Cancer Epidemiology, Biomarkers & Prevention

ABSTRACTS • 38th Annual Meeting • American Society of Preventive Oncology, Hyatt Regency Crystal City, Arlington, VA, March 9–11, 2014

The following are the 16 highest scoring abstracts of those submitted for presentation at the 38th Annual ASPO meeting held March 9–11, 2014, in Arlington, VA.

Clinic Type and Patient Characteristics Affecting Time to Resolution after an Abnormal Cancer-Screening Exam

Krok JL, Kurta ML, Weier RC, Young GS, Carey AB, Tatum CM, Paskett ED

Research shows that multilevel factors influence health care delivery and patient outcomes. The goal of this study was to examine how clinic type (primary care clinic within an academic medical center (AMC) or federally-qualified health center (FQHC)) and patient characteristics influence time to resolution (TTR) among individuals enrolled in a patient navigation (PN) intervention. Data were obtained from the Ohio Patient Navigation Research Project, a group randomized trial in which 862 patients from 18 clinics in Columbus, OH participated. Patient's TTR after an abnormal breast, cervical, or colorectal test and the clinics' patient and provider characteristics were obtained. Descriptive statistics and Cox shared frailty proportional hazards regression models of TTR were used to analyze the data. The mean patient age was 44.8 years and 71% of patients were White. In models adjusted for study arm, the interaction between time and study arm and a clinic random effect, FQHC patients had a 39% lower rate of resolution than AMC patients (HR = 0.61, p = 0.004); college educated patients had an 87% higher rate of resolution than patients with less than a high school education (HR = 1.87, p = 0.0007); privately insured patients had a 79% higher rate of resolution than uninsured patients (HR = 1.79, p < 0.0001); patients with annual incomes ≥$50,000 had a 51% higher rate of resolution than patients with annual incomes <$10,000 (HR = 1.51, p = 0.02); and there was a 4% increase in the rate of resolution for each five year increase in patient age (HR = 1.04, p = 0.004). After using multiple imputation to impute income and insurance status where missing, factors that potentially confounded the effect of clinic type on TTR were assessed using forward selection. After adjustment for patient insurance status, education level and age, clinic type was not significantly associated with TTR. Controlling for clinic type, patient insurance status and age were significantly associated with TTR (p = 0.005 and p = 0.01, respectively) and patient education level was marginally significant (p = 0.06). These results suggest that TTR among individuals participating in PN programs is influenced by multiple socioeconomic (SES) patient-level factors rather than clinic type. Consequently, PN interventions should be tailored to address SES factors that influence TTR within patient populations.

Published online March 7, 2014.
doi: 10.1158/1055-9965.EPI-14-0066

Neighborhood Socioeconomic Status in Relation to Cancer Mortality in the Black Women's Health Study, 1995–2011

Bethea TN, Palmer JR, Rosenberg L, Cozier YC

Neighborhood socioeconomic status has been associated with a range of cancer health outcomes, but longitudinal data in African Americans, who tend to live in more deprived neighborhoods, is lacking. We assessed the relation of neighborhood socioeconomic status (SES) to cancer mortality in a prospective cohort of African American women. Participants enrolled in the Black Women's Health Study in 1995 by completing mailed questionnaires. Exposure information and incident diagnoses are updated through biennial questionnaires. Neighborhood SES was measured by a factor score based on census block group data for 6 indicators of income and education – median household income, median housing value, percent of households receiving interest/dividend/rental income, percent of adults who are college graduates, percent of white-collar workers, and percent of households not headed by a single female. Deaths through 2011 and cause of death were identified through linkage to the National Death Index. Cox proportional hazard models were used to estimate hazard ratios (HRs) and 95% confidence intervals (CIs) with control for age, education, marital status, cigarette smoking, physical activity, time spent watching TV, and dietary pattern. Based on 819 cancer deaths that occurred from 1995–2011, neighborhood SES was inversely associated with cancer mortality. The age-adjusted HR for lowest quartile of neighborhood SES relative to highest quartile was 1.63, 95% CI 1.33–2.00; control for covariates reduced the HR to 1.29, 95% CI 1.05–1.60. In analyses restricted to participants with 16 or more years of education, the multivariable HR for lowest relative to highest quartile of neighborhood SES was 1.38 (95% CI 1.01–1.90). Our results suggest that neighborhood SES is associated with

an individual's risk of cancer mortality and that the association is mediated in part by diet, physical activity, and sedentary behavior. The finding that this association was present even among college graduates is of particular relevance to African Americans, who are more likely to live in disadvantaged neighborhoods regardless of their individual income or educational attainment.

Published online March 7, 2014.
doi: 10.1158/1055-9965.EPI-14-0067

Changes in the Breast Cancer Risk Distribution among Women Utilizing Screening Mammography in Vermont Between 2001 and 2012

Bolton KC, Mace JL, Vacek PM, Geller BM, Weaver DL, Sprague BL

We previously reported a decline in overall breast cancer screening rates in Vermont following 2009. During this period, there has been debate regarding the role of patient context in decisions about when and how often to get screened, as well as increased interest in risk- based screening to optimize the balance between the potential benefits and harms of screening. The purpose of the current study was to evaluate whether the breast cancer risk distribution of the screened population in Vermont has changed during the observed decline in utilization rates. We examined the distribution of breast cancer risk among the screened population in Vermont from 2001 to 2012 using cross-sectional data from the statewide Vermont Breast Cancer Surveillance System. We employed the Breast Cancer Surveillance Consortium risk model to estimate each individual's risk of developing breast cancer within 5 years according to age, breast density, race/ethnicity, family history of breast cancer, and biopsy history. Among women ages 40 to 74 who received screening mammograms, the absolute number of visits dropped by 4,257, from 54,415 to 50,158 (−7.3%; 95% CI: −7.5, −7.1) between 2009 and 2012. Concurrently, the number of screened women who were estimated to be at low risk of developing breast cancer decreased by 4,240 (95% CI: 3,907, 4,573), representing the bulk of the overall decrease. There was no significant change in the aggregate number of women estimated to be at higher risk (−17 women; 95% CI: −350, 316). The outsized proportion of the decline attributed to women at low estimated risk held across younger and older age groups: among women ages 40 to 49, the absolute number screened dropped by 3,337, with 2,495 (95% CI: 2,389, 2,601) reflected by declines among women at low risk; among women ages 50 to 74, the absolute number screened dropped by only 920, however this value reflects a decrease of 1,763 (95% CI: 1,519, 2,007) for the low risk category, and gains totaling 843 (95% CI: 599, 1,087) among higher risk categories. We conclude that the observed decline in women screened in Vermont since 2009 is largely attributable to reductions in visits by women who are estimated to be at low risk of developing breast cancer, and that this trend generally holds across age groups.

Published online March 7, 2014.
doi: 10.1158/1055-9965.EPI-14-0068

Adherence to Multiple Cancer Screening Tests among Appalachian Women

Katz ML, Young GS, Pennell ML, Reiter PL, Paskett ED

Appalachian populations suffer from higher rates of cancer incidence and mortality than non-Appalachian populations. Research has documented disparities in the receipt of within guideline cancer screening tests for each test individually (mammography (MA), Pap Test (PT) and colonoscopy, flexible sigmoidoscopy or FOBT (CRC)), however, no study has documented disparities in the receipt of multiple screening tests in this population. Methods. As part of a larger study using community-based participatory research strategies to reach Appalachian community members about the need for CRC screening, we surveyed 643 women aged 51–75, inclusive who agreed to complete a phone survey after being randomly selected from commercially available address lists for 12 Appalachian Ohio counties. The survey included questions about the receipt of screening tests within guidelines: PT (within 3 years), MA (within the past year), and CRC (FOBT: past year; FS: last 5 years; or colonoscopy: last 10 years). The frequencies of each test received within guidelines as well as the number of tests (0, 1, 2, 3) women were adherent to, were calculated. Odds ratios and 95% confidence intervals for being within guidelines were calculated using multiple logistic regression (performed for within guidelines for each test and for all 3 tests vs. 0–2 tests). Results. Women not screened within guidelines by self-report were 33% for PT, 46% for MA, and 48% for CRC. Only 31% of the women were within guidelines for all 3 tests, with 18% reporting not being within guidelines for any of the 3 tests. Predictors of within screening guidelines for all three tests include having a check-up in the past two years (OR = 14.7; 1.94, 111.5; $p < 0.01$) and not being a current or former smoker (OR = 0.28; 0.11, 0.72; $p < 0.01$ and OR = 0.48; 0.25, 0.93; $p < 0.01$, respectively). Conclusions. Few women in Appalachia Ohio are adherent to currently recommended cancer screening tests. Only about a third of the women were adherent to all three screening tests and almost a fifth of the women were not adherent to any of the three screening tests. These findings suggest that interventions should focus on improving multiple screening behaviors to reduce the high cancer rates in this underserved population.

Published online March 7, 2014.
doi: 10.1158/1055-9965.EPI-14-0069

Collagen Fiber Alignment in Relation to Prognostic Markers for Ductal Carcinoma In Situ of the Breast

Trentham-Dietz A, Sprague BL, Conklin MW, Hampton JM, Gangnon RE, Eliceiri KW, Newcomb PA, Friedl A, Kelly PJ

Almost 20% of new diagnoses of breast cancer are ductal carcinoma in situ (DCIS). DCIS increases risk for invasive breast cancer, and new prognostic markers of disease-free survival are needed to complement the few that are known. Limited studies have investigated the prognostic value of the tumor microenvironment, which is increasingly recognized as potentially playing a key role in tumor invasion and progression. Collagen is the most abundant component of the stroma surrounding the breast ducts, and laboratory studies suggest that collagen alignment facilitates cancer cell invasion and migration. Here we examined whether collagen alignment patterns in human DCIS specimens correlate with known prognostic markers. We evaluated collagen fiber alignment in 235 Wisconsin women diagnosed with DCIS in 1997–2000 who participated in a clinicopathologic cohort study. Fiber alignment was evaluated from routine H&E tissue slides prepared at the time of diagnosis using second harmonic generation (SHG) microscopy, a label-free multiphoton laser scanning technique that selectively images collagen. Images were evaluated for the presence of collagen fibers arranged in a radial pattern (approximately 75- to 90-degree angles) with respect to the DCIS lesion/stroma boundary, a phenotype termed TACS (Tumor Associated Collagen Signature). Chi-square tests were used to compare presence or absence of TACS with prognostic factors from a central review of pathology reports and slides, and analysis of tissue for ER, PR, Ki-67, and HER2. Overall, slides for about half (49.8%) of DCIS cases showed the TACS phenotype. TACS was not associated with age of the cases ($P = 0.29$), size of the lesion ($P = 0.76$), grade ($P = 0.61$), or margin size ($P = 0.77$). However, results suggested that TACS was more common (63.1%) among DCIS cases detected symptomatically than by mammography (47.3%, $P = 0.09$). TACS was more common among cases that were ER-negative ($P = 0.002$), PR-negative ($P = 0.02$), Ki-67 positive ($P = 0.06$), and HER2-positive ($P = 0.002$). This study underscores the relevance of the tumor microenvironment, in particular the arrangement of the collagen fiber matrix. On-going analysis will examine disease-free survival among DCIS cases according to patterns of collagen fiber alignment.

Published online March 7, 2014.
doi: 10.1158/1055-9965.EPI-14-0070

Improving the Diagnostic Accuracy of a Stratified Screening Strategy by Identifying the Optimal Risk Cutoff

Brinton JT, Hendrick RE, Ringham BM, Glueck DH

We give a novel decision-theoretic approach for finding the optimal risk cutoff for additional breast cancer screening for women who have a high model-predicted risk of breast cancer. Methods: The American Cancer Society (ACS) suggests a stratified screening strategy for breast cancer. The strategy includes assessing women's risk of breast cancer using a risk model, screening women at high risk of breast cancer with both contrast-enhanced breast MRI and mammography, while screening women at low risk of breast cancer with mammography alone. The ACS used expert consensus opinion to choose the risk cutoff for additional screening. Instead, we suggest a risk cutoff chosen to maximize the full area under the receiver operating characteristic curve for the strategy. We use three inputs to find the cutoff, including: 1) the distribution of five-year breast cancer risk scores, 2) the probability of breast cancer given the risk score, and 3) the diagnostic accuracies of digital mammography, and contrast-enhanced screening breast MRI. No data were publicly available for testing the performance of stratified screening strategies based on the ACS suggested risk models. Instead, we used publicly available Breast Cancer Screening Consortium (BCSC) risk data to seek an optimal risk cutoff. A previous study suggests that the BCSC risk model has similar predictive accuracy as the Tyrer-Cuzick and Claus models. For comparison, we used a hypothetical risk model with much better predictive accuracy than the BCSC model. Results: For the BCSC risk model, the strategy with the highest diagnostic accuracy for the entire population is to screen almost all women with both digital mammography and contrast- enhanced breast MRI. Under the strategy based on the hypothetical risk model, only women at 18% or higher five-year risk would receive dual modality screening. Conclusion: The results occur because the BCSC risk model does not accurately predict which women will or will not develop breast cancer. However, if there were a more accurate risk model, a stratified screening strategy would offer benefits for the entire population by balancing the harms of breast cancer screening with the potential for improved breast cancer detection.

Published online March 7, 2014.
doi: 10.1158/1055-9965.EPI-14-0071

Clinical and Genetic Predictors of Impaired Fertility in Female Survivors of Childhood Cancer

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An important late effect among female survivors of childhood cancer is treatment-related ovarian damage

and impaired fertility. While chemotherapy and radiation therapy are associated with impaired fertility, few other risk factors have been identified. Furthermore, little is known about the role of genetic susceptibility to these late effects. Objective: As Anti-Müllerian Hormone (AMH) is a demonstrated marker of ovarian reserve; our objective was to identify clinical and genetic predictors of AMH levels in female survivors of childhood cancer. Methods: Female childhood cancer survivors (n = 181) were recruited from the Texas Children's Cancer Center Long Term Survivor Program (LTSP). AMH (ng/mL) was measured using an enzyme-linked immunosorbent assay. Information on age at diagnosis and enrollment, race, ethnicity, cancer diagnosis, pelvic radiation, and use of alkylating agents was abstracted from medical records. The following single nucleotide polymorphisms (SNPs) were selected based on known or suspected function: AMHR2 rs2002555; CYP2C9*4 rs56165452; CYP2C19*2 rs4244285; and CYP2C19*3 rs4986893. SNPs were genotyped using TaqMan assays. Linear regression was used to determine the association between selected factors and AMH levels. As AMH levels were not normally distributed, the dependent variable was expressed as log10(AMH+1). Results: The mean age at enrollment in the LTSP was 12.4 years. The most common cancer diagnosis was acute lymphoblastic leukemia (47.2%), and a substantial proportion of the population was Hispanic (41.0%). The following variables were significantly associated with lower AMH levels: pelvic radiation (beta = −0.61, P < 0.001) and treatment with alkylating agents (beta = −0.09, P = 0.04). Age at enrollment was associated with higher AMH levels (beta = 0.01, P = 0.04). Hispanic ethnicity was marginally associated with lower AMH levels (beta = −0.08, P = 0.08). There were no significant genetic associations. Conclusions: In one of the largest studies of its kind, our results confirm previous associations between treatment-related factors and ovarian damage. While the SNPs evaluated were not predictive of AMH levels, more work is needed to explain why some survivors experience impaired fertility, while others do not, despite similar therapy.

Published online March 7, 2014.
doi: 10.1158/1055-9965.EPI-14-0072

Accuracy of Self-Report of Nevus and Pigmentation Phenotype Compared to Clinical Assessment in Young Australian Adults

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There is no formal community-wide melanoma screening program in Australia, but the importance of early detection and regular skin self-examination is generally well understood. It is important that individuals are able to identify key melanoma risk factors so that those at high risk can modify their sun-related behaviours and take appropriate preventative actions from a young age. Aims: 1) To evaluate the accuracy of self-reported pigmentation and nevus phenotype compared to clinical assessment, and 2) to examine agreement between clinically-measured whole-body nevus count and clinically-measured nevus count on selected anatomical regions, given that localised mole count is often used as a proxy measure. Methods: The sample included 456 cases with invasive cutaneous melanoma diagnosed between ages 18–39 years and 538 controls from the population-based Australian Melanoma Family Study. Participants completed a questionnaire regarding their pigmentation and nevus phenotype, and attended a clinical skin examination with a dermatologic trainee. Results: There was strong agreement between self-reported and clinical measurement for eye color (weighted kappa, Kw, = 0.83, 95% confidence interval (CI) 0.80–0.86); and moderate agreement for hair color (Kw = 0.52, 95% CI 0.47–0.56). There was poor agreement for skin color when using spectrophotometer-derived individual typography angle (ITA) scores as the objective measure (Kw = 0.18, 95% CI 0.14–0.22). Participants underestimated their nevus counts. The Spearman correlation was 0.43 (95% CI 0.38–0.49) when comparing clinically-measured total body nevus count (≥2 mm) with self-reported nevus density categories, and the intraclass correlation was 0.36 (95% CI 0.30–0.41) when comparing nevus counts on the back. There was good agreement between quartile distributions of clinically-measured site-specific nevus counts with total body nevus counts, particularly for the arms (Kw = 0.76 for men and 0.80 for women). Conclusions: Agreement between self-reported pigmentation and nevus phenotype compared to clinical assessment ranges from poor to excellent, depending on the measure. For studies where a full body nevus count is impractical, measuring nevus counts on the arms would be an acceptable alternative.

Published online March 7, 2014.
doi: 10.1158/1055-9965.EPI-14-0073

Contribution of MC1R Genotype and Novel Common Genomic Variants to Melanoma Risk Prediction

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Genome-wide association studies have identified numerous common genomic variants associated with increased susceptibility to melanoma, but there is limited knowledge about the utility of adding them to risk prediction models for melanoma. Individuals diagnosed at a young age might have an underlying genetic susceptibility to melanoma, and young adulthood is a key age period for targeting primary prevention strategies for melanoma. Aim: To evaluate the contribution of melanocortin-1 receptor (MC1R) gene variants and novel common genomic variants to melanoma risk prediction, among young Australian adults. Methods: The sample

included 552 cases with invasive cutaneous melanoma diagnosed between ages 18–39 years and 405 controls from an Australian population-based, case-control-family study. MC1R genotype was sequenced, and through a genome-wide association study we obtained genotype data for single nucleotide polymorphisms from 18 selected gene regions. Measures of discriminatory accuracy included the area under receiver operating characteristic curves (AUC) and net reclassification improvement (NRI), calculated based on predicted probabilities of melanoma from unconditional logistic regression models. We used 10-fold cross-validation and bootstrap methods to assess internal validation. Results: The AUC increased from 0.76 (95% CI 0.73–0.79) for the non-genetic multivariate model containing demographic and self-reported risk factors (UV exposure, phenotype, nevi, etc), to 0.81 (95% CI 0.78–0.84) for the genetic model that additionally included MC1R genotype and novel common genomic variants. The combined contribution to the AUC of the novel common genomic variants identified through genome-wide association studies was similar to that contributed from the known common variants in MC1R and CDKN2A. Inclusion of genomic variants in the multivariate model improved the quartile classification of predicted risk (NRI) by a net 17% (95% CI 9–24) compared to the non-genetic model. Conclusions: Our results suggest that MC1R and other common genomic variants could considerably improve risk prediction models for early-onset melanoma, and may have a role in primary prevention of melanoma.

Published online March 7, 2014.
doi: 10.1158/1055-9965.EPI-14-0074

Retention of Black and White Populations in the Selenium and Vitamin E Cancer Prevention Trial

Arnold KB, Hermos JA, Anderson KB, Minasian LM, Cook ED

Background: Adequate retention of Black (African-American) participants in long-term, randomized trials is important for achieving broadly applicable results. Purpose: To determine the incidence of retention failures and the individual and study site factors associated with retention failure among White and Black participants from the Selenium and Vitamin E Cancer Prevention Trial (SELECT), a phase III study of selenium and vitamin E for prevention of prostate cancer. Methods: SELECT randomized 35,533 participants from 427 study sites. Age eligibility was >55 years for Whites, >50 years for Blacks; race was determined by self-report. The primary analysis included 28,118 (87%) White and 4,322 (13%) Black men. Time to retention failure was defined as days to the earliest of either (1) the second consecutive missed in-person or phone visit or (2) refusal of future contact with study staff. Covariates included participant demographic and clinical characteristics, reasons for participating in SELECT and study site characteristics. Results: In SELECT, Blacks had a higher age-adjusted risk of disengagement than Whites [HR = 1.9; 95% CI 1.7–2.0; p-value <.0001]. Younger Black participants, age 50–54, representing 32% of Black participants, were at three times the risk of disengagement than those age 65+ [HR = 3.34, 95%CI 2.24, 4.94, p < .0001]. Blacks age 65+ had 1.6 times the risk of disengagement than Whites age 65+ [HR = 1.58, 95% CI 1.37, 1.83, p < .0001]. By six years post-randomization, 83% of Whites were still retained on the study compared to 68% of Blacks. Among Whites, participant risk factors for disengagement were Hispanic ethnicity, graduate degree, living alone or current smoking; among Blacks, younger age and current smoking were risk factors. The site characteristic associated with disengagement among both racial groups was staff missing SELECT training sessions. Sites with a low staff attendance at training sessions had a high percentage of disengaged participants of either race. Both Whites and Blacks at sites receiving SELECT retention and adherence grants had lower risks for retention failure. Conclusion: These results may be useful in identifying personal and study site characteristics to guide recruitment and enhance retention of both Black and White men in long-term prevention trials.

Published online March 7, 2014.
doi: 10.1158/1055-9965.EPI-14-0075

Physical Activity and Quality of Life among Elderly Cancer Survivors Compared to Women without Cancer: The Iowa Women's Health Study

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Few studies have examined lifestyle factors and health-related quality of life (QOL) in elderly, long-term cancer survivors compared to a cancer-free comparison group. We examined the degree to which physical inactivity is associated with poor QOL among elderly, female cancer survivors compared to similar-aged women without cancer. Methods: Subjects included women enrolled in the Iowa Women's Health Study in 1986 who completed the 2004 questionnaire (at ages 71–89 years) and were alive through 2005. The 2004 questionnaire asked participants about recreational physical activity and included the Medical Outcomes Study Short Form-36 (SF36) QOL assessment. Physical inactivity was defined as moderate or vigorous activity less than once per week. Logistic regression was used to compute the odds of poor QOL for each SF36 subscale (<0.5 SD below the mean score of women without cancer) associated with physical inactivity between 4 groups based on the cross-classification of cancer history (no/yes) and physical inactivity (no/yes) (referent group = No/No). Results: Analyses included 12,067 women without a history of cancer and 1,707 women diagnosed with cancer between 1986 and 2002. Inactive cancer survivors were significantly more likely

to report poor QOL for each SF36 subscale compared to the referent group (Odds Ratios (OR) 1.7 to 4.5), independent of age, comorbidity, BMI, and diet quality. Compared with the other 3 groups, inactive cancer survivors had the greatest odds of poor Physical Function (inactive cancer survivors [OR = 4.5, 95% CI 3.9–5.3], inactive women without cancer [OR = 3.8, 95% CI 3.5–4.2], active cancer survivors [OR = 1.0,95% CI 0.8–1.2]) and poor General Health (inactive cancer survivors [OR = 3.2, 95% CI 2.7–3.8], inactive women without cancer [OR = 2.8, 95% CI 2.5–3.0), active cancer survivors [OR = 1.2, 95% CI 0.98–1.4]). Among physically active women, cancer survivors had similar QOL as women without a cancer history. Conclusions: Physical inactivity was more strongly associated with poor General Health and Physical Function in elderly, long-term cancer survivors compared to women without cancer. These findings support the need for interventions to help older women maintain or regain a physically active lifestyle after a cancer diagnosis.

Published online March 7, 2014.
doi: 10.1158/1055-9965.EPI-14-0076

Quality of Life and Comorbidities Impact Education and Employment for Survivors of Adolescent and Young Adult Cancers

Kirchhoff AC, McFadden M, Warner EL, Kinney AY

Survivors of adolescent and young adult (AYA) cancers have a high risk of chronic conditions such as cardiovascular disease and asthma. These conditions may affect their ability to attend school or to work. We examined the impact of quality of life (QOL) and comorbidities on educational attainment and employment status for survivors of AYA cancers relative to a non-cancer comparison group. Methods: Using data from the 2009 Behavioral Risk Factor Surveillance System (BRFSS), we identified 7,471 individuals who were diagnosed with cancer between ages 15 and 39 and were ≥5 years from diagnosis and 326,821 controls without a history of cancer. Participants were ≥25 years of age. QOL was measured by a general health measure (excellent/very good/good/fair/poor). Comorbidities included self-reported cardiovascular disease, hypertension, asthma, and diabetes. Multivariable regressions using BRFSS survey weights were adjusted for sex, race/ethnicity and age, and compared the effects of QOL and comorbidities on educational attainment (college graduate or more vs. less education) and being employed or unable to work (compared to out of work or not in labor force) among the survivor and control groups. Results: Compared to controls, survivors in fair-poor health were less likely to be college graduates or more (survivors 18.5% vs. controls 37.9%, $p < 0.01$) and less likely to be employed (survivors 31.7% vs. controls 61.6%, $p < 0.001$), whereas survivors in good-excellent health did not differ from controls for either outcome. In addition, survivors in fair-poor health self-reported being unable to work more often than controls (31.4% vs. 5.4%, respectively; $p < 0.001$). For comorbidities, inability to work ranged from 14.9% of survivors with hypertension to 27.9% of survivors with cardiovascular conditions compared to 5.4% of controls (all $p < 0.001$), while survivors with no comorbidities did not differ from controls. Conclusions: AYA cancer survivors with ongoing health problems may face educational or work-related limitations. Early detection and management of health problems could help AYA cancer survivors control health problems before their ability to attend school or employment is disrupted.

Published online March 7, 2014.
doi: 10.1158/1055-9965.EPI-14-0077

The Association Between Sexual Abuse and Adherence to Risk-Appropriate Cervical Cancer Screening Guidelines: A Study of Women in Appalachian Ohio

Kurta ML, Krok JL, Hade EM, Williams J, Nemeth J, Paskett ED

Our objective was to determine if a history of forced sex influenced the likelihood of meeting risk-appropriate cervical cancer (CC) screening guidelines among women in Appalachian Ohio. Methods: We used data collected from initial recruitment for Community Awareness Resources and Education (CARE) I projects 1 and 2. Women were randomly selected from 14 Ohio Appalachian clinics. Risk-appropriate guidelines were defined as having had a Pap smear within 13 months of study interview among high risk women and within 37 months of interview among low risk women. High risk was defined as meeting any of the following criteria: 5 or more sexual partners during their lifetime; intercourse before 18; a current smoker; diagnosis of an STI; or a sexual partner diagnosed with an STI. Low-risk women did not meet any of these criteria. Associations between meeting guidelines and patient characteristics were evaluated by calculating odds ratios (OR) and corresponding 95% confidence intervals (CI) using logistic mixed model regression, with clinic incorporated as a random effect. Significant factors were included in a multivariable regression model assessing the association between exposure to forced sex and meeting CC screening guidelines. Results: Of the 571 women in this study, 105 (18.4%) reported being forced to have sex, 456 (79.9%) did not report forced sex, and 10 (1.8%) refused to answer or didn't know. We observed significant crude associations between meeting risk-appropriate CC screening guidelines and potential confounders: socioeconomic status (low vs. intermediate: OR = 2.46, CI: 1.48–4.09; low vs. high: OR = 2.78, CI: 1.65–4.72), marital status (divorced/widowed/separated vs. married/member of couple: OR = 2.03, CI: 1.90–6.92; divorced/widowed/separated vs. never married: OR = 3.63, CI: 1.90–6.92), and smoking

status (never vs. former: OR = 2.46, CI: 0.32–0.84; never vs. current: OR = 0.51, CI: 0.33–0.78). Adjusted for these factors and current age, women forced to have sex had significantly lower odds of being within screening guidelines (OR = 0.32, CI: 0.20–0.53). Conclusions: Women exposed to forced sex have lower odds of meeting risk-appropriate CC screening guidelines. This population needs additional efforts to ensure adherence to CC screening guidelines.

Published online March 7, 2014.
doi: 10.1158/1055-9965.EPI-14-0078

Trajectories of Depressive Symptoms 24 Months Following Breast Cancer Diagnosis

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The majority of studies on depression among cancer survivors report means or percentages which obscure the heterogeneity of women's responses to cancer. Trajectory analysis provides a more nuanced picture of different patterns of response. Purpose: To identify, in a large sample of breast cancer survivors, distinct groups of women exhibiting different patterns (trajectories) of depressive symptoms up to 24 months following a breast cancer diagnosis, and to identify characteristics associated with these patterns. Methods: 653 women within 8 months of initial breast cancer diagnosis completed questionnaires at baseline and 6, 12, and 18 months after baseline on contextual/patient characteristics, symptoms, and psychosocial variables. Chart reviews provided cancer and treatment-related data. The primary outcome was depressive symptomatology assessed by the Beck Depression Inventory (BDI). Finite mixture modeling was used to identify trajectories of depressive symptoms. Results: Based on a combination of the Bayesian Information Criterion and observation of trajectory distinctiveness, a 6-trajectory model was chosen. Almost half of the sample had a consistently very low (3.8%) or low (46%) level of depressive symptoms over time that was well below the traditional BDI cut-point of 10 thought to be indicative of clinically significant depression; 29.8% had a consistently borderline BDI score that hovered around 10; 12.1% had initially high BDI, but showed a decline over time; 7.2% showed an increased BDI over time; and a small but distinct group (1.2%) reported a chronically high BDI above 25. Women in the lower depressive symptom groups were older, had fewer physical symptoms (fatigue and pain), less rigorous chemotherapy, and lower levels of illness intrusiveness. Additional analyses also showed that to some degree, illness intrusiveness, pain, and social support scores over time paralleled BDI trajectories. Conclusions: Trajectory analysis allowed us to detect heterogeneity among women in reporting depressive symptoms following a breast cancer diagnosis. Our larger sample size identified more trajectories than other smaller studies. Mean levels of various characteristics at baseline and over time were identified that were significantly associated with each trajectory.

Published online March 7, 2014.
doi: 10.1158/1055-9965.EPI-14-0079

Neighborhood and Geographic Factors Associated with Diagnostic Resolution After an Abnormal Breast or Cervical Cancer Screening Test Among Women Enrolled in a Patient Navigator Program

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This study's aim was to assess the associations between neighborhood and geographic factors and diagnostic resolution within 12 months following an abnormal screening test for breast or cervical cancer among participants of the Ohio Patient Navigator Research Program. Methods: Patient (demographic, psychosocial, and socioeconomic status [SES]) and neighborhood (SES, racial segregation, healthcare access) factors of 776 women attending one of 16 clinics and living in one of 285 census tracts in greater Columbus, Ohio were examined. Women were randomized at the clinic level to determine receipt of the navigation intervention. Multilevel logistic regression was used to estimate associations between these factors and diagnostic resolution while controlling for clinic and neighborhood clustering. Spatial analysis assessed the presence of geographic disparities (i.e., regions of significantly high odds of not resolving). Results: After adjustment for individual-level SES and the receipt of the clinic-level navigation intervention, there was a significant inverse association between neighborhood-level percent of residents without a bachelor's degree and odds of diagnostic resolution (odds ratio = 0.79, 95% confidence interval = 0.63–0.98). Adjustment for neighborhood percent of residents without a bachelor's degree accounted for geographic disparities in diagnostic resolution. Racial segregation, home-to-clinic distance and PN were not associated with odds of resolution. Conclusions: Women were more likely to have diagnostically resolved 12 months following an abnormal breast or cervical cancer screening test if they lived in neighborhoods of higher SES. Geographic disparities in diagnostic resolution could be reduced if there was no variation in neighborhood SES.

Published online March 7, 2014.
doi: 10.1158/1055-9965.EPI-14-0080

Smoking History in Relation to Survival after a Breast Cancer Diagnosis

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Smoking history is associated with increased risk of most cancers, including breast cancer. Given the per-

sistent effects of tobacco carcinogens, smoking history may also influence breast cancer survival. The few previous studies assessing this association were hindered by limited numbers of outcomes. METHODS: We assessed pre-diagnosis tobacco smoking in relation to survival in 22,870 female residents of Wisconsin, Massachusetts, or New Hampshire who were diagnosed with incident, invasive breast cancer between 1988–2008 at ages 20–79. All women reported pre-diagnosis tobacco use, as well as other known and suspected breast cancer risk factors. Information on breast cancer staging was obtained from state cancer registries. Proportional hazards regression with baseline hazard stratified on state of residence and study phase was used to estimate adjusted hazard ratios (HR) and 95% confidence intervals (CI) for cause-specific death according to current smoking (at the time of the breast cancer diagnosis) and long-term (>30 years) smoking (prior to the diagnosis) adjusting for age at diagnosis, stage of disease at diagnosis, family history of breast cancer, age at first birth, menopausal status, hormone therapy use, body mass index, alcohol consumption, education, and mammography. RESULTS: During a median follow-up of 11.3 years from diagnosis, 7,807 deaths occurred, including 3,483 attributed to breast cancer, 328 to lung cancer, 415 to respiratory disease, and 1,553 to cardiovascular disease. Compared to nonsmokers, the HR were 1.2 (1.1–1.3. P = trend = 0.0003) for current smokers and 1.2 (1.1–1.3, P trend = 0.01) for >30 years of smoking. Current smoking was also associated with increased mortality from lung cancer, HR = 14.5 (10.1–20.8), cardiovascular disease, HR = 2.2 (1.9–2.5), and respiratory disease HR = 6.3 (4.8–8.2). CONCLUSIONS: In this large population-based sample of breast cancer cases, current and long-term smokers at the time of diagnosis were 20% more likely to die from breast cancer than never smokers adjusting for breast cancer stage. The elevated mortality risk observed here for known smoking-related diseases adds confidence to the breast cancer findings.

Published online March 7, 2014.
doi: 10.1158/1055-9965.EPI-14-0081

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Cancer Epidemiol Biomarkers Prev 2014;23:569-570.