



## Selección de Resúmenes de Menopausia

Semana del 1 al 7 de Febrero de 2017

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**JAMA Oncol. 2017 Feb 2. doi: 10.1001/jamaoncol.2016.6326. [Epub ahead of print]**

### **Population-Attributable Risk Proportion of Clinical Risk Factors for Breast Cancer.**

Engmann NJ, Golmakani MK, Miglioretti DL, Sprague BL, Kerlikowske K; Breast Cancer Surveillance

Importance: Many established breast cancer risk factors are used in clinical risk prediction models, although the proportion of breast cancers explained by these factors is unknown. Objective: To determine the population-attributable risk proportion (PARP) for breast cancer associated with clinical breast cancer risk factors among premenopausal and postmenopausal women. Design, Setting, and Participants: Case-control study with 1:10 matching on age, year of risk factor assessment, and Breast Cancer Surveillance Consortium (BCSC) registry. Risk factor data were collected prospectively from January 1, 1996, through October 31, 2012, from BCSC community-based breast imaging facilities. A total of 18 437 women with invasive breast cancer or ductal carcinoma in situ were enrolled as cases and matched to 184 309 women without breast cancer, with a total of 58 146 premenopausal and 144 600 postmenopausal women enrolled in the study. Exposures: Breast Imaging Reporting and Data System (BI-RADS) breast density (heterogeneously or extremely dense vs scattered fibroglandular densities), first-degree family history of breast cancer, body mass index ( $>25$  vs  $18.5$ - $25$ ), history of benign breast biopsy, and nulliparity or age at first birth ( $\geq 30$  years vs  $<30$  years). Main Outcomes and Measures: Population-attributable risk proportion of breast cancer. Results: Of the 18 437 women with breast cancer, the mean (SD) age was 46.3 (3.7) years among premenopausal women and 61.7 (7.2) years among the postmenopausal women. Overall, 4747 (89.8%) premenopausal and 12 502 (95.1%) postmenopausal women with breast cancer had at least 1 breast cancer risk factor. The combined PARP of all risk factors was 52.7% (95% CI, 49.1%-56.3%) among premenopausal women and 54.7% (95% CI, 46.5%-54.7%) among postmenopausal women. Breast density was the most prevalent risk factor for both premenopausal and postmenopausal women and had the largest effect on the PARP; 39.3% (95% CI, 36.6%-42.0%) of premenopausal and 26.2% (95% CI, 24.4%-28.0%) of postmenopausal breast cancers could potentially be averted if all women with heterogeneously or extremely dense breasts shifted to scattered fibroglandular breast density. Among postmenopausal women, 22.8% (95% CI, 18.3%-27.3%) of breast cancers could potentially be averted if all overweight and obese women attained a body mass index of less than 25. Conclusions and Relevance: Most women with breast cancer have at least 1 breast cancer risk factor routinely documented at the time of mammography, and more than half of premenopausal and postmenopausal breast cancers are explained by these factors. These easily assessed risk factors should be incorporated into risk prediction models to stratify breast cancer risk and promote risk-based screening and targeted prevention efforts.

**J Fam Pract. 2016 Dec;65(12):933-934.**

### **Clinical Inquiries: Does vitamin D without calcium reduce fracture risk?**

Daly S, Allison C, Nashelsky J.

Supplemental vitamin D without calcium--in doses averaging as much as 800 IU per day--doesn't reduce the risk of hip, vertebral, or nonvertebral fractures in postmenopausal women and older men.

**Cancer Epidemiol Biomarkers Prev. 2017 Feb 1. doi: 10.1158/1055-9965.EPI-16-0761. [Epub ahead of print]**

### **Metabolic Phenotype and Risk of Colorectal Cancer in Normal-Weight Postmenopausal Women.**

Liang X, Margolis KL, Hendryx M, Rohan TE, Groessl EJ, Thomson CA, Kroenke CH, Simon MS, Lane D, et al.

BACKGROUND: The prevalence of metabolically unhealthy phenotype in normal-weight adults is 30%, and few studies have explored the association between metabolic phenotype and colorectal cancer incidence in normal-weight individuals. Our aim was to compare the risk of colorectal cancer in normal-weight postmenopausal women who were characterized by either the metabolically healthy phenotype or the metabolically unhealthy phenotype. METHODS: A large prospective cohort, the Women's Health Initiative, was used. The analytic sample included 5,068 postmenopausal

women with BMI 18.5 to <25 kg/m<sup>2</sup> Metabolic phenotype was defined using the Adult Treatment Panel-III definition, excluding waist circumference; therefore, women with one or none of the four components (elevated triglycerides, low high-density lipoprotein cholesterol, elevated blood pressure, and elevated fasting glucose) were classified as metabolically healthy. Multivariable Cox proportional hazards regression was used to estimate adjusted HRs for the association between metabolic phenotype and risk of colorectal cancer. RESULTS: Among normal-weight women, those who were metabolically unhealthy had higher risks of colorectal cancer (HR, 1.49; 95% CI, 1.02-2.18) compared with those who were metabolically healthy. CONCLUSIONS: A metabolically unhealthy phenotype was associated with higher risk of colorectal cancer among normal-weight women. IMPACT: Normal-weight women should still be evaluated for metabolic health and appropriate steps taken to reduce their risk of colorectal cancer.

**J Clin Oncol. 2012 Sep 20;30(27\_suppl):25. doi: 10.1200/jco.2012.30.27\_suppl.25.**

### **Metformin and breast cancer risk: A meta-analysis and critical literature review.**

Ochs L, Springmann V, Aragaki AK, Chlebowski RT.

Background: Observational studies have suggested that metformin, commonly used for diabetes treatment that increases insulin sensitivity and improves glycemic control, decreases the incidence of several common cancers. However, findings regarding metformin and breast cancer incidence have been mixed. To explore this issue, a systematic literature review and meta-analysis were performed with a focus on potential biases. METHODS: We conducted a comprehensive literature search for all pertinent studies addressing metformin use and breast cancer risk by searching Pub Med, Cochrane Library, Scopus (which includes Embase, ISI Web of Science) using the Mesh terms: "metformin" or "biguanides" or "diabetes mellitus, type 2/therapy" and "cancer" or "neoplasms". When multiple hazard ratios (HR) or odds ratio (OR) were reported, the most adjusted estimate was used in the base-case analysis. We pooled the adjusted HR using and performed sensitivity analyses on duration of metformin use (> or < 3 years use), study quality (assessed using the GRADE system), and initial observation year of the cohort (before vs after 1997). RESULTS: From a total of 421 citations, 13 full-text articles were considered, and 7 independent studies were included. All were observational (4 cohort and 3 case control). Our combined OR for metformin association with invasive breast cancer of all 7 studies was 0.83 (95% CI, 0.71-0.97). Funnel plot analyses did not suggest publication bias. Stronger associations were found when analyses were limited to studies estimating the impact of longer metformin duration (OR = 0.75, 95% CI, 0.62-0.91) or among studies that began observing their cohort before 1997 (OR=0.68, 95% CI, 0.55-0.84). Stratification according to study quality did not affect the combined OR but higher quality studies had smaller CI and achieved statistical significance. Interpretation is limited by the observational nature of reports and different comparison groups. CONCLUSIONS: Our analyses support a protective effect of metformin on invasive breast cancer incidence among postmenopausal women with diabetes. Clinical trials are needed to determine whether metformin reduces breast cancer risk.

**Clin Nutr. 2017 Jan 13. pii: S0261-5614(17)30006-7. doi: 10.1016/j.clnu.2016.12.030. [Epub ahead of print]**

### **Extra virgin olive oil consumption reduces the risk of osteoporotic fractures in the PREDIMED trial.**

García-Gavilán JF, Bulló M, Canudas S, Martínez-González MA, Estruch R, Giardina S, Fitó M, Corella D, et al.

BACKGROUND & AIMS: The incidence of osteoporotic fractures is lower in countries in the Mediterranean basin. Virgin olive oil, a key component of the Mediterranean Diet (MDiet), with recognised beneficial effects on metabolism and cardiovascular health, may decrease the risk of osteoporotic fractures. The aim to this study was to explore the effect of chronic consumption of total olive oil and its varieties on the risk of osteoporosis-related fractures in a middle-aged and elderly Mediterranean population. METHODS: We included all participants (n = 870) recruited in the Reus (Spain) centre of the PREvención con Dieta MEDiterránea (PREDIMED) trial. Individuals, aged 55-80 years at high cardiovascular risk, were randomized to a MedDiet supplemented with extra-virgin olive oil, a MedDiet supplemented with nuts, or a low-fat diet. The present analysis was an observational cohort study nested in the trial. A validated food frequency questionnaire was used to assess dietary habits and olive oil consumption. Information on total osteoporotic fractures was obtained from a systematic review of medical records. The association between yearly repeated measurements of olive oil consumption and fracture risk was assessed by multivariate Cox proportional hazards. RESULTS: We documented 114 incident cases of osteoporosis-related fractures during a median follow-up of 8.9 years. Treatment allocation had no effect on fracture risk. Participants in the highest tertile of extra-virgin olive oil

consumption had a 51% lower risk of fractures (HR:0.49; 95% CI:0.29-0.81. P for trend = 0.004) compared to those in the lowest tertile after adjusting for potential confounders. Total and common olive oil consumption was not associated with fracture risk. CONCLUSIONS: Higher consumption of extra-virgin olive oil is associated with a lower risk of osteoporosis-related fractures in middle-aged and elderly Mediterranean population at high cardiovascular risk.

**Menopause. 2017 Jan 30. doi: 10.1097/GME.0000000000000824. [Epub ahead of print]**

### **Association of sleep disturbance and sexual function in postmenopausal women.**

Kling JM, Manson JE, Naughton MJ, Temkit M, Sullivan SD, Gower EW, Hale L, Weitlauf JC, Nowakowski S, et al. OBJECTIVE: Sleep disturbance and sexual dysfunction are common in menopause; however, the nature of their association is unclear. The present study aimed to determine whether sleep characteristics were associated with sexual activity and sexual satisfaction. METHODS: Sexual function in the last year and sleep characteristics (past 4 wk) were assessed by self-report at baseline for 93,668 women age 50 to 79 years enrolled in the Women's Health Initiative (WHI) Observational Study (OS). Insomnia was measured using the validated WHI Insomnia Rating Scale. Sleep-disordered breathing (SDB) risk was assessed using questions adapted from the Berlin Questionnaire. Using multivariate logistic regression, we examined cross-sectional associations between sleep measures and two indicators of sexual function: partnered sexual activity and sexual satisfaction within the last year. RESULTS: Fifty-six percent overall reported being somewhat or very satisfied with their current sexual activity, and 52% reported partnered sexual activity within the last year. Insomnia prevalence was 31%. After multivariable adjustment, higher insomnia scores were associated with lower odds of sexual satisfaction (yes/no) (odds ratio [OR] 0.92, 95% CI, 0.87-0.96). Short sleep duration (<7-8h) was associated with lower odds of partnered sexual activity (yes/no) ( $\leq 5$ h, OR 0.88, 95% CI, 0.80-0.96) and less sexual satisfaction ( $\leq 5$ h, OR 0.88, 95% CI, 0.81-0.95). CONCLUSIONS: Shorter sleep durations and higher insomnia scores were associated with decreased sexual function, even after adjustment for potential confounders, suggesting the importance of sufficient, high-quality sleep for sexual function. Longitudinal investigation of sleep and its impact on sexual function postmenopause will clarify this relationship.

**J Am Heart Assoc. 2017 Jan 29;6(2). pii: e004545. doi: 10.1161/JAHA.116.004545.**

### **Postmenopausal Women With Greater Paracardial Fat Have More Coronary Artery Calcification Than Premenopausal Women: The Study of Women's Health Across the Nation (SWAN) Cardiovascular Fat Ancillary Study.**

El Khoudary SR, Shields KJ, Janssen I, Budoff MJ, Everson-Rose SA, Powell LH, Matthews KA.

BACKGROUND: Volumes of paracardial adipose tissue (PAT) and epicardial adipose tissue (EAT) are greater after menopause. Interestingly, PAT but not EAT is associated with estradiol decline, suggesting a potential role of menopause in PAT accumulation. We assessed whether volumes of heart fat depot (EAT and PAT) were associated with coronary artery calcification (CAC) in women at midlife and whether these associations were modified by menopausal status and estradiol levels. METHODS AND RESULTS: EAT and PAT volumes and CAC were measured using electron beam computed tomography scans. CAC was evaluated as (1) the presence of CAC (CAC Agatston score  $\geq 10$ ) and (2) the extent of any CAC (log CAC Agatston score  $> 0$ ). The study included 478 women aged 50.9 years (58% pre- or early perimenopausal, 10% late perimenopausal, and 32% postmenopausal). EAT was significantly associated with CAC measures, and these associations were not modified by menopausal status or estradiol. In contrast, associations between PAT and CAC measures were modified by menopausal status (interaction- $P \leq 0.01$ ). Independent of study covariates including other adiposity measures, each 1-SD unit increase in log PAT was associated with 102% higher risk of CAC presence ( $P = 0.04$ ) and an 80% increase in CAC extent ( $P = 0.008$ ) in postmenopausal women compared with pre- or early perimenopausal women. Additional adjustment for estradiol and hormone therapy attenuated these differences. Moreover, the association between PAT and CAC extent was stronger in women with lower estradiol levels (interaction  $P = 0.004$ ). CONCLUSIONS: The findings suggest that PAT is a potential menopause-specific coronary artery disease risk marker, supporting the need to monitor and target this fat depot for intervention in women at midlife.