

ABSTRACTS • 34th Annual Meeting • American Society of Preventive Oncology, Bethesda, Maryland • March 20-23, 2010

The following are the 17 highest scoring abstracts of those submitted for presentation at the 34th Annual ASPO meeting to be held March 20-23, 2010 in Bethesda, MD.

Up-regulation of Endothelin-2 as a Common and Early Event in localized Clear Cell Renal Cell Carcinoma

Parker A, Bot B, LeGrand S, Eckel-Passow J

Purpose: Despite incidence rates that have been rising for decades, the molecular underpinnings that support the development of clear cell renal cell carcinoma (ccRCC) remain unclear. Herein, we evaluate expression levels of the hypoxia-induced autocrine survival factor endothelin-2 (EDN2) in patient-matched ccRCC and normal kidney samples.

Methods: We identified 169 patients who underwent nephrectomy for histologically confirmed, localized ccRCC at our institution from 2000 to 2003 and had fresh-frozen tumor and normal kidney samples available. After mRNA was extracted from microdissected tissue, we conducted real time PCR to determine expression levels of EDN2. We normalized the expression data using four control genes and then fit linear mixed models to evaluate differential expression between tumor and normal samples. In addition, we explored potential interactions with relevant clinicopathologic characteristics including tumor stage and grade.

Results: Of the 161 patients analyzed, 65% were male, 58% were stage pT1, and 43% were nuclear grade 1 or 2. Overall, EDN2 expression was higher in tumor samples compared to paired normal samples with an average fold change (FC) of 2.0 (P -value < 0.0001). This over-expression in tumor versus normal tissue was apparent in early stage (pT1) tumors but not later stage (pT2, pT3) tumors (FC of 2.9 v. 1.1 respectively; interaction P -value = 0.001). Similarly, over-expression was more pronounced in low grade (1, 2) tumors compared to high grade (3, 4) tumors (FC of 3.5 v. 1.3 respectively; interaction P -value = 0.0002).

Conclusions: While independent validation is required, our patient-based data suggest that up-regulation of EDN2 is a common and early event in localized ccRCC. If confirmed in future studies, EDN2 could represent a target for the development of novel chemopreventive or neo-adjuvant therapeutics for ccRCC.

Published OnlineFirst 02/16/2010.

doi: 10.1158/1055-9965.EPI-19-3-ASPO

©2010 American Association for Cancer Research.

Circulating 25-Hydroxyvitamin-D and Risk of Colorectal Adenomas and Hyperplastic Polyps

Adams S, Newcomb P, Burnett-Hartman A, Mandelson M, Potter J

Background: Colorectal adenomas are clear precursors of cancer; hyperplastic polyps have recently been hypothesized to also have malignant potential. However, these two distinct colorectal lesions are probably on different molecular pathways to neoplasia. An inverse association between vitamin D and adenoma risk has been reported, but this is the first study, to our knowledge, that examines circulating 25(OH)D in relation to risk of hyperplastic polyps.

Methods: We conducted a colonoscopy-based case-control study of adenomas and hyperplastic polyps among 474 members of a large integrated health plan. Self-administered questionnaires provided data on demographics and colorectal polyp risk factors, and we assayed plasma samples donated by participants at the time of the colonoscopy for total 25-hydroxyvitamin-D (25(OH)D) concentration. Polytomous regression was used to estimate separate odds ratios for adenomas ($n = 153$) and hyperplastic polyps ($n = 91$) by tertile of 25(OH)D.

Results: An inverse association between 25(OH)D and adenomas was observed (comparing upper to lower tertiles: adjusted OR [95%CI]: 0.60 [0.34-1.08]). After restriction of the analyses to study participants with no history of polyps, this OR estimate moved further from the null and became statistically significant (adjusted OR [95% CI]: 0.43 [0.20-0.96]). In comparison, no statistically significant association between hyperplastic polyps and 25(OH)D was observed among the full study participants (adjusted OR [95%CI]: 1.12 [0.59-2.13]) nor among those without prior polyps (adjusted OR [95%CI]: 1.27 [0.57-2.35]).

Conclusions: There is no evidence in our study that the established inverse association between circulating 25(OH)D and colorectal adenoma applies to hyperplastic polyps.

PACE+ Nutrition and Exercise Counseling for Obese Patients Based on Stage of Change at an Urban Primary Care Clinic

Sun G, Peechakara S, Thomas CL, Seeholzer EL

Background: Obesity screening and behavioral counseling for adults is recommended but rarely feasible to reduce the risk of developing cancer and many chronic

diseases. We initiated obesity screening at an urban clinic and offered obese patients tailored counseling using PACE+, a validated tool designed for the primary care setting.

Aim: To evaluate obesity screening rates, readiness to change, preferences for change and change in BMI in patients counseled with PACE+.

Methods: Electronic medical record (EMR) review of patient data from May 2006 to March 2008. Analyses comparing stage of change to patient characteristics was conducted using the Cochran-Armitage Trend Test. Bivariate comparisons of the continuous items were analyzed using the Chi-square.

Results: Of 5,390 patients in the clinic practice, 2532 (47%) were obese, 2269 (42%) were normal or overweight, and 589 (11%) were not screened. PACE+ educators counseled 843 obese patients (33%) May 2006-March 2008. Mean age 50, mean BMI 39, 79% female and 98% African American. 31% of PACE+ participants had hypertension, diabetes mellitus and hyperlipidemia. Stage of change for exercise was most often contemplation (38%) and preparation (40%). The preferred activity was walking (62%). Most cited reasons to change behavior were to lower blood pressure, improve health, reduce weight, and increase energy. Most reported activity barriers were pain (20%), weather (13%), and time (10%). Most patients rated their stage of change for reducing calories as preparation (62%). Anticipated nutrition adherence barriers were "will-power," cost, and time. Participants rated their self-confidence for activity and dietary changes highly. A trend to weight stabilization and weight loss was observed with follow-up.

Conclusion: Obesity screening and a structured low-intensity behavioral counseling by educators was feasible and reached 33% of obese patients in the practice. PACE+ evaluation in the EMR provides retrievable and measurable information about patient stage of change, preferences and perceived adherence barriers. This data can direct efforts to link community and personal resources to optimize behavioral and weight outcomes. Pain cited as an activity barrier by 20% needs further study.

Socioeconomic Status and Survival after an Invasive Breast Cancer Diagnosis

Sprague BL, Ramchandani R, Trentham-Dietz A, Newcomb P, Gangnon R, Remington PL, Hampton JM

Significant progress has been achieved in the United States in improving survival rates following an invasive breast cancer diagnosis. Previous studies have shown, however, that women living in geographic areas with high poverty and low education levels experience poorer survival. However, nearly all of these studies have been restricted to use of community-level data (e.g. US Census) on socioeconomic status (SES), and thus have been limited in their ability to identify individual-level factors

associated with the disparity in survival. We examined individual-level SES in relation to breast cancer survival in a population-based cohort of invasive breast cancer survivors, ages 20-69, diagnosed in Wisconsin during 1995-2003 (N = 5,865). Information on household income, household size, and education was obtained during telephone interviews conducted shortly after diagnosis. Vital status was determined through December 31, 2006, using automated searches of the National Death Index. A total of 676 deaths (461 from breast cancer) were observed during 41,751 person-years of follow-up. Compared to college graduates, women with no further education beyond high school were more likely to die from breast cancer (Hazard Ratio, HR: 1.39; 95% CI: 1.10, 1.76) and from all causes (HR 1.42; 95% CI: 1.17, 1.73) following their breast cancer diagnosis. Similarly, women with household income less than 2.5 times that of the poverty level were more likely to die from breast cancer (HR 1.46; 95% CI: 1.03, 2.08) and from all causes (HR 1.64; 95% CI: 1.20, 2.24) compared to women with household income at least 5 times the poverty level. Women with lower education and income levels were less likely to have had annual mammograms prior to diagnosis. There was little difference in stage at diagnosis according to education level, but women with low income levels were 2.7 (95% CI: 1.2, 6.2) times more likely than women with high income to be diagnosed with distant-stage breast cancer. Adjustment for these factors attenuated, but did not eliminate, the association between SES and survival after diagnosis. Thus, the disparities in breast cancer survival that exist according to individual-level SES cannot be fully explained by variation in mammography use and stage at diagnosis.

A Pooled Analysis on the Associations between Involuntary Smoking and Lung Cancer Risk by Histological Types

Lee YA, Hung R, Boffetta P, Brennan P, Yang P, Zhang ZF, et al.

Background: While the association between involuntary tobacco smoke exposure and lung cancer is well established, few studies with sufficient power have been conducted to evaluate the relationship between involuntary smoking (IS) and lung cancer by histological type, especially for the association between IS and small cell lung cancer among nonsmokers.

Methods: We evaluated the associations between IS and lung cancer by histological type based on a pooled data of the International Lung Cancer Consortium (ILCCO). The individual-level epidemiological data from 17 participating studies were pooled, including 2,218 non-smoking lung cancer cases and 6,243 non-smoking controls. Logistic regression models were used to obtain adjusted odds ratios (OR) and 95% confidence intervals (CI), using SAS v9. Likelihood ratio tests were used to assess heterogeneity by study site.

Results: Among never tobacco smokers, IS exposure was associated with lung cancer with an adjusted OR of 1.33 (95% CI 1.18, 1.50), compared to never exposure to IS, when adjusting for age, sex, ethnicity, and study site. Similar associations were observed in different histological types of lung cancer with adjusted ORs of 1.38 (95% CI 0.97, 1.98) for squamous cell carcinoma, 1.26 (95% CI 1.08, 1.46) for adenocarcinoma, 2.92 (95% CI 1.55, 5.48) for small cell lung cancer, and 1.30 (95% CI 1.14, 1.49) for non-small cell lung cancer. Similar associations with ever IS exposure were observed when the overall population including nonsmokers and smokers was included in the analysis. No apparent association was observed with IS exposure in childhood.

Conclusion: This is the first study with a relatively large sample size investigating the relationship between IS exposure and small cell lung cancer among non-smokers. Our results corroborated the association between IS and lung cancer regardless of histological types, including adenocarcinoma, and we observed the strongest association between IS and small cell lung cancer. Our study provides more precise estimates of the impact of IS on major histological types of lung cancer and suggests the importance of smoking intervention for lung cancer prevention, especially for small cell lung cancer type.

Oral Contraceptive, Menopausal Hormone Therapy Use and Risk of non-Hodgkin Lymphoma in the California Teachers Study

Lu Y, Sullivan-Halley J, Henderson KD, Ma H, Duan L, Wang SS, Lacey J, Chang ET, Deapen D, Bernstein L

Objective: To evaluate whether use of oral contraceptives (OCs) or menopausal hormonal therapy (MHT) is associated with B-cell non-Hodgkin lymphoma (NHL).

Methods: Within the prospective California Teachers Study cohort, women under age 85 with no history of hematopoietic cancer were followed from 1995 through 2007 for diagnosis of B-cell NHL. Overall, 547 women of 116,779 women eligible for analysis of OC use and 402 of 54,758 postmenopausal women eligible for analysis of MHT use developed B-cell NHL. Relative risks (RR) and 95% confidence intervals (CI) were estimated by fitting multivariable Cox proportional hazards models.

Results: Women who used OCs had marginally lower risk of B-cell NHL than women who had never used OCs (RR = 0.86, 95% CI = 0.69-1.06). The reduced risk was most pronounced among women who started OCs before age 25, but did not decrease with increasing duration. No association with MHT was observed when MHT ever users were compared to the never users (RR = 1.05, 95% CI = 0.83-1.33); this result was consistent across formulations of MHT [unopposed estrogen therapy (ET), combined estrogen and progestin therapy (EPT)]. Among women who had never used MHT, women with a bilat-

eral oophorectomy had three times greater risk than those with natural menopause (RR = 3.15, 95% CI = 1.62-6.13), whereas there was no association with bilateral oophorectomy among women who had used MHT. In stratified analyses according to hysterectomy and oophorectomy status, ET and EPT did not affect risk for women with natural menopause or those with hysterectomy who had at least part of an ovary remaining. Among women who had a bilateral oophorectomy, ET reduced risk of NHL (RR = 0.41, 95% CI = 0.21-0.82).

Conclusion: These data suggest that ET use decreases the risk of B-cell NHL among women with both ovaries removed, but not among women retaining at least part of an ovary. In other subgroups MHT does not influence risk. Additional study of associations of MHT and OCs with B-cell NHL are warranted.

Higher Bone Density is Associated with a Decreased Risk of Colon Adenomas in Women

Nock NL, Patrick-Melin A, Cook M, Thompson C, Kirwan JP, Li L

Purpose: Bone mass has been proposed as a biomarker of the cumulative exposure to calcium, vitamin D and endogenous and exogenous estrogens. Postmenopausal women with higher levels of bone mass have a decreased risk of colon cancer. No prior studies, however, have examined the role between bone mass and the risk of colon adenomas, which are precursor lesions that, if not removed, may lead to colon cancer.

Methods: We evaluated the potential association between bone mass, as measured by bone mineral density (BMD) using dual-energy X-ray absorptiometry (DXA), and colon adenomas in 167 patients who underwent colonoscopy screening at University Hospitals in Cleveland, Ohio.

Results: We found that women with a total body BMD exceeding 1.294 g/cm² (third tertile) compared to those with a total body BMD less than 1.167 g/cm² (first tertile) had a much lower risk of colon adenomas (OR = 0.10; 95% C.I.: 0.02-0.74; *P* = 0.02). Similarly, women with a total body BMD between 1.167 and 1.294 g/cm² (second tertile) compared to those with a BMD less than 1.167 g/cm² had a decreased risk for colon adenomas (OR = 0.15; 95% C.I.: 0.03-0.80; *P* = 0.03; *p*-trend = 0.01). Postmenopausal women with a total body BMD in the second and third highest tertiles combined compared to those in the first tertile also had a decreased risk of colon adenomas.

Conclusions: Our results show, for the first time, that bone mass, as measured by total body BMD, is inversely associated with colon adenomas in women, which suggests the mechanisms underlying the synergistic actions of calcium, vitamin D, estrogen exposure and other factors affecting BMD including exercise are key to preventing the development of colonic lesions, particularly among women.

Associations of Telomere Length and Diabetes with Pancreatic Cancer

Skinner H, Gangnon R, Chari S, Johnson R, Boardman L

Risk for pancreatic cancer increases strongly with older age, and diabetic conditions have been consistently associated with pancreatic cancer, although the temporal relation between diabetes and pancreatic cancer remains uncertain. Telomeres are complexes of proteins and hexameric DNA repeats that cap and protect the ends of chromosomes. Telomere length decreases with subsequent cell divisions and the length of telomeres in peripheral blood leukocytes (PBL) has been observed to be shorter with older age, and shorter among cases of several cancer types than in controls. We conducted a hospital-based case-control study with 500 cases of pancreatic cancer, and 1,000 controls without pancreatic cancer (500 diabetic and 500 non-diabetic). We examined associations between PBL telomere length and pancreatic cancer status using generalized additive models (GAM), adjusting for age, body mass index, and gender. We observed significant heterogeneity in the association between PBL telomere length and pancreatic cancer by fasting blood glucose status ($P < 0.003$). Among those with impaired fasting blood glucose (>100 mg/dL) there was a continuous inverse association between pancreatic cancer and telomere length in the GAM adjusted for age, body mass index, sex, and cigarette smoking status. The adjusted odds ratio for pancreatic cancer comparing the 10th percentile of telomere length (4,184 bp) to the 90th percentile (7,823 bp) was 3.21 (95% C.I. 1.87, 5.52). In contrast, no significant association was found between telomere length and pancreatic cancer status among those with normal fasting blood glucose (OR = 0.67; 95% C.I. 0.39, 1.05; comparing 10th to 90th percentiles). We did not find strong evidence for effect modification of the relation between PBL telomere length and pancreatic cancer by age, gender, or cigarette smoking status. Shorter telomeres in peripheral blood may portend higher risk for pancreatic cancer among those with impaired fasting blood glucose, or may indicate cases who are more likely to have tumors that result in diabetes.

Do Early Screening Mammography Outcomes <Age 40 Adversely Impact the Timing of Screening Mammography >40 Differentially by Race?

Kapp JM, Walker R, Haneuse S, Yankaskas BC

Purpose: Previous studies suggest 29% of women ages 30-39 report having had a mammogram; this varies by race/ethnicity. Black women have a greater odds than White women of reporting multiple mammograms <40; yet ≥ 40 , Black and Asian women are less likely to receive adequate mammography screening. Could early mammography testing adversely impact future mammography use? Our objective is to determine whether racial/ethnic differences and the outcome of a first mammo-

gram <40 (false positive (FP) or true negative (TN)) may delay the age of the first mammogram ≥ 40 .

Methods: Data were pooled from seven mammography registries of the National Cancer Institute's Breast Cancer Surveillance Consortium (BCSC), a network created to study performance and outcomes in community practice. Using 1996-2006 data, we identified 29,158 women with a screening mammogram between ages 40-45 who also underwent screening mammography for the first time ever at an age <40 in the BCSC data. We used logistic regression to examine the association between race/ethnicity and first mammography outcomes on the odds of delayed mammography after 40 (ages 43-45 compared to 40-42).

Results: Overall, 96% of these women's first screens <40 were at ages 35 or later, and 93% of their first screens >40 were at ages 40-42. Regression models adjusted for age at first screen suggest: (1) Hispanic women have an increased odds of waiting to screen until 43-45 compared to White women, regardless of first screening outcome <40; (2) White and Black women whose first screen <40 was a FP have less odds of delaying future screening than those with a TN; and (3) among women with a TN, Black women have an increased odds of waiting to screen until 43-45 relative to White women, with no observed difference between Asian and White women.

Conclusions: Findings suggest a differential impact of early mammography outcomes on future mammography use by race/ethnicity, among the women in our sample with a known first screening mammogram before and after age 40. The concern for harmful effects of over-screening young women drives the need for additional work in this area.

Reaching Underserved Women with Mammography: 15 month experience with a Mobile Prevention Unit and Prevention Program

Davis ET, Hembree T, Beache SC, Ballard D, Brooks SE

Objective: There is much debate regarding the efficacy of mammography screening in women <50. No cost and low cost service providers may be required to target screening to the population at highest risk in order to maximize utility of resources. We sought to describe outcomes of women >40 undergoing mammography screening in underserved areas through a mobile unit and prevention program affiliated with a large network cancer program in Louisville, Kentucky.

Methods: We conducted a retrospective review of women undergoing mammography during the period 3/08-6/09. Locations determined to be high risk by GIS analysis, income and cancer incidence. Analyses included: descriptive analyses, calculation of odds ratios and confidence intervals and regression analyses.

Results: Of the 1702 women, 735 (43%) were white, 884 (52%) were African American, 54 (3%) other and 236 (14%) Hispanic/Latina. The mean age was 54 (std.dev.

9.4). Twenty-eight percent of the women (471/1702) had either never had a mammogram or not had one in 5 years. Fifty-one percent were uninsured. Of the 1702 women, 662(39%) were between the ages of 40-49 (Group A) and 1040 (61%) were >49 (Group B). The majority of women resided in high risk areas (74% Group A, 51% Group B). Twelve percent (206/1702) of the mammograms were abnormal and required follow up. Women in Group A were 1.4 times more likely than women in Group B to have a screening mammogram classified as abnormal (OR 1.4 95% CI 1.05-1.88). Four women were diagnosed with cancer in group A (0.6%) and 9 in group B (0.8%), $P = ns$. The median age of women with cancer was 52, mean = 58, range 42-83, (std. dev. 12.5). The overall follow up rate was 92%. All women with cancer received treatment. Logistic regression analysis demonstrated women of African American race and women who had never been screened were more likely to have abnormal results ($P < 0.0001$ and $P = 0.03$ respectively).

Conclusion: Our targeted approach of community based screening was successful in identifying a sub-population of women who are not regularly screened and are at risk for abnormal screening mammograms and breast cancer. Further studies are needed to determine if recommendations for screening should be based on factors other than age.

Maternal Cultural Barriers Correlate with Adolescent HPV Vaccine Use

Carlos RC, Resnicow K, Dempsey AF, Patel D, Ruffin M, Dalton VA

Purpose: Determine maternal cultural barriers in mothers who adhere to their own cancer preventive behavior that correlate with HPV vaccination in their adolescent daughters.

Methods: We conducted a cross-sectional mailed survey of women attending breast and cervical cancer screening at two diverse institutions; one serving mostly black (54.1%) urban inner-city population and another serving a mostly (87.5%) white suburban population. Surveys queried the adolescent daughter's HPV vaccination status (adolescent defined as 9-17 years old), general health beliefs; HPV-specific beliefs; knowledge, perceived benefits and barriers to HPV vaccination; perceived social/peer group attitudes about HPV vaccines. HPV vaccine completion (receipt of all three doses) is the primary outcome. Cultural differences between groups were assessed using linear regression. Correlates of the primary outcome were assessed using univariate logistic regression.

Results: 33% response rate with 68 black and 164 non-black mothers. 6.8% of adolescent daughters of black mothers adhering to breast/cervical cancer screening completed HPV vaccination, compared 24.5% of non-blacks. In 11-12 year olds, for whom the CDC recom-

mends universal vaccination, none of the daughters of black mothers completed HPV vaccination, compared to 17.5% in nonblacks. Black mothers more likely agreed with "Giving my daughter a new vaccine is like performing an experiment on her" (coefficient 0.38, $P = 0.038$). Overall knowledge about HPV lagged in black mothers (mean knowledge index 0.587 (95%CI 0.531-0.643)) compared to nonblacks (0.73(95%CI 0.70-0.76)). Black mothers more likely to score lower on the vaccine benefit scale (coef -0.31, $P = 0.007$, $\alpha = 0.76$) and more likely scored higher on the peer group disapproval scale (coef 0.44, $P = 0.010$, $\alpha = 0.73$). Belief about vaccine experimentation on her daughter decreased adolescent HPV vaccine use by black moms (OR 0.15, $P = 0.002$).

Conclusion: HPV vaccine completion in adolescent daughters of mothers who already participate in their own cancer preventive behavior remains suboptimal with significant racial disparity in vaccine use. Significant cultural differences correlate with decreased vaccine completion in daughters of black mothers.

Test of a Weight Gain Prevention Intervention in Stage II and III Breast Cancer Patients Receiving Neoadjuvant Chemotherapy

Basen-Engquist K, Perkins H, Carmack C, Hughes D, Jovanovic J, Arun B, Murray J

Purpose: Weight gain is common in women with breast cancer and is worrisome, as it may affect prognosis and risk of other chronic diseases. This randomized pilot test was conducted to evaluate the feasibility and preliminary effectiveness of a weight gain prevention intervention for breast cancer patients receiving neoadjuvant chemotherapy.

Method: Breast cancer patients receiving neoadjuvant chemotherapy were randomized to the weight gain prevention intervention or usual care. The intervention used a size acceptance approach, which emphasized changes in diet (low energy density food) and exercise behavior (resistance training) rather than focusing on weight loss. It was administered in weekly sessions delivered in-person and by telephone. Assessments were done at baseline, mid-chemotherapy, end of chemotherapy, after surgical recovery, after a post-surgical booster intervention, and 6 months after surgery. The data from baseline (BL), mid-chemotherapy (MC), and end of chemotherapy (EC) are presented.

Results: 38 participants were randomized to the intervention ($n = 19$) or usual care ($n = 19$). 68% had stage II and 32% had stage III breast cancer. Their mean age was 50.0 (SD = 11.0), and 55% were premenopausal. Mean BMI was 29.1 (SD = 6.2) and 69% were physically inactive. The sample was diverse with regard to self-reported ethnicity (58% white, 27% African-American, 8% Hispanic, 6% other). Data collected at MC and EC indicated a trend toward greater reduction in BMI in the intervention than the control group (intent to treat analysis, $P = 0.10$).

When the analysis was conducted without the 4 intervention participants who attended less than 60% of the sessions (analyze as treated) the differences were more marked (group difference: 0.5 kg/m² at MC and 0.9 kg/m² at EC, $P = 0.025$). Similar results were found for waist circumference and SF-36 physical component score, but no differences were found in the SF-36 mental component score.

Conclusions: Based on a preliminary analysis, there was a trend toward improvements in body composition and physical aspects of quality of life from a diet and exercise intervention based on the size acceptance approach. These results indicate this intervention should be tested in a larger randomized controlled trial.

Menopausal Hormone Therapy influences Lung Cancer Survival but not Lung Cancer Risk: Results from the California Teachers Study

Clague J, Reynolds P, Chang E, Henderson KD, Ma H, Anton-Culver H, Bernstein L

Purpose: Most studies have shown a protective or null effect of postmenopausal hormone therapy (HT) on lung cancer risk, whereas the recent post-hoc analysis of the Women's Health Initiative (WHI) showed that estrogen +progestin (E+P) decreased lung cancer survival. Given the substantial clinical implications, it is vital that the risk and survival associations be validated.

Methods: We examined the associations between HT use and lung cancer risk and survival among 60,592 postmenopausal women enrolled in the prospective California Teachers Study cohort. Between 1995 and 2007, 727 women (184 never smokers) were diagnosed with lung cancer; 441 of these died as of December 31, 2007. Age-stratified, multivariable Cox proportional hazards regression was used to calculate hazard ratios (HR).

Results: After adjusting for potential confounders, various measures of HT use were not associated with lung cancer risk. However, any HT use (vs. no use) was associated with a statistically significant increase in lung-cancer-specific survival [HR, 0.70; 95% confidence interval (CI), 0.56-0.87]. Among women who only used E, statistically significant increases in lung cancer survival were seen for recent use (HR, 0.59; 95% CI, 0.43-0.80), but not former use; use of only E+P was not associated with survival. Shorter duration of recent E-only use was associated with improved survival (0-5 years of use: HR, 0.29, 95% CI, 0.12-0.68; 5-15 years of use: HR, 0.60, 95% CI, 0.35-1.05; >15 years of use: HR, 0.58, 95% CI, 0.39-0.88) (trend $P = 0.005$). Similarly, women who reported recently using E-only for 0-5 years had a median survival time of 42.1 months versus women who reported 5-15 years of use (31 months), >15 years of use (19.1 months), or no HT use (15.6 months) (log-rank $P = 0.009$). Among former users of HT, a statistically significant 63% (95% CI, 0.16-0.87) decrease in lung-cancer-specific death was observed for E-only use

<5 years prior to baseline, but not for E-only use >5 years prior to baseline or E+P-only use.

Conclusions: Contrary to the recent finding that lung cancer survival is poorer among women in WHI taking E+P, our results suggest no effect of E+P. By contrast, postmenopausal E-only use, specifically recent use, is associated with increased lung cancer survival.

Expression of Inflammatory Molecules Among Breast Cancer Patients Receiving Different Chemotherapies: Implications for Chemobrain

Janelins M, Roscoe J, Mustian K, Palesh O, Peppone L, Sprod L, Morrow G

Increased levels of MCP-1, IL-8 and IL-6 are associated with mild cognitive impairment, defined as frequent and irregular bouts of forgetfulness, difficulties with attention and/or difficulties with language—a condition with comparable symptomology reported by cancer patients experiencing chemobrain. High levels of these molecules may compromise neuronal and synaptic integrity, leading to cognitive impairment. Patients receiving doxorubicin-based (with cyclophosphamide, or cyclophosphamide and fluorouracil; AC/CAF) chemotherapy or a combination of cyclophosphamide, methotrexate, and fluorouracil (CMF) chemotherapy report experiencing chemobrain, but MCP-1, IL-8 and IL-6 may be differentially influenced by these regimens. The purpose of this study was to examine changes in expression of these molecules among breast cancer patients (N = 54) receiving combinations of AC/CAF or CMF. Changes in MCP-1, IL-8 and IL-6 were assessed at baseline (T1) and after 2 chemotherapy cycles (T2). *T*-tests were used to compare between group and within group differences on raw means and mean change (T2-T1). IL-6 significantly increased in the AC/CAF group (4.95 pg/mL, SEM = 2.31; $P < 0.05$), but MCP-1 (42.8 pg/mL; SEM = 40.36) and IL-8 (0.25 pg/mL; SEM = 1.19) did not. IL-6 (-1.46 pg/mL, SEM = 0.94), MCP-1 (-15.8 pg/mL, SEM = 49.95) and IL-8 (-0.79 pg/mL, SEM = 1.04) all decreased in the CMF group; however, none of these changes were significant. No significant differences in IL-6 (1.06 pg/mL, SEM = 1.05), MCP-1 (73.48 pg/mL, SEM = 67.30), or IL-8 (-1.95 pg/mL, SEM = 3.28) at T1 were observed between AC/CAF and CMF groups. At T2, there was a significant difference in IL-6 (7.72 pg/mL, SEM = 3.82; $P \leq 0.05$) between AC/CAF and CMF groups, but not in MCP-1 (131.91 pg/mL, SEM = 87.09) or IL-8 (5.72 pg/mL, SEM = 4.0). A significant change (T2-T1) in IL-6 (6.41 pg/mL, SEM = 2.57; $P < 0.05$) between AC/CAF and CMF groups was observed. Changes in MCP-1 (58.65 pg/mL, SEM = 63.94) and IL-8 (1.08 pg/mL, SEM = 1.58) between groups were not significant. These results suggest AC/CAF and CMF chemotherapy regimens elicit distinct inflammatory response patterns in MCP-1, IL-8 and IL-6 suggesting different mechanisms may be responsible for the development of chemobrain. Future

research is needed to confirm these findings. Funding: NCI R25CA10618.

Focus on Survivorship: Refining Complete Prevalence Estimates Using Local Cancer Registry Data

Wobker S, Yeh W, Carpenter W

Purpose: This study applies NCI's ComPrev software to ten years of North Carolina Central Cancer Registry (NCCCR) data to demonstrate the added value of using complete prevalence (CP) methods to estimate cancer prevalence compared with the prior standard, limited-duration prevalence (LDP).

Methods: All cases for years 1995-2004 were obtained from the NCCCR and merged with vital status and date of death from the NC State Center for Health Statistics' vital statistics to form the "case data." Population data for four expanded races and individual ages, originally from the U.S. Census Bureau, were obtained from the SEER program. Case and population data were integrated using SEER*Prep software. SEER*Stat software was used to calculate 10-year LDP based on first primary cancer as of January 1, 2005. ComPrev software was subsequently used to convert LDP into CP for each cancer site, gender, and race combination. CP applies a completeness index based on incidence and survival to adjust for underascertainment of cases due to limited years of surveillance, providing a more accurate estimate of survivor burden.

Results: LDP methods estimated 228,457 cancer survivors living in NC as of January 1, 2005. CP methods estimated 371,537 individuals living with cancer, 63% more than LDP estimates. Compared to cancers with typically short survival duration or later age at diagnosis, cancers of greater survival duration or earlier age at diagnosis tended to have greater difference between LDP and CP estimates. Breast, prostate, colorectal, and melanoma comprise 205,747 (55%) of the cancer survivors in NC as estimated by CP methods.

Conclusions: The number of cancer survivors in the US is expected to grow from the 2006 estimate of >11 million, and more refined prevalence estimates are needed for survivorship planning. In North Carolina, the commonly used method of LDP based on SEER data underestimates the survivor burden by nearly 40%. Regional, gender-based, and racial differences suggest local programs should understand their community's prevalent cancer population when prioritizing local survivorship services. Future analysis will use MIAMOD methods as a supporting method of estimating CP, and updated case data to generate January 1, 2008 prevalence estimates.

The Effect of Smoking on Side Effects Among Cancer Patients Throughout Treatment: a URCC CCOP Study of 947 Patients

Peppone L, Mustian K, Palesh O, Piazza K, Janelins M, Roscoe J, Sprod L, Morrow G

Background: Cigarette smoking during cancer treatment adversely affects overall survival, disease-free survival, and disease recurrence. Very few studies investigated the effect of smoking on cancer-related side effects, but smoking in cancer patients represents an important problem because it may exacerbate side effects, which could lead to treatment interruptions and compromised treatment efficacy.

Purpose: To examine the influence of cigarette smoking on side effects among 947 cancer patients throughout treatment.

Methods: Patients diagnosed with cancer and scheduled to receive chemotherapy and/or radiation therapy reported on current smoking status (yes, no) and the severity (on an 11-point scale ranging from 0 gNot Presenth to 10 = "As Bad as You Can Imagineh) of 12 side effects (fatigue, hair loss, memory, nausea, depression, sleep, pain, concentration, hot flashes, weight loss, skin problems, and shortness of breath) at pre-treatment, during treatment, and 6-month follow-up. The total mean of the aforementioned side-effects was determined for self-reported smokers (S) and non-smokers (NS) using ANCOVA controlling for sociodemographic variables, treatment, cancer site, and Karnofsky score.

Results: S were more likely to be non-Caucasian, younger, single, and less educated (all $P < 0.05$) than NS. S reported a higher total mean side effect severity than NS prior to treatment ($S = 1.73$ vs. $NS = 1.47$; $P = 0.02$), during treatment ($S = 3.91$ vs. $NS = 3.43$; $P = 0.03$), and at 6-month follow-up ($S = 2.34$ vs. $NS = 1.80$; $P < 0.01$). S also reported a greater increase in total mean side effect severity from pre-treatment to treatment ($S = +2.48$ vs. $NS = +2.05$; $P = 0.04$). S who quit smoking (Q) between baseline and 6-month follow-up reported lower total mean side effect severity than S who continued to smoke at 6-month follow-up ($Q = 1.36$ vs. $S = 2.34$; $P = 0.04$).

Conclusion: S reported greater side effect severity compared to NS prior to treatment, during treatment, and at 6-month follow-up. S also experienced a greater increase in side effect severity than NS from pre-treatment to treatment. S who quit reported lower side effect severity than S who continued smoking. Targeted cessation efforts for S to decrease side effect severity may limit the likelihood of treatment interruptions.

Neighborhood Socio-Economic Status and Individual Smoking Status Interact to Predict PAH-DNA Adduct Levels in Prostate Tissue

Richards C, Rybicki B, Tang D, Neslund-Dudas C, Rundle A

Background: We extend our work studying environmental and genetic determinants of polycyclic aromatic hydrocarbon (PAH) DNA adducts in radical prostatectomy specimens, to consider cross-level interactions between cigarette smoking and indicators of neighborhood level socio-economic status.

Methods: PAH-DNA adducts were measured in 397 prostatectomy specimens from the Henry Ford Health System using immunohistochemistry with image analysis to measure staining intensity in optical density units. Subjects' home addresses were geo-coded to Census tracts and linked to 2000 Census data. Tracts were classified for educational attainment using the median value across tracts for the percentage of residents who graduated college. GEE models, accounting for clustering at the Census tract level, were used to determine if smoking was associated with adduct levels in tumor tissue by strata of neighborhood educational attainment. Analyses adjusted for race, age, tumor volume, primary Gleason grade and PSA level at diagnosis.

Results: Among those living in tracts with high educational attainment, smoking status predicted adduct levels. The covariate adjusted mean staining intensity for current smokers was 0.17 (95% CI = 0.15-0.19), for ex-smokers was 0.16 (95% CI = 0.15-0.17) and

never-smokers was 0.13 (95% CI = 0.12-0.14). For those living in tracts with low educational attainment there was no significant difference in adduct levels by smoking status, the covariate adjusted mean staining intensity for current smokers was 0.16 (95% CI = 0.14-0.18), for ex-smokers was 0.15 (95% CI = 0.14-0.16) and for never smokers was 0.16 (95% CI = 0.15-0.17). The *P*-value for the interaction term between smoking status and tract level educational attainment was 0.02. Further adjustment for individual level education and for tract median household income did not alter these results.

Conclusion: The results suggest that neighborhood context modifies the relationship between individual smoking status and PAH-DNA adduct levels in prostate tissue; smoking is only predictive of adduct levels in higher SES tracts. The spatial segregation of income groups in and around Detroit suggests that indicators of lower neighborhood SES serve as a proxy for other environmental sources of PAH.