

## ABSTRACTS

### 28th Annual Meeting • American Society of Preventive Oncology Bethesda, Maryland • March 14-16, 2004

Following are the 16 highest-scoring abstracts of those submitted for presentation at the 28th Annual ASPO meeting to be held March 14-16, 2004.

Ovarian Cancer and Endometriosis. F. Modugno\*, R. Ness, G. Allen, J. Schildkraut, F. Davis and M. Goodman.

Background: Women with endometriosis may be at an increased risk of ovarian cancer. It is not known whether reproductive factors that reduce the risk of ovarian cancer in general also reduce risk in women with endometriosis. Methods: We pooled data on history of endometriosis from 4 population-based case-control studies of epithelial ovarian cancer, comprising 2083 cases and 2923 controls. We obtained data on oral contraceptive (OC) use, childbearing, breastfeeding, gynecologic surgeries and other reproductive factors on each woman. Multivariable unconditional logistic regression was used to calculate odds ratios (OR) and 95% confidence intervals (CI) for ovarian cancer among women with compared to women without endometriosis. Similar methods were used to assess the frequencies of risk factors among women with and without endometriosis. Adjustments were made for age, parity, oral contraceptive use, tubal ligation, family history of ovarian cancer and study site. Results: Women with endometriosis were at an increased risk of ovarian cancer (OR=1.32, 95% CI=1.06-1.65). Using OCs, bearing children, and having a tubal ligation or hysterectomy were associated with a similar reduction in the ORs for ovarian cancer among women with and without endometriosis. Notably, OCs use for 10+ years was associated with a substantial reduction in risk among women with endometriosis (OR=0.21; 95%CI=0.08-0.58). Conclusions: Endometriosis increases the risk of ovarian cancer. Long-term OC use provides substantial protection against the disease in this high-risk population.

Effect of Fraternal vs. Paternal Prostate Cancer on Ovarian Cancer. F. Modugno\*, R. Ness and G. Allen. Background: Sex hormones may play a role in the etiology of ovarian and prostate cancers, yet there are limited data linking the two diseases. Methods: Multivariable logistic regression was used to examine the association between ovarian cancer and family history of prostate cancer in a population-based study comparing incident cases (n=512) to community controls (n=946). Results: Compared to women with no family history of the disease, women reporting a brother with prostate cancer were at an increased risk of ovarian cancer (OR=3.02; 95%CI=1.19-7.69, adjusted for age, parity, tubal ligation and OC duration). No increase in risk was associated with paternal prostate cancer (OR=1.07; 95%CI=0.68-1.70). Oral contraceptive use was associated with decreased risk among women without a family history of prostate cancer (OR= 0.71; 95%CI=0.55-0.92) and among women with a paternal history (OR=0.46; 95% CI=0.22-0.97), but not among women reporting fraternal prostate cancer (OR=3.42; 95%CI=0.75-15.66). Mucinous tumors were overrepresented in women with a brother with prostate cancer compared to women with no family history of the disease (35.7% vs 13.8%, p=.02). Conclusion: Only fraternal prostate cancer may be a risk factor for ovarian cancer, suggesting recessive or X-linked susceptibility genes may play a role in the etiology of both diseases. Tumor histology and risk factor differences between fraternal versus paternal prostate cancer suggest different etiologies for ovarian cancers associated with different prostate cancer family history.

Evidence of overdiagnosis in lung cancer screening. PM Marcus, EJ Bergstralh, MH Zweig, A Harris, KP Offord, RS Fontana.

A troubling aspect of cancer screening is that detection of disease with little or no clinical relevance (overdiagnosis) may occur. Such diagnoses waste health care resources; furthermore, evaluation and treatment can lead to morbidity and even premature mortality. The strongest evidence of overdiagnosis comes from a randomized controlled trial (RCT) in which no mortality benefit is observed but an excess of cases persists in the intervention arm after screening stops and time passes. Overdiagnosis is of particular concern in lung cancer (LC) screening because new imaging modalities can identify small nodules of unknown significance. To examine the possibility of overdiagnosis in LC screening, we conducted extended LC incidence follow-up among Mayo Lung Project (MLP) participants. The MLP, an RCT of LC screening (1971-1983, 9211 male smokers, intense regimen of chest x-ray and sputum cytology vs. usual care) showed no reduction in lung cancer mortality, but showed an excess of 46 cases in the intervention arm at the end of the study (1983). To identify LC diagnosed between 1983 and 1999, we investigated the LC status of the 7118 MLP participants who, as of 1983, were alive and had not been diagnosed with LC. Medical records, surveys mailed to participants or next-of-kin, and state death certificates were utilized, and information on 6101 (86%) of the 7118 participants was available. From 1971-1999, a total of 585 participants in the MLP intervention arm were diagnosed with lung cancer versus 500 in the usual care arm. The persistence of excess cases after 16 additional years of follow-up provides continued evidence for overdiagnosis in the MLP and lung cancer screening in general.

Gender of Offspring and Ovarian Cancer G.L. Gierach, F. Modugno and R.B. Ness, University of Pittsburgh. Purpose: Sex steroids have been implicated in the etiology of both breast and ovarian cancers. Recent data suggest that gender of offspring, a potential marker of maternal hormone milieu, may be associated with differences in breast cancer risk. We sought to determine whether a similar relationship exists for ovarian cancer. Methods: We compared 511 parous women with incident ovarian cancer to 1136 community controls participating in a population-based study of ovarian cancer conducted in the Delaware Valley from 1994-98. After stratifying by number of offspring, we used multivariable logistic regression to assess the relationship between ovarian cancer and offspring gender, adjusting for age, race, education, oral contraceptive duration, tubal ligation, and family history of ovarian cancer. Results: Compared to having all girls, having a male offspring was inversely associated with ovarian cancer (OR=0.67, 95%CI=0.51-0.87). This result was consistent among women with only one birth (OR=0.68, 95% CI=0.40-1.13) and among those with 3 births (OR=0.43, 95% CI=0.21-0.86; OR=0.48, 95%CI=0.24-0.96; OR=0.50, 95% CI=0.20-1.23; for 1, 2 and 3 boys, respectively, compared to no boys). Among women with two births, the association was observed for those with 1 male offspring (OR=0.65, 95% CI=0.41-1.02), but not for those with two male offspring (OR=1.14, 95%CI=0.69-1.88). Conclusions: Bearing a male offspring may be associated with a decrease in maternal ovarian cancer risk.

Zablotska L and Neugut A., "Esophageal Cancer Following Radiation Therapy in Women Treated with Lumpectomy or Mastectomy for Primary Breast Cancer."

1. Purpose: to investigate the impact of postmastectomy and postlumpectomy radiation treatment (RT) on second primary esophageal cancer (EC); to explore the relationship between RT and histological type of EC; to examine the location of the second EC in relation to the primary field of irradiation.

2. Methods: a prospective cohort analysis of the data from the population-based SEER registry, encompassing approximately 10% of the U.S. population, from 1973 to 2000. Cox regression was used to estimate the relative risk (RR) for second primary EC among women treated with RT as compared to those who received surgery alone as a function of time interval since treatment. Hazard ratios were calculated for EC overall and separately for the histological subtypes, and for EC originating in the different parts of esophagus in the mastectomy group.

3. Results: 5-9 years following post-mastectomy RT the relative risk of second EC increased to 2.86 (95% CI, 1.50-5.44). The excess risk was found for both major histologic subtypes (adenocarcinoma and squamous cell carcinoma). The increase was mainly present for tumors located in the upper (cervical) and middle (thoracic) third of esophagus, with risks of 9.09 (95% CI, 1.22-67.74) and 2.54 (95% CI, 0.99-6.50). All risks remained increased with increased length of follow-up. There was no increase in risk following lumpectomy and RT.

4. Conclusions: Postmastectomy RT gives a moderate increase in risk of EC starting 5 years after exposure; increased risk persists for more than 10 years. Postlumpectomy RT does not appear to incur an increased risk. These findings should be reassuring to women treated with either type of RT, but the excess risk in the postmastectomy group should be considered in the choice between treatment options.

Dietary Folate and Alcohol Intake and Ovarian Cancer  
LE Kelemen, TA Sellers, RA Vierkant, L Harnack, JR Cerhan  
Studies evaluating the association of ovarian cancer (OC) with alcohol intake are inconsistent, and few have evaluated this association in the context of folate consumption. Dietary folate and alcohol intakes were assessed with a validated food frequency questionnaire administered in 1986 to postmenopausal (PM) women aged 55-69 years followed prospectively for 15 years for risk of epithelial OC in the Iowa Women's Health Study. Self-reported lifestyle and medical information was collected by questionnaire. Among 25,598 eligible women free of baseline cancer and diabetes, 145 incident epithelial OC cases were identified by linkage to a cancer registry. Compared to the highest quartile of total folate (food plus supplement) intake (greater than or equal to 541 ug/d), the multivariable risk ratios (RRs) for decreasing quartiles were 1.0 (referent), 0.81, 0.94, 0.65 (95% confidence interval [CI], 0.34-1.25; P for trend, 0.30). The results were similar for folate from food sources only. Compared to non-drinkers, the multivariable RRs for increasing alcohol intake were 1.0 (referent), 0.77 for 0.01-3.9 g/d, 0.74 for 4.0-9.9 g/d and 0.51 for greater than or equal to 10.0 g/d (95% CI, 0.26 - 0.99; P for trend, 0.04). The apparent risk reduction was limited to women with total folate intake above the median (greater than or equal to 331 ug/d) and alcohol intake greater than or equal to 4 g/d (RR, 0.36, 95% CI, 0.16-0.83) compared to women with folate intake above the median and alcohol intake < 4 g/d (P for interaction = 0.02). The RR was independent of baseline age, age at menopause, PM hormone use, family history of breast or ovarian cancer and intake of antioxidants. PM women who consume folate greater than or equal to 331 ug/d and alcohol greater than or equal to 4 g/d may be at lower risk of developing OC than women with this level of folate intake and no or little alcohol consumption.

African American Recruitment in Prostate Cancer Research: Unprecedented Success with Relationship Marketing  
Deborah Watkins Bruner, Sabriya Linton, Susan Mazzoni, Mary Daly, Natalie Dewberry-Moore, Andre Konski, Robert G. Uzzo

Purpose: This descriptive study reports on results of African American (AA) recruitment for The Prostate Cancer Risk Assessment Program (PRAP) at the Fox Chase Cancer Center (FCCC), a screening program and registry developed for those at high-risk for the disease. Methods: Recruitment used a multifaceted approach including a technique called "Relationship Marketing", which employs building ethnically and culturally sensitive relationships that are sustained over long periods. Results: AAs account for 256 of 436 PRAP participants. Mean age for the total sample and for AA participants is 49 years. Education levels were similar among ethnic groups but there were differences in income. Recruitment patterns differed widely by ethnicity with radio advertising accounting for 78% and 18%, newspaper 3% and 13%, relative referrals 3% and 21%, TV 4% and 1%, and friend referrals 6% and 4% of AA and white recruitment respectively. Conclusion: While most clinical trials accrue <5% AA's, PRAP has accrued 58% AA's, which is also 40% greater than the 13.5% AA population in the FCCC primary catchments. Two lessons can be learned, one type of recruitment strategy does not fit all, and relationship marketing may enhance minority recruitment.

Pulmonary Findings in a Cohort of Current and Ex-cigarette Smokers Undergoing Lung Cancer Screening  
J.G. Schragin, F.C. Scieurba, D.O. Wilson, C.R. Fuhrman, R.M. Rogers, and J.L. Weissfeld. University of Pittsburgh  
Purpose of Study: To determine the prevalence of chronic obstructive lung disease (COPD) by Global Initiative for Obstructive Lung Disease (GOLD) Criteria and qualitative CT interpretation in a community-based cohort recruited for lung cancer screening. Methods: Participants, 2143, were recruited from the Allegheny County, PA area. Eligibility criteria include age 50-79 years and history of smoking 11 or more cigarettes per day for at least 25 years and, if quit, quit no more than 10 years before study entry. All participants received office-based pulmonary function (PFT) tests from a trained technician, completed a medical questionnaire, and underwent spiral CT scanning for lung cancer screening and qualitative evidence of emphysema. Results: In a group of 50-79 year-old persons, without self-reported prior MD diagnosis of emphysema, bronchitis, or asthma, undergoing CT lung cancer screening due to cigarette related risk, we found 22.8% prevalence of moderate to very severe COPD, GOLD Stages II-IV, on PFT's and a 35.0% prevalence of CT radiographic evidence for emphysema. Of the persons with none to mild COPD, GOLD Stages 0-I, 29.5% have qualitative CT evidence for emphysema. Conclusion: Lung cancer screening in persons at risk due to cigarette exposure detects a significant amount of undiagnosed COPD creating the opportunity for early medical intervention. Further characterization of CT-determined emphysema by quantitative methods may be useful in lung cancer screening.

### A Tetranucleotide Repeat Polymorphism of CYP19 and Risk of Prostate Cancer: A Sibling-Matched Case-Control Study

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The CYP19 gene codes for aromatase, a key steroidogenic enzyme involved in the conversion of C19 androgen to aromatic C18 estrogen. The prostate is influenced by estrogen from peripheral sources as well as through aromatase activity in its stroma. A (TTTA)<sub>n</sub> repeat polymorphism in intron 4 of CYP19 has been inconsistently associated with prostate cancer in previous studies. We investigated the relationship of this polymorphism in CYP19 and prostate cancer risk in a sibling-matched case-control study. Included in our analysis are 440 cases and their 480 control siblings from 414 discordant families. We observed 9 different CYP19 alleles in our study population. No statistically significant difference in the CYP19 allelic distribution was found between the cases and the controls ( $\chi^2=5.14$ ,  $p=0.74$ ). Age-adjusted odds ratios (ORs) and 95% confidence intervals (95% CIs) were estimated by conditional logistic regression models. Compared to those with no (TTTA)<sub>10</sub> allele, the OR was 0.65 (95% CI=0.30-1.41) for those with (TTTA)<sub>10</sub> allele ( $p=0.27$ ). When compared to those with no (TTTA)<sub>12</sub> allele, the OR was 0.91 (95% CI=0.45-1.83) for those with (TTTA)<sub>12</sub> allele ( $p=0.78$ ). Analysis at the genotype-level yielded similar results. Further analysis stratified by disease aggressiveness or case's age at diagnosis did not alter the results. Our study indicates that the CYP19 (TTTA)<sub>n</sub> polymorphism is unlikely to play an important role in the development of prostate cancer.

Interrelation of energy intake, body size, and physical activity with breast cancer in the PLCO Screening Trial

Chang SC, Leitzmann MF, Stolzenberg-Solomon R, Lacey J, Huang WY, Ziegler R, Buys S, Johnson K, Hoover R, Hartge P, Schatzkin A.

**Background:** We assessed prospectively whether an energy-rich diet, body mass, and physical exercise influence breast cancer development in postmenopausal women directly, or through a combination of each.

**Methods:** 27,534 women, aged 55–74 years at baseline, were recruited from multiple centers in USA from 1993 to 1997. During follow-up from 1993 to 2000, 764 incident breast cancer cases were ascertained. Cox proportional hazards regression was applied for data analysis.

**Results:** Women in the highest quartile of energy intake, as compared to those in the lowest quartile, had a significantly increased risk for breast cancer (RR=1.25; 95% CI=1.02, 1.54;  $p$  for trend=0.07). Body mass index (BMI) at baseline was also suggestively positively associated with risk of breast cancer (RR comparing extreme categories=1.26; 95% CI=0.99, 1.60;  $p$  for trend=0.06). Women with vigorous activity • 4 hrs/wk at baseline had a significantly lower risk of breast cancer than those with <4 hrs/wk (RR=0.83; 95% CI=0.69, 1.00). When we jointly evaluated energy intake, body mass, and physical activity, women with the most unfavorable energy balance (i.e. women with the highest energy intake, highest BMI, and lowest physical activity level) were at greatest risk for developing breast cancer (RR=2.11; 95% CI= 1.28, 3.48).

**Conclusion:** These results suggest that energy intake, body mass, and physical activity are independently associated with risk of breast cancer and that these three factors act jointly in determining breast cancer risk.

Dietary B vitamins and the risk of lymphoid cancers in male smokers. U. Lim, R. Stolzenberg-Solomon, J. Virtamo, P. Pietinen, P.R. Taylor, D. Albanes.

Genetic polymorphisms in folate-regulating enzymes have been suggested to alter the risk of lymphoid cancers through their impact on one-carbon metabolism and DNA stability. We prospectively examined the association of dietary factors of one-carbon metabolism with lymphoid cancers on the 27,111 healthy male smokers who completed dietary questionnaires in the Alpha-Tocopherol Beta-Carotene Cancer Prevention Study Cohort. During up to 15 years of follow-up (1985–1999), 147 non-Hodgkin's lymphoma (NHL) and 42 chronic lymphocytic leukemia (CLL) cases were diagnosed (N = 189). Cox proportional hazard models were used to estimate relative risks (RR) and 95% confidence intervals (CI). The adjusted RR for combined lymphoid cancers comparing the highest to the lowest quintiles of energy-adjusted dietary vitamin B12 intake was 0.54 (95% CI, 0.34-0.86;  $p$  – trend = 0.01), with a stronger inverse association primarily for NHL (RR = 0.42; 95% CI, 0.24 – 0.72;  $p$  – trend = 0.001). There was no significant association between folate (RR = 0.75; 95% CI, 0.45 – 1.27) and lymphoid cancers. There was a borderline significant inverse association between dietary vitamin B6 intake and NHL (RR = 0.59; 95% CI, 0.35, 1.01) comparing the highest to the lowest quintiles. Our results support the hypothesis that dietary one-carbon sources may be inversely associated with NHL.

### Diet and Risk of Biliary Tract Cancers: A Population-based Study in Shanghai, China

Tanuja Rastogi, Gao Y, Gridley G, Rashid A, Deng J, Fraumeni JF, Hsing AW

**Purpose:** To clarify the role of diet in biliary tract cancer etiology, we conducted a population-based case-control study in Shanghai, China, where incidence of biliary cancers has doubled in recent years. **Methods:** In-person interviews were administered to patients newly diagnosed with primary biliary tract cancers (n=661), biliary stones (n=1037), and 959 healthy controls randomly selected from the general population (age and gender matched). A food frequency questionnaire was used to assess usual dietary intake. **Results:** The association between intake of 43 food groups and the risk of biliary tract cancers was examined using unconditional logistic regression. Higher intake of preserved foods was associated with increased risk of biliary stones and cancers: subjects in the highest compared to lowest quartile of intake had an elevated risk for gallstones (OR=1.23,  $P$ , trend =0.04), bile duct stones (OR=1.32,  $P$ , trend =0.06), gallbladder cancer (OR=1.6,  $P$ , trend =0.07) and bile duct cancer (OR=1.57,  $P$ , trend=0.04). In contrast, compared to subjects in the lowest quartile of allium vegetable consumption, those in the highest had a reduced risk for gallstones (OR=0.70;  $P$ , trend =0.03) and for gallbladder cancer (OR=0.65;  $P$ , trend =0.08). Higher intake of red meat was associated with a non-significant elevation in risk for both gallstones and bile duct stones, with persons in the highest quartile having a 1.35-fold risk of gallstones ( $P$ , trend=0.08) and a 1.24-fold risk for bile duct stones ( $P$ , trend= 0.2), relative to those in the lowest. **Conclusions:** These findings suggest that consumption of nitrates from preserved foods may have an adverse role in pathogenesis of biliary stones and cancers, while the anti-inflammatory property of allium vegetables may be associated with reduced risk of both gallstones and gallbladder cancer.

Colonoscopy for colorectal cancer screening in average risk subjects: prevalence of neoplasia, complications and cost-effectiveness.

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**Background:** The ideal screening modality for CRC in average-risk population is still in debate. Colonoscopy is the most effective screening method, but its role in screening programs and cost-effectiveness remain to be proven.

**Aims:** To evaluate the benefits, risk and cost-effectiveness of primary screening colonoscopy in asymptomatic subjects at average-risk of CRC.

**Methods:** 1040 asymptomatic subjects without a personal or family history of CR neoplasia underwent a full colonoscopy: 787 persons were aged 50-75 years, 178 aged 40-49 and 75 subjects aged 76-80 years.

**Results:** In the age group 50-75, overall CR neoplasia was detected in 23.8%, advanced neoplasia in 8% and CRC in 1.4%. Proximal neoplasia without distal lesions was 34%. In the age group of 40-49 years, overall CR neoplasia rate was 9.5%, including advanced adenoma in 1.1% and no CRC. Among the elderly (76-80 yrs), the prevalence of CR neoplasia, advanced neoplasia and CRC was 27.9%, 14.6% and 2.7%, respectively. Morbidity rate was very low with no perforations, bleeds or mortality. Using a Partially Observed Markov Decision Process designed for the health services in Israel, colonoscopy once in 10 years was shown to be the most cost-effective screening modality, compared with 5-year sigmoidoscopy and annual fecal occult blood test, with \$5,690 per life year gained.

**Conclusions:** Colonoscopy is a sensitive, safe, feasible and highly cost-effective screening modality for asymptomatic individuals at average-risk of CRC, beginning at age 50.

A focused CQI intervention can increase colorectal cancer screening rates among Veterans: results from the Chicago VA project

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This study examined whether a combined patient and physician intervention increased adherence to colorectal cancer (CRC) screening. A randomized controlled intervention was conducted with outpatients at VA Chicago-Lakeside Division. One firm, with 979 patients, was assigned to the intervention, and the other, with 941 patients, to usual care. The patient intervention involving an educational brochure and video included male Veterans, age 50 and older, who had not undergone recent CRC screening. Literacy was measured using the Rapid Estimate of Adult Literacy in Medicine (REALM). The physician component included quarterly anonymous "report cards" indicating screening recommendation and adherence rates. Patient mean age was 67.8 years. 44% were white and 50% were African-American. After 6-12 months of follow-up, a higher rate of screening recommendations was observed in the intervention arm compared to the control arm (76% vs. 70%,  $p=0.038$ ), as well as a higher rate for completed screening tests (41% vs. 33%,  $p=0.008$ ). The intervention had a greater effect on the rate of completed screening tests among low-literate patients (55.8% vs. 32.1%,  $p=0.007$ - low literacy group; 40.2% vs. 37.2%,  $p=0.67$ - high literacy group). This intervention significantly increased screening recommendations and adherence to CRC screening among Veterans, especially persons with poor literacy skills.

Cooked Meat and Breast Cancer in the Carolina Breast Cancer Study Steck-Scott, S. Arab, L., Tseng, M., Tse, C.K., Millikan, R. Well-done cooked meat contains carcinogens and may be related to an increased risk of breast cancer. We examined the association of meat cooked with various preparation methods and to varying degrees of doneness with risk of breast cancer in a large (1,449 cases, 1,231 controls), population-based case-control study conducted in North Carolina between 1997 and 2001. A questionnaire that captured intake of 8 different types of meat with 3 different preparation methods, as well as preference for doneness of meat, was administered by interview. Logistic regression was used to calculate adjusted odds ratios (OR) for breast cancer by level of meat intake. Increased risk of breast cancer was observed for women who consumed fried or broiled beef steak once per week (OR=1.53, 95% confidence interval (CI): 1.19, 1.96), for women who consumed pan-fried chicken >once per week (OR=1.24, 95%CI: 0.92, 1.66), and for women who often or always ate drippings or gravy from cooked meat (OR=1.23, 95%CI: 0.97, 1.55) relative to non-consumers. These associations were observed in both African-American and white women. Associations were stronger in women who preferred meat cooked to medium-well or well-done compared to women who preferred rare to medium meat. Joint effects were observed for high consumption of cooked meat and low intake of fruits and vegetables. Future analyses will examine the interactions between cooked meat intake and polymorphisms in DNA repair genes. In conclusion, intake of meat cooked by methods that promote carcinogen formation was associated with a modest increased risk of breast cancer.

#### THE INCIDENCE OF COLORECTAL CANCER FOLLOWING THE IDENTIFICATION OF A SINGLE TUBULAR ADENOMA AT SCREENING FLEXIBLE SIGMOIDOSCOPY

Doria-Rose VP, Newcomb PA, Levin TR, Selby JV, Weiss NS

**Purpose of study:** To examine the incidence of colorectal cancer (CRC) following the identification of a single very small (< 5 mm) or small (6-9 mm) tubular adenoma (TA) at a baseline screening sigmoidoscopy, in order to assess whether a 5-year surveillance interval is adequate, and whether colonoscopy is indicated.

**Methods:** Men and women aged 50 and above, who were considered not to be at high risk of CRC, and who had a single very small ( $n=1,860$ ) or small ( $n=302$ ) TA discovered at a baseline sigmoidoscopy between 1994 and 1996, were identified using a computerized database of participants in the Colon Cancer Prevention (CoCaP) program of Kaiser Permanente of Northern California. Five-year incidence rates of distal and proximal CRC were compared to rates in a cohort of CoCaP participants who had no polyps at baseline ( $n=72,483$ ).

**Results:** For those who had a single TA < 1 cm that was completely removed, the five-year incidence of distal CRC was 14.2 per 100,000 person-years, which was similar to the incidence in those with no polyps at baseline (9.9 per 100,000). The incidence rates of proximal CRC were elevated in those with a small (154.3 per 100,000), but not in those with a very small (12.4 per 100,000) TA (compared to rates of 27.2 per 100,000 in those with no polyps).

**Conclusions:** Although we cannot rule out chance as a cause of these findings, our results suggest that there would not be a large benefit to screening those with a single TA less than one centimeter more often than every five years, and that only those with TAs greater than 5 mm should receive colonoscopy.