ABSTRACTS
27th Annual Meeting • American Society of Preventive Oncology
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Following are the 16 highest-scoring abstracts of those submitted for presentation at the 27th Annual ASPO meeting to be held March 9–11, 2003, in Philadelphia, Pennsylvania

FOLIC ACID FORTIFICATION AND RATES OF NEUROBLASTOMA IN ONTARIO

AE French, R Grant, S Weitzman, L Sung, M Greenberg, J Ray, M Vermeulen, and G Koren

Purpose To investigate the effect of folate fortification of flour on the incidence of neuroblastoma (NB), based on maternal intake during gestation.

Methods We compared the rates of NB, as well as infant (< 1 year) acute lymphoblastic leukemia (ALL) and hepatoblastoma (HB), registered by the Pediatric Oncology Group of Ontario, which captures 95% of all pediatric cancers in Ontario, before and after the introduction of folate fortification.

Results The introduction of folate fortification was associated with a significant decrease in rates of NB in Ontario (from 1:6100 to 1:12000 births, P = 0.003), and conferred a 51% protective effect (RR 0.51, 95% CI 0.33-0.79). In contrast, folate fortification was not associated with a decrease in rates of infant ALL (RR 1.15, 95% CI 0.48-2.75) or HB (RR 0.83, 95% CI 0.35-1.94).

Conclusions Fortification of flour with folic acid, previously shown to double erythrocyte folate levels in Ontario, appears to have a significant protective effect against NB. Longer follow-up of NB rates, investigation into other embryonic cancers, the potential impact of treating NB with folate, and higher levels of folate fortification should be considered.

Aspirin use and risk of leukemia in post-menopausal women

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Regular use of aspirin and other non-steroidal anti-inflammatory drugs (NSAIDs) may be associated with reduced risk of some types of malignancy. We explored whether NSAIDs might also be associated with reduced risk of leukemia in a prospective cohort of over 28,000 post-menopausal women. Eighty-one incident leukemia cases were identified during the period 1993-2000. After controlling for age, education, smoking and previous blood transfusion, the relative risk (RR) of leukemia was 0.45 (95% confidence interval (CI): 0.27-0.75) for women who reported using aspirin two or more times per week compared to women who reported no use. In contrast, for women who reported using non-aspirin NSAIDs two or more times per week compared to women who reported no use, the RR of leukemia was 1.30 (95% CI: 0.77-2.21). Similar associations were observed for the two subtypes of leukemia analyzed (acute myeloid leukemia and chronic lymphocytic leukemia). Analyses that excluded cases diagnosed prior to 1995 did not notably alter results. Our data suggest that aspirin use is associated with a decreased risk of leukemia. Given the growing body of evidence implicating aspirin as a chemopreventive agent, and the lack of etiological data with respect to adult leukemia, it will be necessary for other large cohort studies to evaluate NSAID use and leukemia risk.

Gender Differences in Response to Bupropion Treatment in a Randomized Placebo-Controlled Smoking Cessation Trial

Collins, B, Wyleto, E, Patterson, F, Audrain-McGovern, J, Hawk, L, Kaufmann, V, Pinto, A, Niaura, R, Epstein, L, Lerman, C

The literature shows that women have greater difficulty quitting smoking than men. We hypothesized that bupropion (Bp) would attenuate this gender disparity among 555 smokers enrolled in this randomized trial with 300 mg Bp. Participants were 18-75 y.o. and smoked at least 10 cigarettes per day for =one year. The primary outcome was prolonged abstinence at end of treatment (EOT, 8 weeks post quit date) and 6-month follow-up. Univariate analyses showed a large drug effect for women at EOT (51.8% quit on Bp vs. 26.8% on placebo (Pl), x^2=17.27, p< .001) that was not sustained through 6 months. The drug effect for men was not large (EOT: 52.0% quit on Bp vs. 42.0% on Pl) and not sustained. Six-mo. logistic regression, controlling for base-line education, CES-D, FTND, ethnicity and recruitment site, showed gender x drug and gender x drug x baseline-smoking-rate interactions and a main effect for marital status. A Cox regression model showed similar factors suggesting that through 6 mo., females on Pl had a significantly shorter time to relapse than females on Bp, whereas little difference between men on Bp vs. Pl emerged. The gender x drug interaction may indicate that women respond more favorably than men to Bp+counseling, or that men simply respond more favorably to Pl+counseling than women. The moderating effect of smoking rate suggests that for heavier smokers, Bp+behavioral counseling alone may not be a sufficient smoking cessation treatment, particularly for women. Clinical implications also include the possibility that females could benefit from longer Bp trials for smoking cessation.

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Tea drinking, colorectal adenomas, and apoptosis

Il'yasova D, Martin C, Galanko J, Sandler RS

Tea polyphenols have induced apoptosis in experimental studies. We analyzed the relationship between tea consumption and apoptotic activity in rectal mucosa as well as the associations with colorectal adenomas in 173 cases and 323 adenoma-free controls. Subjects were recruited from consecutive patients who underwent colonoscopy. Cases were ascertained through complete visualization of colon to the cecum. Apoptotic activity in biopsies of rectal mucosa was assessed by the TUNEL method; the score varied from 1.14 to 3.25.

After adjusting for gender, age, race, smoking status, the prevalence of adenoma(s) was negatively associated with tea consumption (OR 0.5; 95%CI 0.3 – 1.0 for ≥2 cups/day vs. < 2 cups/day) and with apoptotic activity of rectal mucosa (OR 0.5; 95%CI 0.4 – 0.7 for the difference between 75th and 25th percentile of the TUNEL score). Tea consumption (cup/day) was not correlated with apoptotic activity: r = -0.02, p-value 0.6. Tertiles of apoptotic activity score were not associated with the three levels of tea consumption (non-consumers, <2, and ≥2 cups/day): p-value for general association χ^2-test was 0.5.

Our results suggest that apoptotic activity and tea drinking are independently associated with lower prevalence of colorectal adenomas. Exposure to tea polyphenols does not induce apoptosis in normal rectal mucosa.

Obesity, weight gain and metabolic hormones in breast cancer survivors

Irwin M, Gilliland F, Ballard-Barbash R, Baumgartner R, Bernstein L, Tworoger S, LaCroix K, McTiernan A

Purpose: To examine the cross-sectional and longitudinal associations of c-peptide, leptin, IGF-I, and IGFBP-3 levels with BMI and weight gain among 181 breast cancer survivors in the Health, Eating, Activity, and Lifestyle (HEAL) Study.
Methods: Women living in the greater Seattle area, diagnosed with *In Situ* to Stage III breast cancer, and ages 40 to 65 years at study enrollment, had body weight and height measured during a baseline (i.e., ~6 months after diagnosis) and 24-month clinic visit. A fasting blood draw was also obtained at baseline and 24-months. Adjusted least-square mean hormone levels across categories of BMI and weight gain were calculated by linear regression.
Results: A higher BMI at 24-months (BMI < 25 versus ≥30 kg/m^2) was associated with higher c-peptide (2.89 ± 0.10 versus 1.52 ± 0.10 ; P for trend = 0.0001) and leptin (36.5 ± 1.3 versus 10.2 ± 1.3; P for trend = 0.0001) levels adjusted for disease stage, tamoxifen use, and age. Weight gain from baseline to 24 months was associated with a 3% and 38% increase in c-peptide (P-value = 0.0001) and leptin (P-value = 0.0001)) levels, respectively, compared to a weight-loss associated 16% and 15% decrease in c-peptide and leptin levels. BMI and weight gain were not associated with IGF-I and IGFBP-3 levels.
Conclusions: This is the first report of an inverse association between BMI or weight change and c-peptide and leptin levels in breast cancer survivors. This association may represent one mechanism by which obesity and weight gain adversely affect breast cancer prognosis.

Social Connectedness and Female Long-term Cancer Survivors' Quality of Life

Sapp AL, Trentham-Dietz A, Newcomb PA, Moinpour C, Remington PL

Social connectedness can be a powerful predictor of how cancer survivors fare—physically and mentally—in the years following their diagnosis. A study of female colorectal cancer survivors residing in Wisconsin examined quality of life nine years after cancer diagnosis (n=257). The study consisted of a self-administered questionnaire containing the Medical Outcomes Study Short Form 36 Health Status Survey (SF-36) as well as questions based on Berkman's literature on social networks and health. For each respondent, a Mental Component Summary (MCS) and Physical Component Summary (PCS) were calculated from the SF-36. These scores, along with a single-item score for self-reported "general health" were tested, using Spearman's Correlation Coefficient, for associations with overall and individual components of "social connectedness," calculated from social network and SF-36 questions. After controlling for potential confounders including age and co-morbidities, mental, physical, and general health were positively associated with overall social connectedness (r = 0.57, 0.52, 0.65 respectively). Mental, physical, and general health were positively associated with individual components of social connectedness as well. Most notable were associations between self-reported general health and the frequency with which the study participants saw their friends (r = 0.24), but not their family members (r = 0.005). Study results suggest that, for female colorectal cancer survivors, social connectedness can play an integral role in improving quality of life.

Insulin-Like Growth Factor-1 (IGF-1): An Exploration of Serum Levels, Binding Protein (IGFBP-3) and IGF-1 CA Repeat Genotype, and the Risk of Prostate Cancer

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IGF-1 is a mitogen and has been associated with prostate cancer risk. We undertook a study to explore the relationship between serum IGF-1, IGFBP-3, IGF-1 CA repeat alleles and the risk of prostate cancer in black and white men.

Prostate cancer cases (N=99) and controls (N=91) 40-74 years old were identified at the Durham Veterans Administration Medical Center over a two and a half-year period. Controls were frequency-matched to cases on the basis of race (black or white) and age (5-year age categories). Multivariate logistic regression was used to determine associations between prostate cancer risk and serum IGF-1 and IGFBP-3 concentrations, as well as associations between prostate cancer risk and polymorphisms in the IGF-1 gene.

Serum IGF-1 concentrations in the highest quartile were associated with a 3-fold increased risk of prostate cancer (OR = 3.31; 95% CI = 1.32, 8.34). After adjusting for serum IGFBP-3, this association persisted among blacks but not whites. A decreased risk of prostate cancer (OR = 0.35; 95% CI = 0.14, 0.88) also was observed among those homozygous for the common IGF1 allele (188 bp). The prevalence of the homozygote 188 genotype was found to be higher in whites than in blacks.

Serum IGF-1 and the common CA repeat allele in the IGF1 gene may, in part, be responsible for the increased incidence and mortality of prostate cancer in blacks compared to whites. Further research is needed to confirm these findings.

RCT of a New Interactive Electronic Program to Promote Colorectal Cancer Screening

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Purpose: To determine if an interactive educational electronic program significantly increased screening for colorectal cancer.
Methods: A randomized controlled trial of adults 50 years and older in need of screening for colorectal cancer recruited from three communities in Michigan. Participants were randomly assigned to a standard electronic program with no interaction or promotion of choice or the new program that was interactively promoted making a choice of which test to use for screening. The content of both programs was identical. After each participant was exposed to the assigned program, interviews by telephone were done at 2 weeks, 8 weeks, and 24 weeks. The primary outcome is completion of any colorectal screening procedure.
Results: 200 participants have been recruited to the trial with 50% men and 50% African Americans. The trial is still ongoing at this date and will be finished in time for complete data presentation. Preliminary analysis: participants exposed to the interactive program had a significantly higher knowledge score (p=0.05) and were more likely to have a preferred screening method (p=0.05) than those exposed to the standard program. The participants exposed to the interactive program are more likely to have made plans to get screened or completed screening (p=0.05) than those exposed to the standard program.
Summary: This preliminary analysis suggests that an interactive educational electronic program that promotes making a choice among the various screening options for colorectal cancer moves more adults to completion of screening than a non-interactive educational program.

Topical all-trans Retinoic Acid for CIN II/III
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Unger, E Centers for Disease Control and Prevention
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Purpose: To determine if doses of all-trans Retinoic Acid (atRA) less than 0.37% delivered with a cervical cap and sponge for four days to women with CIN II/III were equally effective as 0.37%. Second goal was to determine if cervical HPV status, sexual behaviors, other demographic factors, and disease state predicted response to atRA.
Methods: 175 women age 14 and older with biopsy proven CIN II/III were randomized to four consecutive days of atRA with a cervical cap and sponge at one of three doses (0.16%, 0.28%, and 0.36%) or placebo. The outcome of interest at 12 weeks was whether there was treatable disease CIN II or worse. All subjects underwent a repeat colposcopy evaluation and biopsy of the cervix by the same provider as baseline.
Results: The disease response to atRA or placebo was not significantly different (p=0.28). 94% of participants were HPV+, which was not effected by the exposure to atRA or placebo (p=0.41). HPV status and risk behaviors did not predict response to atRA. Participants with CIN II at baseline were more likely to be free of disease at 12 weeks than participants with CIN III at baseline (p=0.0003).
Summary: Four consecutive days of treatment with topical atRA was not any more effective than placebo even at doses previously proven to be effective given repeatedly over a year. HPV status appears not to be effected by atRA, which may account for treatment failures.

Food Groups and Colon Cancer Risk

J. Satia Abouta, PhD, MPH; J. A. Galanko, MS; R.S. Sandler, MD

This abstract describes associations of food groups with colon cancer risk in African Americans and Whites using data from a large case-control study in North Carolina. Incident cases of colon cancer, age 40-85 (n=613), were identified from the North Carolina Colon Cancer Registry and matched controls (n=996) were selected from Department of Motor Vehicle lists and the Center for Medicare and Medicaid Services. In-person interviewers collected dietary data over the year prior to diagnosis or interview date using a validated food frequency questionnaire. Odds ratios (OR) were based on quartile cut points in race-specific controls and were adjusted for dietary and other colon cancer risk factors. Overall, White participants had higher intakes (frequency and amounts) of fruits and fruit juices, vegetables, and dairy products than African Americans. Regardless of race, cases generally reported higher mean intakes of cereals, red meats, and fats, oils, and sweets than controls (all $p<0.05$). In both racial groups, high fruit and vegetable intakes (particularly dark green leafy vegetables) were protective, consistent with 30-50% reductions in colon cancer risk, e.g., OR=0.5 (95% CI, 0.3, 0.8) for vegetables in African-Americans. In contrast, cereals, red meats, and fats, oils, and sweets were positively associated with colon cancer risk in Whites, e.g., for cereals, OR=2.4, 95% CI, 1.6, 3.7; while dairy products were only associated with increased risk in African Americans (OR=1.8, 95% CI, 1.0, 3.2). These findings add to the growing body of evidence that plant foods may protect against colon cancer and suggest that red meats and refined carbohydrates may increase colon cancer risk.

Prostatic Concentrations of Polyunsaturated Fatty Acids Independently Predict Risk of Extracapsular Disease in Men with Clinically Localized Prostate Cancer. *VL Freeman, M Meydan, K Hur, RC Flanigan*

PURPOSE: To evaluate the relation between prostatic exposure to individual fatty acids and locally advanced prostate cancer. **METHODS:** We identified 197 men (175 whites, 22 blacks) awaiting radical prostatectomy for clinically localized prostate cancer. Baseline clinical, demographic and lifestyle data were collected via self-administered questionnaires and medical records review. Fatty acids were measured using capillary gas chromatography in fresh, non-malignant tissue collected at the time of surgery. Two sample t-tests compared mean prostatic fatty acid concentrations in men found to have extracapsular disease (n=52) vs. organ-confined controls (n=145). Logistic regression accounted for simultaneous effects of age at treatment, clinical stage, Gleason sum, pre-operative PSA and ethnicity. **RESULTS:** Percent tPUSF was associated with a lower risk of any extracapsular disease, after adjustment for patient demographic and clinical characteristics (RR= 0.93 [0.87, 0.99], p=0.349). Limiting cases to just those with seminal vesicle involvement (n=20) seemed to strengthen this relation (RR = 0.86 [0.79, 0.94], $p \leq 0.001$ and RR = 0.49 [0.29, 0.84] p=0.009, for percent tPUSF and percent omega-3 fatty acid [eicosapentanoic + docosahexanoic acids], respectively.) **CONCLUSIONS:** Exposure to polyunsaturated fatty acids may help regulate prostate carcinogenesis

DNA Repair Capacity for UV-induced DNA Damage and Risk of Non-Melanoma Skin Cancers – A Hospital-based Case-control Study. Wei Q, Strom SS, Wang L, Lippman SM, Clayman GL, El-Naggar AK, Dùvic M, Goldberg L, Lee JJ, Kripke ML. The University of Texas M. D. Anderson Cancer Center, Houston, Texas, 77030.
Non-melanoma skin cancers (NMSCs), including basal cell carcinoma (BCC) and squamous cell carcinomas (SCC), are the most common human malignancy, and sunlight exposure is the predominant risk factor. To test the hypothesis that there was an association between DRC and NMSCs and tumor aggressiveness, we conducted a study of 322 NMSC patients (186 BCC and 136 SCC) and 322 cancer-free control subjects. All subjects were non-Hispanic whites. The DRC was measured by the host-cell reactivation assay with a reporter gene damaged by UVL. Multivariate logistic regression analysis with adjustment for age, sex, known risk factors, and assay correlates was used to calculate the odds ratios (ORs) and 95% confidence intervals (CIs). Overall, low DRC in cases (8.47%) compared with controls (10.1%) ($P < 0.01$) was associated with an increased risk of NMSCs (adjusted OR=1.55; 95% CI=1.06-2.25) by using the control median DRC level as the cutoff value. However, the risk was more pronounced for BCC (adjusted OR=1.66; 95% CI=1.10-2.53) than for SCC (adjusted OR = 1.26; 95% CI = 0.73-2.17). A dose-dependent increased risk using the tertiles of the controls' DRC values ($P_{trend} = 0.019$) was evident in BCC but not in SCC. Furthermore, there was no evidence that reduced DRC was associated with aggressive tumor pathology. These findings suggest that low DRC is an independent risk factor for BCC but not for SCC and not for tumors having aggressive features. (Supported by the NIH grant CA68233).

Outcome of a Tailored Print and Phone Counseling Trial to Increase Cancer Screening in 5 Ethnic Groups

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Purpose: Among individual-directed interventions to increase cancer screening in underserved communities, personal outreach is effective but costly. This was a randomized, controlled trial to increase screening and minimize cost. Methods: A cohort of 1463 African American, Chinese, Filipina, Latina, and white women was recruited by phone; participants were interviewed in their language at baseline and at a median 10 and 26 months. Individually tailored print brochures were sent to women in the intervention group after the first survey. After the second survey, an updated brochure was mailed and a telephone counseling intervention initiated by a multi-ethnic team of lay health workers. Results: The effects of the mailing alone differed significantly across ethnic groups and were associated with greater use of mammography among Latinas (p=0.02) and both mammography (p=0.005) and Pap tests (p=0.03) among Filipinas compared to their control counterparts. Following counseling, recent screening was overall significantly greater in the intervention group than in the control group for mammography (76% vs. 69%, p=0.004) and Pap tests (73% vs. 64%, p=0.001). The counseling intervention effects did not differ significantly across ethnic groups. Conclusion: Tailored phone counseling may be a cost-effective alternative to in-person outreach; tailored print material merits further exploration in some ethnic groups.

Tobacco Use Among Lung Cancer Screening Participants

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Purpose: The NCI's Lung Screening Study (LSS) was a feasibility study for conducting a randomized controlled trial of lung cancer screening with spiral CT. As an ancillary study of the LSS, we assessed the impact of study participation and screening result on smoking status and readiness to quit smoking among current smokers. Method: We conducted telephone interviews (N=144; 60% current smokers) prior to the second annual screening exam (T1), 3 weeks post receipt of screening result (T2), and are completing final 4-month follow-up interviews (T3). Subjects were: M=64 years (sd=5.2), 55% male, 90% white, 65% married, and 58% had at least a college degree. Results: T1 results revealed the usual distribution on readiness to quit (36% were not thinking of quitting, 44% were thinking of quitting in the next 6 months, and 20% planned to quit in the next 30 days). The mean FTND score was 4.4 (sd=2.1), cigarettes/day = 23 (sd=14), and 52% had made a 24h quit attempt in the past year. Although little change occurred in smoking status at T2 (5% quit), there was a significant increase in intention to quit (p<0.001). Furthermore, those who received an *abnormal* result had greater intention to quit (i.e., stage shift toward cessation) relative to those with a normal result (p=0.01). Regarding interest in cessation treatment, 69% expressed interest in NRT, and 66% would participate in counseling as part of a research study. T3 results will also be reported. Conclusions: These results indicate that lung cancer screening may serve as a teachable moment for smoking cessation, and that the screening setting represents a unique opportunity for assisting this challenging, high-risk group of smokers.

SEVERITY OF CANCER RISK AND HEALTH MOTIVATION TO CHANGE DIET AT BASELINE DO NOT PREDICT ADHERENCE TO MAJOR DIETARY CHANGE IN BREAST CANCER PATIENTS.

L. Madlensky, L. Natarajan and J.P. Pierce for the WHEL study group.

Purpose: To determine whether adherence to a high-vegetable dietary intervention is related to breast cancer family history (FH), stage of initial breast cancer or belief that diet will effect recurrence in the Women's Healthy Eating and Living (WHEL) Study. *Methods:* We consider 613 women randomized to the intervention group who were in the lower half of the distribution for dietary pattern at baseline (from sets of 24 hour recalls). We compare women in the highest vs. lowest tertile of dietary change at one year . *Results:* The intervention was associated with major dietary change, including among women in those with the poorest dietary patterns at baseline. The lowest tertile improved by 50% with the highest improving threefold. Controlled for age, neither Stage (I vs. II/IIIA OR=1.1, 95% C.I. 0.7-1.6) FH (none vs. 2 or more affected relatives OR=0.8, 95% C.I. 0.4-1.5) nor health motivation to change diet (not strong vs. very strong OR= 1.5, 95% C.I. 0.9-2.4) predicted which people would make the most vs. the least dietary change in response to the intervention. *Conclusions:* The telephone counseling intervention led to major dietary change that was not dependent on either the risk of recurrence or initial belief that changing diet would reduce that risk.

Psychological Influences on Lymphoproliferative Responses to HPV

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Purpose: Data suggest that psychosocial factors can influence immunocompetence, which plays an important role in controlling progression of cervical lesions. The purpose of this study was to examine the relationship between psychosocial and immune factors in women diagnosed with cervical intraepithelial neoplasia (CIN). **Methods:** Participants were 65 women undergoing diagnostic follow-up (i.e., colposcopy) for an abnormal Pap smear result. All participants completed psychosocial assessments (e.g., perceived stress, perceived control over one's health). A cervical specimen was obtained for human papillomavirus (HPV)-typing, and a blood sample was drawn to assess relevant immune measures, including T-cell proliferative response to HPV16, which is a specific marker of immune function that has been shown to be associated with viral clearance and disease regression. **Results:** At present, immune results are available for 30 participants. Regression analyses revealed that a lower lymphoproliferative response to HPV16 E7 peptides was associated with greater perceived stress (β = -0.60, $p < .05$) and lower perceived control ($\beta = 0.37$, $p < .05$), after controlling for potential confounding variables (i.e., age, smoking status). **Conclusion:** These findings, although preliminary, suggest that psychosocial factors may indirectly influence progression of precancerous cervical lesions through their effects on cell-mediated immune response to HPV16.

ASPO Abstracts

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