



## Selección de Resúmenes de Menopausia

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**Environ Health Perspect. 2017 Jul 6;125(7):077004. doi: 10.1289/EHP943.**

### **Serum Vitamin D and Risk of Breast Cancer within Five Years.**

O'Brien KM, Sandler DP, Taylor JA, Weinberg CR.

**BACKGROUND:** Vitamin D is an environmental and dietary agent with known anticarcinogenic effects, but protection against breast cancer has not been established. **OBJECTIVE:** We evaluated the association between baseline serum 25-hydroxyvitamin D [25(OH)D] levels, supplemental vitamin D use, and breast cancer incidence over the subsequent 5 y of follow-up. **METHODS:** From 2003-2009, the Sister Study enrolled 50,884 U.S. women 35-74 y old who had a sister with breast cancer but had never had breast cancer themselves. Using liquid chromatography-mass spectrometry, we measured 25(OH)D in serum samples from 1,611 women who later developed breast cancer and from 1,843 randomly selected cohort participants. We estimated hazard ratios (HRs) and 95% confidence intervals (CIs) for the risk of developing breast cancer using Cox proportional hazards models. **RESULTS:** We found that 25(OH)D levels were associated with a 21% lower breast cancer hazard (highest versus lowest quartile: adjusted; CI: 0.63, 0.98). Analysis of the first 5 y of follow-up for all 50,884 Sister Study participants showed that self-reported vitamin D supplementation was associated with an 11% lower hazard [ (CI: 0.81, 0.99)]. These associations were particularly strong among postmenopausal women [ (CI: 0.57, 0.93) and (CI: 0.74, 0.93), respectively]. **CONCLUSIONS:** In this cohort of women with elevated risk, high serum 25(OH)D levels and regular vitamin D supplement use were associated with lower rates of incident, postmenopausal breast cancer over 5 y of follow-up. These results may help to establish clinical benchmarks for 25(OH)D levels; in addition, they support the hypothesis that vitamin D supplementation is useful in breast cancer prevention.

**Sci Rep. 2017 Jul 19;7(1):5803. doi: 10.1038/s41598-017-06036-y.**

### **Mammographic density, blood telomere length and lipid peroxidation.**

Erdmann NJ, Harrington LA, Martin LJ.

Extensive mammographic density is a strong risk factor for breast cancer, but may also be an indicator of biological age. In this study we examined whether mammographic density is related to blood telomere length, a potential marker of susceptibility to age-related disease. We measured mammographic density by a computer assisted method and blood telomere length using a validated PCR method. Urinary malondialdehyde (MDA), a marker of lipid peroxidation, was measured in 24 hour urine collections. In the 342 women examined telomere length was negatively correlated with age, was lower in postmenopausal compared to premenopausal women and in smokers compared to non-smokers, and was positively correlated with urinary MDA. Telomere length was not associated with percent mammographic density or dense area, before or after adjustment for risk factors and MDA. However, there was a significant interaction between telomere length and MDA in their association with mammographic density. At lower levels of MDA, mammographic density and telomere length were inversely associated; while at high levels of MDA, there was evidence of a J-shaped association between mammographic density and telomere length. Further work is need to replicate these results and to examine the association of mammographic density with age-related chronic disease and mortality.

**Diabetologia. 2017 Jul 18. doi: 10.1007/s00125-017-4346-8. [Epub ahead of print]**

### **Age at natural menopause and risk of type 2 diabetes: a prospective cohort study.**

Muka T, Asllanaj E, Avazverdi N, Jaspers L, Stringa N, Milic J, Ligthart S, Ikram MA, Laven JSE, et al.

**AIMS/HYPOTHESIS:** In this study, we aimed to examine the association between age at natural menopause and risk of type 2 diabetes, and to assess whether this association is independent of potential mediators. **METHODS:** We included 3639 postmenopausal women from the prospective, population-based Rotterdam Study. Age at natural menopause was self-reported retrospectively and was treated as a continuous variable and in categories (premature, <40 years; early, 40-44 years; normal, 45-55 years; and late menopause, >55 years [reference]). Type 2 diabetes events were diagnosed on the basis of medical records and glucose measurements from Rotterdam Study visits. HRs and 95% CIs were calculated using Cox proportional hazards models, adjusted for confounding factors; in another model, they were additionally adjusted for potential mediators, including obesity, C-reactive protein, glucose and insulin, as well as for levels of total

oestradiol and androgens. **RESULTS:** During a median follow-up of 9.2 years, we identified 348 individuals with incident type 2 diabetes. After adjustment for confounders, HRs for type 2 diabetes were 3.7 (95% CI 1.8, 7.5), 2.4 (95% CI 1.3, 4.3) and 1.60 (95% CI 1.0, 2.8) for women with premature, early and normal menopause, respectively, relative to those with late menopause (p trend <0.001). The HR for type 2 diabetes per 1 year older at menopause was 0.96 (95% CI 0.94, 0.98). Further adjustment for BMI, glycaemic traits, metabolic risk factors, C-reactive protein, endogenous sex hormone levels or shared genetic factors did not affect this association. **CONCLUSIONS/INTERPRETATION:** Early onset of natural menopause is an independent marker for type 2 diabetes in postmenopausal women.

**Menopause. 2017 Jul 17. doi: 10.1097/GME.0000000000000929. [Epub ahead of print]**

### **Lifelong estradiol exposure and risk of depressive symptoms during the transition to menopause and postmenopause.**

Marsh WK, Bromberger JT, Crawford SL, Leung K, Kravitz HM, Randolph JF, Joffe H, Soares CN.

**OBJECTIVE:** Depression risk increases during the menopausal transition (MT) and initial postmenopausal years—both times of significant fluctuations of estrogen. Research to date provides limited support for the hypothesis that estrogen fluctuations play a role in the greater susceptibility to midlife depression. Importantly, not all women report depressive symptoms during the MT, and recent reports suggest that duration of exposure to estradiol throughout the adult years may also play a role in vulnerability to depression. This study examines patterns of estrogen exposure during the reproductive years and risk of depression during the MT and early postmenopausal years. **METHODS:** A longitudinal, US community-based, multiethnic study of menopause. Data were collected at baseline and annually for 10 years, and included 1,306 regularly menstruating premenopausal women, aged 42 to 52 years at study entry. The main outcome was incidence of high level of depressive symptoms, Center for Epidemiological Studies Depression Scale (CES-D) score at least 16, in the MT and initial postmenopausal years, independent of premenopausal depression symptoms. Risk factors examined were duration of estrogen exposure (menarche to MT), duration of hormonal birth control use, pregnancies, and lactation. **RESULTS:** In a multivariate adjusted model, longer duration of estrogen exposure from menarche to MT onset was significantly associated with a reduced risk of depression (CES-D  $\geq$ 16) during the MT and 10 years or less postmenopause (odds ratio 0.85, 95% confidence interval 0.78-0.92). Longer duration of birth control use was associated with a decreased risk of CES-D at least 16 (odds ratio 0.90, 95% confidence interval 0.83-0.98), but number of pregnancies or breastfeeding was not. **CONCLUSIONS:** Patterns of reproductive lifetime exposure to estrogen are associated with risk of high depressive symptoms during the MT and initial postmenopausal years; longer exposure to estrogen seemed protective.

**Menopause. 2017 Jul 17. doi: 10.1097/GME.0000000000000949. [Epub ahead of print]**

### **The bidirectional relationship between vasomotor symptoms and depression across the menopausal transition: a systematic review of longitudinal studies.**

Natari RB, Clavarino AM, McGuire TM, Dingle KD, Hollingworth SA.

**OBJECTIVE:** To explore the nature of the bidirectional relationship between vasomotor symptoms (VMS) and depression, and to determine whether hot flashes and night sweats differentially affect the association between VMS and depression through their effect on sleep disruption. **METHODS:** Multiple databases were searched from 1961 until July 31, 2016, and a manual search of reference lists of identified articles was conducted. Sixteen articles that involved 10,008 participants were identified and analyzed. **RESULTS:** The methods of analyses and measurement of VMS and depression varied across the studies. Two studies explored the bidirectional association, but only one was significant in both directions (odds ratio [OR] depression to VMS 3.06, 95% confidence interval [CI] 1.43-6.58; OR VMS to depression 8.88, 95% CI 2.57-30.68). In both cases, the association between VMS leading to depressive symptoms was stronger than the opposite. Eleven studies examined VMS leading to depression, but only five showed a significant effect (OR 1.57-1.81,  $P \leq 0.02$ ). Treating VMS and depressive symptoms as continuous variables ( $n=3$ ) diminished the relationship. Three studies showed a significant association of depression leading to VMS (OR 1.62-1.94,  $P \leq 0.01$ ). We found little evidence for a specific effect of night sweats on the association between VMS and depressive symptoms. The effect might not be related to sleep disruption. **CONCLUSIONS:** There is a bidirectional association between VMS and depressive symptoms. The menopausal transition appears to increase the risk of recurrent episodes of depression that might not be explained only by VMS. Further investigation is needed to explain the differential effect of night sweats and hot flashes on depression.

**Arch Osteoporos. 2017 Dec;12(1):66. doi: 10.1007/s11657-017-0361-0. Epub 2017 Jul 17.**

## Sunscreens block cutaneous vitamin D production with only a minimal effect on circulating 25-hydroxyvitamin D.

Libon F, Courtois J, Le Goff C, Lukas P, Fabregat-Cabello N, Seidel L, Cavalier E, Nikkels AF.

**PURPOSE:** Sunscreen use, highly advocated for preventing cutaneous carcinogenesis, is potentially leading to an aggravation of vitamin D deficiency with its consequences on bone health. The effect of sunscreens on circulating vitamin D levels remains debated. This study investigated the effect of sunscreen on cutaneous vitamin D production and circulating 25(OH)D3 levels, according to different body surface areas (BSA). **METHODS:** Vitamin D and 25(OH)D3 levels were measured in four groups exposed to a single nbUVB exposure on 9% (group I: head and hands), 23% (group II: head, hands and arms), 50% (group III: head, hands, arms and legs) and 96% (group IV: total body) of the body surface without and with a 50+ sun protection factor sunscreen. **RESULTS:** Sunscreen use decreased by 83, 88.3, 75.7 and 92.5% the cutaneous vitamin D production in groups I to IV, respectively, but only by 13.2, 10.5, 7.7 and 10.4% the values of circulating 25(OH)D3, correspondingly. **CONCLUSIONS:** Although a 50+ sunscreen decreases significantly cutaneous vitamin D production following a single nbUVB exposure, and independently from the BSA, the circulating 25(OH)D3 levels were only minimally affected. This could be explained by a switch to another endogenous source of precursors. Short-term sunscreen use probably does not affect circulating vitamin D levels and hence does not increase the risk for osteoporosis. The effect of long-term sunscreen use remains however to be determined.

**Osteoporos Int. 2017 Jul 16. doi: 10.1007/s00198-017-4144-7. [Epub ahead of print]**

## One and two-year persistence with different anti-osteoporosis medications: a retrospective cohort study.

Reyes C, Tebe C, Martinez-Laguna D, Ali MS, Soria-Castro A, Carbonell C, Prieto-Alhambra D.

**PURPOSE:** The purpose of this study was to estimate real-world persistence amongst incident users of anti-osteoporosis medications. **METHODS:** This is a retrospective cohort using data from anonymised records and dispensation data (www.sidiap.org). Eligibility comprised the following: women aged  $\geq 50$ , incident users of anti-osteoporosis medication (2012), with data available for at least 12 months prior to therapy initiation. Exclusions are other bone diseases/treatments and uncommon anti-osteoporosis drugs ( $N < 100$ ). Follow-up was from first pharmacy dispensation until cessation, end of study, censoring or switching. Outcomes are 2- and 1-year persistence with a permissible gap of up to 90 days. Persistence with alendronate was compared to other bisphosphonates, strontium ranelate, selective oestrogen receptor modulators, teriparatide and denosumab. Cox models were used to estimate hazard ratios of therapy cessation according to drug used after adjustment for age, sex, BMI, smoking, alcohol drinking, Charlson co-morbidity index, previous fractures, use of anti-osteoporosis medication/s, oral corticosteroids and socio-economic status. **RESULTS:** A total of 19,253 women were included. Unadjusted 2-year persistence [95% CI] ranged from 10.3% [9.1-11.6%] (strontium ranelate) to 45.4% [43.1-47.8%] (denosumab). One-year persistence went from 35.8% [33.9%-37.7%] (strontium ranelate) to 65.8% [63.6%-68.0%] (denosumab). At the end of the first year and compared to alendronate users, both teriparatide and denosumab users had reduced cessation risk (adjusted HR 0.76, 95% CI 0.67-0.86 and 0.54, 95% CI 0.50-0.59 respectively) while at the end of the second year, only denosumab had a lower risk of discontinuation (adjusted HR 0.60, 95% CI 0.56-0.64). **CONCLUSIONS:** Unadjusted 2-year persistence is suboptimal. However, both teriparatide and denosumab users had better 1-year persistence and only denosumab had 2-year better persistence compared to alendronate users. Unmeasured confounding by indication might partially explain our findings.

**Oxid Med Cell Longev. 2017;2017:5982809. doi: 10.1155/2017/5982809. Epub 2017 Jun 20.**

## Dietary Polyphenol Intake, but Not the Dietary Total Antioxidant Capacity, Is Inversely Related to Cardiovascular Disease in Postmenopausal Polish Women: Results of WOBASZ and WOBASZ II Studies.

Witkowska AM, Waskiewicz A, Zujko ME, Szczeñiewska D, Pająk A, Stepaniak U, Drygas W.

The aim of the study was to assess the relationship between the dietary polyphenol intake (DPI) and the dietary total antioxidant capacity (DTAC) and the prevalence of cardiovascular disease (CVD) in postmenopausal women. Participants were 916 postmenopausal women diagnosed with CVD and 1683 postmenopausal women without history of CVD, who took part in the population-based studies carried out in Poland: WOBASZ (2003-2005) and WOBASZ II (2013-2014). Nutritional data were collected using a single 24-hour dietary recall. DPI and DTAC in the CVD women were significantly lower and accounted for 1766.39 mg/d and 10.84 mmol/d, respectively, versus 1920.57 mg/d and 11.85 mmol/d in the women without CVD, but these differences disappeared after the standardization for energy input. Also, in the multiple-adjustment model, higher DPI, but not DTAC, was associated with the reduced odds ratio for the

prevalence of CVD. Beverages, mainly coffee and tea, contributed in more than 40% to DPI and in more than a half to DTAC. In this study, higher dietary polyphenol intake, but not the dietary total antioxidant capacity, was inversely associated with CVD in postmenopausal women, which points to the health benefits of increased polyphenol intake from food sources for these women.