



## Selección de Resúmenes de Menopausia

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### **Repletion of vitamin D associated with deterioration of sleep quality among postmenopausal women.**

Mason C, De Dieu Tapsoba J, Duggan C, Imayama I, Wang CY, Korde L, McTiernan A.

Reduced health-related quality of life (HRQOL), depressive symptoms and poor sleep quality are important health issues among postmenopausal women and may be associated with low vitamin D status. Overweight postmenopausal women, with serum 25-hydroxyvitamin D [25(OH)D] 10-32ng/mL, were recruited in Seattle, WA (2010-2012) and randomly assigned to 12 months of weight loss +2000IU oral vitamin D3/day or weight loss+daily placebo. The weight-loss program included a reduced-calorie diet and 225min/week of moderate-to-vigorous aerobic activity. Eight subscales of HRQOL were assessed by the MOS 36-Item Short-Form Health Survey. Depressive symptoms were assessed using the Brief Symptom Inventory-18, and sleep quality was assessed using the Pittsburg Sleep Quality Index (PSQI). Mean 12-month changes in HRQOL, depressive symptoms and sleep quality were compared between groups (intent-to-treat) using generalized estimating equations. Compared to placebo, women receiving vitamin D did not experience any significant change in depressive symptoms ( $p=0.78$ ), HRQOL subscales (all  $p>0.05$ ), or overall sleep quality ( $p=0.21$ ). However, a greater magnitude of change in serum 25(OH)D was associated with an increased need to take medications to sleep ( $p_{trend}=0.01$ ) and overall worse sleep quality ( $p_{trend}<0.01$ ). Women who became vitamin D replete ( $\geq 32\text{ng/mL}$ ) also showed a deterioration in total PSQI sleep quality score compared to women who remained  $<32\text{ng/mL}$  despite supplementation, even after adjusting for relevant covariates (Non-Replete: -5.7% vs. Replete: +6.2%,  $p<0.01$ ). Vitamin D supplementation of 2000IU/d may result in overall worse sleep quality for postmenopausal women with low circulating vitamin D undergoing weight loss.

**Medicine (Baltimore). 2016 Sep;95(39):e4918. doi: 10.1097/MD.0000000000004918.**

### **GABA+ levels in postmenopausal women with mild-to-moderate depression: A preliminary study.**

Wang Z, Zhang A, Zhao B, Gan J, Wang G, Gao F, Liu B, Gong T, Liu W, Edden RA.

**BACKGROUND:** It is increasingly being recognized that alterations of the GABAergic system are implicated in the pathophysiology of depression. This study aimed to explore in vivo gamma-aminobutyric acid (GABA) levels in the anterior cingulate cortex/medial prefrontal cortex (ACC/mPFC) and posterior-cingulate cortex (PCC) of postmenopausal women with depression using magnetic resonance spectroscopy (H-MRS). **METHODS:** Nineteen postmenopausal women with depression and thirteen healthy controls were enrolled in the study. All subjects underwent H-MRS of the ACC/mPFC and PCC using the "MEGA Point Resolved Spectroscopy Sequence" (MEGA-PRESS) technique. The severity of depression was assessed by 17-item Hamilton Depression Scale (HAMD). Quantification of MRS data was performed using Gannet program. Differences of GABA+ levels from patients and controls were tested using one-way analysis of variance. Spearman correlation coefficients were used to evaluate the linear associations between GABA+ levels and HAMD scores, as well as estrogen levels. **RESULTS:** Significantly lower GABA+ levels were detected in the ACC/mPFC of postmenopausal women with depression compared to healthy controls ( $P=0.002$ ). No significant correlations were found between 17-HAMD/14-HAMA and GABA+ levels, either in ACC/mPFC ( $P=0.486$ ;  $r=0.170$ / $P=0.814$ ;  $r=-0.058$ ) or PCC ( $P=0.887$ ;  $r=0.035$ / $P=0.987$ ;  $r=-0.004$ ) in the patients; there is also no significant correlation between GABA+ levels and estrogen levels in patients group (ACC/mPFC:  $P=0.629$ ,  $r=-0.018$ ; PCC:  $P=0.861$ ,  $r=0.043$ ). **CONCLUSION:** Significantly lower GABA+ levels were found in the ACC/mPFC of postmenopausal women with depression, suggesting that the dysfunction of the GABAergic system may also be involved in the pathogenesis of depression in postmenopausal women.

**BMC Cancer. 2016 Sep 29;16(1):761.**

## **Weight and weight changes throughout life and postmenopausal breast cancer risk: a case-control study in France.**

Cordina-Duverger E, Truong T, Anger A, Sanchez M, Arveux P, Kerbrat P, Guénel P.

**BACKGROUND:** Overweight and weight gain throughout adult life have been associated with increased risk of breast cancer after the menopause. However the role of body weight at a young age and of the timing of weight gain over the lifetime in postmenopausal breast cancer is not well documented. **METHODS:** We conducted a population-based case-control study on breast cancer in France that included 739 cases and 815 population controls in postmenopausal women. Height, weight at age 20, 40 and 50 as well as weight one year before diagnosis were obtained during in-person interviews. **RESULTS:** No association between body mass index at the age of 20 years and breast cancer after the menopause was detected. However, we found that postmenopausal breast cancer was associated with weight gain between ages 40 and 50 years (OR per 5 kg/m<sup>2</sup> increase in BMI: 1.45 [95%ci 1.06-1.98]). The increased risk of breast cancer associated with weight gain was more consistent in leaner women at age 20, in older postmenopausal women (>65 years), and in women who did not use menopausal hormone therapy. **CONCLUSIONS:** These findings point to the importance of controlling for weight gain in middle aged-women. The role of low body weight in young adulthood in breast cancer risk after the menopause should be further scrutinized.

**J Clin Endocrinol Metab. 2016 Sep 28;jc20162348. [Epub ahead of print]**

## **Independent Contributions of Nocturnal Hot Flashes and Sleep Disturbance to Depression in Estrogen-Deprived Women.**

Joffe H, Crawford SL, Freeman MP, White DP, Bianchi MT, Kim S, Economou N, Camuso J, Hall JE, Cohen LS.

**CONTEXT:** Women are at increased risk for mood disturbance during the menopause transition. Hot flashes (HFs), sleep disruption, and fluctuating estradiol levels correlate with menopause-associated depression but co-occur, making cause and effect relationships difficult to disentangle. **OBJECTIVE:** Using a GnRH agonist (GnRHa) experimental model, we investigated whether depressive symptoms are associated with HFs and/or are explained by concomitant sleep fragmentation in the absence of estradiol fluctuation. **DESIGN AND INTERVENTION:** Depressive symptoms, objective polysomnographic sleep parameters, subjective sleep quality, serum estradiol, and HFs were assessed before and 4 weeks after open-label depot GnRHa (leuprolide 3.75-mg) administration. **SETTING:** Academic medical center.

**PARTICIPANTS:** Twenty-nine healthy nondepressed premenopausal volunteers (mean age, 27.3 years). **RESULTS:** Serum estradiol was rapidly and uniformly suppressed. HFs developed in 69% of the subjects. On univariate analysis, worsening of mood was predicted by increases in time in light sleep (stage N1), number of transitions to wake, non-REM arousals, subjective sleep quality, and reductions in perceived sleep efficiency (all  $P < .045$ ), as well as the number of nighttime ( $P = .006$ ), but not daytime ( $P = .28$ ), HFs reported. In adjusted models, the number of nighttime HFs reported, increases in non-REM arousals, time in stage N1, transitions to wake, and reduced sleep quality remained significant predictors of mood deterioration ( $P \leq .05$ ). **CONCLUSIONS:** Depressive symptoms emerged after estradiol withdrawal in association with objectively and subjectively measured sleep disturbance and the number of nighttime, but not daytime, HFs reported. Results suggest that sleep disruption and perceived nighttime HFs both contribute to vulnerability to menopause-associated depressive symptoms in hypoestrogenic women.

**Cancer Causes Control. 2016 Sep 28. [Epub ahead of print]**

## **Menopausal vasomotor symptoms and incident breast cancer risk in the Study of Women's Health Across the Nation.**

Hart V, Sturgeon SR, Reich N, Sievert LL, Crawford SL, Gold EB, Avis NE, Reeves KW.

**PURPOSE:** Two case-control studies reported a 50 % decreased breast cancer risk among women who experienced menopausal vasomotor symptoms (VMS), but one cohort study found no association. VMS may be triggered by declining estrogen levels during menopause, whereas elevated estrogen levels have been associated with increased breast cancer risk. VMS may thus be indicative of lower susceptibility to breast cancer. **METHODS:** We evaluated this relationship in the longitudinal Study of Women's Health Across the Nation (SWAN), using discrete survival analysis of approximately annual data on VMS and self-reported breast cancer occurrences for up to 13 years of follow-up in 3,098 women who were pre- or early perimenopausal at enrollment. **RESULTS:** Over an average 11.4 years of follow-up, 129 incident breast cancer cases were self-reported, and approximately 50 % of participants

experienced VMS. Symptomatic women had a reduced risk of breast cancer compared to non-symptomatic women (adjusted HR 0.63, 95 % CI 0.39, 1.00). The association was stronger in the subgroup of women who fully transitioned to postmenopause during follow-up (n = 67 cases, adjusted HR 0.45, 95 % CI 0.26, 0.77). CONCLUSION: VMS appeared to be a marker of reduced breast cancer risk. Future research is needed to understand the biology underlying this relationship.

**Menopause. 2016 Sep 26. [Epub ahead of print]**

### **Menopausal symptoms and cardiovascular disease mortality in the Women's Ischemia Syndrome Evaluation (WISE).**

Thurston RC, Johnson BD, Shufelt CL, Braunstein GD, Berga SL, Stanczyk FZ, Pepine CJ, Bittner V, et al.

OBJECTIVE: Studies have linked vasomotor symptoms (VMS) to markers of cardiovascular disease (CVD) risk, yet few have considered clinical cardiovascular events. Data suggest that associations may depend upon the age that symptoms occur. We examined associations between VMS and cardiovascular events and endothelial function, considering age of symptom onset. METHODS: The Women's Ischemia Syndrome Evaluation enrolled women referred for coronary angiography for suspected myocardial ischemia. A total of 254 women aged more than 50 years, postmenopausal, with both ovaries, not taking hormone therapy underwent a baseline evaluation, were followed annually (median=6.0 y), and the National Death Index was searched to ascertain CVD mortality (median=9.3 y). A subset of participants underwent brachial artery ultrasound for flow-mediated dilation (FMD). Receiver-operating curve analysis was used to determine vasomotor symptom groups (symptoms beginning<age 42 [early onset], beginning  $\geq 42$  [later onset], never) which were examined in relation to cardiovascular events and FMD in Cox proportional hazard and linear regression models. RESULTS: Women reporting early onset VMS (HR=3.35, 95% CI=1.23-7.86, P=0.005) and women who never had VMS (HR=2.17, 95% CI=1.02-4.62, P=0.05) had higher CVD mortality than women with later onset symptoms (multivariable models). Women with early onset VMS had lower FMD than women with later onset symptoms (b=-4.31, SE=2.10, P=0.04, multivariable). CONCLUSIONS: Women with signs and symptoms of ischemia who had VMS beginning early in midlife had higher CVD mortality and reduced endothelial function relative to women with later onset symptoms. Future research should evaluate the vascular phenotype of women with early midlife VMS.

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### **The seasonal importance of serum 25-hydroxyvitamin D for bone mineral density in older women.**

Michaëlsson K, Wolk A, Byberg L, Mitchell A, Mallmin H, Melhus H.

BACKGROUND: The impact of season when determining a serum 25-hydroxyvitamin D (S-25OHD) cut-off level for optimal bone health is unknown. OBJECTIVE: To investigate the relative importance of S-25OHD for bone mineral density (BMD) by season. METHODS: A subcohort of 5002 Swedish women (mean age 68 years), randomly selected from a large population-based longitudinal cohort study with repeat dietary and lifestyle information, was enrolled during 2003-2009 for a clinical examination, which included dual-energy X-ray absorptiometry and collection of fasting blood samples. Categories of vitamin D status were determined by S-25OHD (measured by HPLC-MS/MS). RESULTS: In samples collected during summer, we found a gradual increase in BMD of the total hip up to a S-25OHD level of 40 nmol L<sup>-1</sup> (6% of the cohort). In women with S-25OHD concentrations below 30 nmol L<sup>-1</sup> during summer, adjusted BMD was 11% lower [95% confidence interval (CI) 3-19] and in those with S-25OHD levels of 30-40 nmol L<sup>-1</sup> BMD was 6% lower (95% CI 1-11), compared with women with S-25OHD levels above 80 nmol L<sup>-1</sup>. Low S-25OHD concentrations during summer (<30 nmol L<sup>-1</sup>) were also associated with higher adjusted relative risk of osteoporosis (4.9; 95% CI 2.9-8.4) compared with concentrations above 80 nmol L<sup>-1</sup>. By contrast, no differences in mean BMD values between categories of S-25OHD were found during winter. CONCLUSIONS: Summer concentrations of S-25OHD appear to be the most useful to predict BMD, whereas winter levels have limited value. To determine a S-25OHD cut-off level for vitamin D deficiency, it may be necessary to take into account the season of blood collection.