum tests.

Results: The average age at diagnosis was 54 years; 83% of patients were non-Hispanic white; and 36% were TN IBC. We found that patients with TN IBC had significantly lower frequency ($p = 0.02$) and duration of breastfeeding ($p = 0.02$) compared with non-TN IBC patients. No differences were found in the frequency of other breast cancer risk factors.

Conclusion: The association between breastfeeding and TNBC indicates that stem cells that are retained in the absence of breastfeeding may be the cell of origin for TN IBC. These results highlight the importance of evaluating epidemiologic risk factors of IBC according to receptor subtype, which could lead to the identification of distinct etiologic pathways that could be targeted for prevention.

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Non-Physician Providers, Cancer Screening and Health Behavior Counseling

Kepka D, Yabroff KR

Purpose: Patients who receive a physician's recommendation for cancer screening and behavioral modification are most likely to comply with these recommendations. However, physicians face time constraints that make it nearly impossible to provide all recommended preventive services. The 2010 Affordable Care Act will expand health insurance coverage to 42 million Americans by 2014. Non-physician providers may help meet this new demand for primary care and ensure compliance with preventive services recommendations.

Methods: Data from the 2005 National Health Interview Survey were analyzed using multivariate logistic regression to assess the association between provider type seen in the past 12 months and compliance with U.S. Preventive Services Task Force cancer screening recommendations and receipt of behavior counseling among age-eligible adults ($n = 23,201$). Models were adjusted for age, level of education, and insurance status and stratified by gender.

Results: About 15% of NHIS participants ($N = 4,652$) saw a non-physician provider (nurse practitioner, certified nurse midwife or physician assistant) and a primary care physician. In adjusted analyses, age-eligible women were more likely to be compliant with Pap screening

(OR: 5.0; 95% CI: 4.2–5.9), mammography (OR: 6.6; 95% CI: 5.2–8.4) and colorectal screening recommendations (OR: 7.8; 95% CI: 5.3–11.4) if they saw a non-physician provider and a primary care physician compared to not seeing any provider. Similarly, men were more likely to be compliant with colorectal screening recommendations (OR: 9.6; 95% CI: 6.9–13.5) if they saw a non-physician provider and a primary care physician. Women and men were more likely to report a provider asking about smoking status if they saw a non-physician provider and a primary care physician than those who saw other types of healthcare providers ((OR: 2.2; 95% CI: 2.0–2.4) and (OR: 3.0; 95% CI: 2.4–3.7), respectively).

Conclusions: Seeing a non-physician provider and a primary care physician is related to an increased likelihood of compliance with cancer screening recommendations and receipt of health behavior counseling. Opportunities exist for non-physician providers during this era of healthcare reform.

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Benefits and Harms of Screening Mammography Frequency by Age and Comorbidity Score

Braithwaite D, Zhu W, Hubbard R, O'Meara ES, Miglioretti DL, Geller B, Dittus K, Wernli K, Moore D, Kerlikowske K, for the Breast Cancer Surveillance Consortium

Background: There is uncertainty about the appropriate use of screening mammography in older women. We compared the benefits and harms of screening mammography frequency according to age and comorbidity scores.

Methods: We conducted analyses within a prospective cohort study of four mammography registries in the Breast Cancer Surveillance Consortium that had mammography data linked to Medicare claims information. Participants included 137,949 women aged 66–89 years without breast cancer and 2,993 women with breast cancer. We estimated odds of advanced (IIb, III, IV) stage, large tumor size (>20 millimeters), and estrogen receptor (ER) negative tumors and cumulative probability of false-positive mammography after 10 years of screening by mammography frequency, age and comorbidity score as determined by the Charlson Comorbidity Index.

Results: Mammography biennially vs. annually for women aged 66–89 years does not increase risk of tumors with unfavorable characteristics regardless of women's comorbidity score. Cumulative probability of a false-positive result for annual and biennial screening of women aged 66–89 years with a comorbidity score of ≥ 1 was 48 (46.1, 49.9) and 29 (28.1, 29.9) respectively. False-positives were more common among annual screeners than among those screened biennially irrespective of women's comorbidity score.

Conclusion: Mammography annually vs. biennially does not have added benefit for women aged 66–89 years, even among those in good overall health as reflected by the lack of comorbidity. Risk of false-positive mammography is much higher with annual mammography.

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Immune Responses Contribute to Depression, Fatigue, and Pain in Hematopoietic Stem Cell Transplant Recipients

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Depression, fatigue, and pain are prevalent and distressing quality of life concerns for individuals recovering from hematopoietic stem cell transplantation (HSCT). Recent research in other cancer populations suggests inflammatory cytokines can activate central nervous system pathways, evoking adverse behavioral responses including depressed mood, fatigue, and pain. We hypothesized that inflammatory responses also contribute to these symptoms among HSCT recipients. Participants (24 allogeneic and 68 autologous transplant recipients) completed well-validated measures of depressive symptoms, fatigue, and pain prior to transplant and 30, 100, and 200 days post-transplant. Circulating proinflammatory (IL-6, TNF α) and regulatory (IL-10) cytokines were measured by ELISA in peripheral blood plasma at the same time points. Subject-level fixed effects and mixed effects linear regression models were employed to examine relationships between cytokine levels and quality of life assessments. Results indicated that depression and fatigue were most severe 30 days post-transplant, with allogeneic recipients showing markedly slower improvement than autologous recipients at later assessments. Pain did not change significantly over time. Among individual patients, changes in IL-6 levels across the assessment points were associated with corresponding changes in depressive symptoms ($t = 2.0$, $p = .048$), fatigue ($t = 2.7$, $p = .008$), and pain ($t = 2.0$, $p = .048$), after adjusting for the effects of time since transplant. Similarly, participants with elevated IL-6 levels reported more severe depression ($z = 2.9$, $p = .004$), fatigue ($z = 2.9$, $p = .004$), and pain ($z = 3.0$, $p = .003$) compared to participants with low/normal IL-6 levels. All models adjusted for graft type and recipient's age. Similar relationships were seen for IL-10, while TNF α was not significantly associated with symptoms. Results provide evidence for a novel biobehavioral pathway by which inflammatory processes secondary to treatment and/or treatment-related complications may contribute to depression, fatigue, and pain among HSCT recipients. Findings may assist

health care providers in identifying patients at risk for this constellation of symptoms.

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Race and Risk of Large Bowel Polyps in Younger and Older Patients

Wallace K, Ahnen D, Burke C, Barry E, Bresalier R, Saibil F, Baron J

African Americans (AA) have a higher incidence of colorectal cancer (CRC) compared to European Americans (EA). However, AA are consistently diagnosed with CRC at a younger age suggesting a possible biologic difference in neoplasms by race. Few studies have investigated racial differences in risk of adenomas, precursors to most colorectal cancer and, to our knowledge, none have investigated whether this risk differs by adenoma type or age. To address this gap, we analyzed data pooled from three placebo-controlled adenoma chemoprevention trials to explore racial differences in the risk of large bowel polyps among younger and older subjects. Eligible subjects had at least one documented adenoma and were followed until their next scheduled colonoscopy. Using generalized linear regression, we estimated risk ratios and 95% confidence intervals (CI) as measures of the association between race and risk for one or more adenomas, advanced lesions, or hyperplastic polyps (HP) after randomization adjusting for age, sex, follow-up time, and treatment assignment. We defined advanced lesions as adenomas with at least 25% villous component, high-grade dysplasia, or an estimated size of $1 \geq$ centimeter. We also assessed the potential interaction between race and age on the risk of large bowel polyps. Of the 2683 subjects enrolled, 2605 completed one follow-up exam after randomization (193 AA, 2412 EA). Overall, our results suggested a racial difference in risk for adenomas among younger (<50 years) but not among older (≥ 50 years) subjects (p-for interaction between age and race for any adenoma (p = 0.13) and for advanced adenoma (p = 0.04)). Younger AA, when compared to EA had a significantly higher risk of any adenoma (RR 1.73, 95% CI 1.00–3.00) and advanced lesions (RR 4.40, 95% CI 1.47–13.15) but no difference in risk of HP. Among older patients, using the same comparison, there was no racial difference in risk of adenomas (RR 1.06, 95% CI 0.91–1.25) or advanced lesions (RR 1.06, 95% CI 0.71–1.57) but there was a significantly lower risk of HP (RR 0.64 (95% CI 0.47–0.88)). Our findings suggest that older AA have a lower risk of HP; and AA under the age of 50 years of age are at increased risk of adenomas, especially advanced lesions.

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Relationship Between Use of Different Oral Contraceptive Formulations and Breast Cancer Risk Among Young Women

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Purpose: Prior studies suggest that recent oral contraceptive (OC) use is associated with a modest increased risk of breast cancer among young women. However, the majority of these reports have relied on self-reported use and have not characterized risks associated with newer OC formulations.

Methods: We conducted a nested case-control study among health plan enrollees at a large health maintenance organization, Group Health Cooperative, which serves the greater Seattle-Puget Sound region. Cases consisted of 1,102 women 20–49 years of age diagnosed with invasive breast cancer from 1990–2009. We randomly selected 21,952 controls matched on age, year, and enrollment length. Detailed information on recent OC use, including formulation, dose, and duration was ascertained from electronic pharmacy records. Multivariate-adjusted conditional logistic regression was used to calculate odds ratios (ORs) as estimates of relative risks and 95% confidence intervals (CIs).

Results: Recent OC use (within 1 year of diagnosis) was associated with a 60% (95% CI = 1.3–1.9) increased breast cancer risk. The association was slightly stronger for estrogen receptor (ER) positive compared to ER-negative disease (ER-positive OR = 1.7, 95% CI = 1.3–2.1 and ER-negative OR = 1.2, 95% CI = 0.8–1.8), though this difference was not statistically significant. The ORs varied somewhat by OC formulation, with recent use of OCs containing the progestin ethynodiol diacetate (OR = 2.6, 95% CI = 1.4–4.7) or high dose estrogen (OR = 2.7, 95% CI = 1.2–6.4) associated with particularly elevated risk estimates compared to non-use of OCs in the prior year. In contrast, risk estimates for recent use of OCs with the progestin norgestimate or low dose estrogen suggested either a modest association or no association (OR = 1.2, 95% CI = 0.6–2.2 and OR = 1.0, 95% CI = 0.6–1.7, respectively).

Conclusions: These results suggest that recent use of contemporary OC formulations is associated with an elevated risk of breast cancer among women ages 20–49, with associations varying somewhat by OC formulation. Although breast cancer is rare among young women, the potential risk of breast cancer associated with certain formulations could impact OC recommendations by providers if these findings are confirmed.

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Risk of Non-Hodgkin Lymphoma in Relation to Tricyclic Antidepressant Use

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Purpose: We investigated the relationship between prior use of tricyclic antidepressants (TCA) and risk of non-Hodgkin lymphomas (NHL), both overall and for common subtypes of NHL; previous studies provided some evidence of an association with NHL, but did not assess the risk of specific subtypes of NHL, which have been shown to be etiologically diverse.

Methods: We conducted a population-based matched case-control study among members of Group Health (GH), an integrated healthcare delivery system. Cases included GH members diagnosed with NHL between 1980–2011 at age ≥ 25 with no record of a prior cancer or of certain autoimmune conditions, who had been enrolled for ≥ 2 years at the reference date (date of diagnosis). Eight controls were matched to each case on age, sex, enrollment on the reference date, and length of prior enrollment at GH. Information on prior TCA use, including dose, duration, recency, and type, was ascertained from automated pharmacy data. We calculated odds ratios (ORs) and 95% confidence intervals (CIs) for NHL (and common subtypes) in relation to various patterns of TCA exposure using conditional logistic regression adjusted for confounders.

Results: We identified 2,768 cases and 22,127 matched controls. We did not observe an appreciably increased risk of NHL among persons who had filled ≥ 2 TCA prescriptions prior to the reference date compared to those who had filled none (OR: 1.1; 95% CI: 1.0–1.2). Overall risk of NHL was associated to at most a small degree with longer-term use (OR: 1.2; 95% CI: 1.0–1.4 for ≥ 10 prescriptions), high-dose use (OR: 1.1; 95% CI: 0.8–1.5 for ≥ 50 mg or equivalent), or use that began more than 5 years prior to reference date (OR: 1.0; 95% CI: 0.9–1.2). TCA use was generally not associated with most major NHL subtypes, though longer-term TCA use was associated with increased risk of chronic lymphocytic leukemia/small lymphocytic lymphoma (OR: 1.5; 95% CI: 1.1–2.0).

Conclusions: We found little evidence that TCA use increases risk of NHL, overall or for specific common subtypes of NHL.

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Research Addressing Follow-Up for Abnormal Cancer Screening Tests: NCI Portfolio Analyses

Zapka J, Edwards H, Chollette V, Taplin S

Purpose: The study's purposes were to identify the portfolio of grants awarded by the National Cancer Institute that addressed follow-up to abnormal screening tests for colon, breast and cervical cancer, document key research design characteristics, and discuss questions and issues for future practice and research.

Methods: A standardized form was used to audit grants funded from 2002 through 2011. Grant text was independently reviewed by two auditors; differences in reports were discussed until consensus was reached. The investigators then summarized findings in order to distill trends and issues.

Results: Twelve grants met inclusion criteria; 5, 4, 2 and 1 addressed follow-up of Pap tests, mammography, and colorectal tests and multiple screens respectively. Fifty percent were R01 awards, the majority of which applied group or individual RCT designs. One was a prospective cohort study. R21s typically emphasized qualitative methods and stressed behavioral epidemiology, measurement tool development and intervention planning; several listed aims related to determining prevalence. Definition of outcome measures was variable: e.g. completion of a follow-up test; time to follow-up; and steps until diagnosis. Four studies explicitly focused on ethnic/racial disparities; 5 on low income and underserved populations. Several emphasized measurement development. Three included cost analyses research questions. Most focused on individual level change, although changes in the broader multi-level context were proposed, but at times implicit, often viewed as process measures. A majority included aims related to understanding important mediator and moderator variables. Few explicated multilevel theories, although models reflected an ecological orientation.

Conclusions: Future practice and research priorities include development of clear operational definitions of follow-up; conceptual and descriptive evaluations of how providers, patients, and organizations interact across the steps and interfaces of follow-up care; determination of priorities for multilevel intervention testing and improvement of measures, and application of appropriate and innovative study designs using multi-methods.

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