# Selección de Resúmenes de Menopausia

Semana del 5 a 11 de Septiembre de 2018

María Soledad Vallejo. Clínica Quilín. Universidad de Chile

**Adv Ther. 2018 Sep 6. doi: 10.1007/s12325-018-0779-9. [Epub ahead of print]**

## Real-world Management of Women with Postmenopausal Osteoporosis Treated with Denosumab: A Prospective Observational Study in the Czech Republic and Slovakia.

Růžičková O, Killinger Z, Kasalický P, Hamilton L, Tyl R, Tomková S, Kalouche-Khalil L.

INTRODUCTION: Osteoporosis is characterized by low bone mineral density (BMD) and an increased risk of fracture. In randomized controlled trials, denosumab has been shown to significantly reduce the fracture risk in women with osteoporosis. However, little is known about the real-world management of women who are prescribed denosumab. METHODS: This multicenter, prospective, observational real-world study in the Czech Republic and Slovakia evaluated the baseline characteristics and clinical management of women with postmenopausal osteoporosis prescribed denosumab for 24 months. RESULTS: A total of 600 women were included (300 in each country). In the Czech Republic and Slovakia, respectively, mean age at enrollment was 69.0 and 64.3 years, 67.7% and 30.0% of patients had a previous osteoporotic fracture, and 85.0% and 48.7% had previously received osteoporosis medication. In both countries, 'low BMD T score' and 'a history of osteoporotic fracture' were the main reasons for prescribing denosumab. Most patients received all four post-baseline denosumab injections (Czech Republic, 82.0%; Slovakia, 81.0%), and more than 98% of patients in both countries received all injections at the prescribing center. At 24 months, most patients experienced an increase in BMD T score for the lumbar spine, total hip, or femoral neck (Czech Republic, 69.7-91.7%; Slovakia, 67.1-92.9%). Adverse drug reactions were consistent with the known safety profile of denosumab. CONCLUSION: Baseline characteristics of patients receiving denosumab in the Czech Republic and Slovakia reflect the reimbursement criteria for this agent in each country. The findings of our study in patients who are at high risk for fracture are consistent with the growing body of evidence demonstrating the effectiveness of denosumab in real-world clinical practice.

**J Psychosom Res. 2018 Oct;113:30-36. doi: 10.1016/j.jpsychores.2018.07.009. Epub 2018 Jul 21.**

## Depressive symptoms predict incident chronic disease burden 10 years later: Findings from the English Longitudinal Study of Ageing (ELSA).

Poole L, Steptoe A.

OBJECTIVE: To assess the association between depressive symptoms and incident chronic illness burden in prospective longitudinal analyses. METHODS: We analysed data from 2472 participants (62.88 ± 8.49 years old; 50.8% female) from the English Longitudinal Study of Ageing (ELSA). Depressive symptoms were measured using the Centre for Epidemiological Studies Depression (CES-D) scale at baseline in 2004, and participants were followed up for 10 years. Participants with prevalent illness at baseline (coronary heart disease [CHD], other cardiac illness, stroke, cancer, diabetes/high blood glucose, arthritis, lung disease, osteoporosis and Parkinson's disease) were excluded from models predicting illness burden (the sum of illnesses reported) over follow-up. Linear regression was used controlling for a wide range of covariates. RESULTS: The mean chronic illness burden was 0.57, with 43.1% experiencing at least one incident physical illness. Baseline continuous CES-D score was a significant predictor of incident chronic illness burden up to 10 years later (incident rate ratio = 1.05, 95% confidence intervals = 0.05-0.21, p = .003), independent of sociodemographic, behavioural, cognitive and clinical covariates. Sensitivity analyses excluding participants who developed a chronic illness within the 2 years following baseline corroborated the main results. CONCLUSION: Depressive symptoms were associated with greater incident chronic illness burden 10 years later. These findings have clinical implications for the treatment of depression in physically healthy older adults.

**Hum Reprod. 2018 Aug 21. doi: 10.1093/humrep/dey267. [Epub ahead of print]**

## Physical activity is not related to risk of early menopause in a large prospective study.

Zhao M, Whitcomb BW, Purdue-Smithe AC, Manson JE, Hankinson SE, Rosner BA, Bertone-Johnson ER.
STUDY QUESTION: Is physical activity associated with incident early menopause? SUMMARY ANSWER: Physical activity is not associated with incident early menopause. WHAT IS KNOWN ALREADY: Lifestyle factors such as physical activity may influence menopause timing, but results from prior research are inconsistent. STUDY DESIGN, SIZE, DURATION:We evaluated the association between physical activity and the occurrence of early natural menopause in a prospective cohort study, the Nurses' Health Study II. Women were followed prospectively from 1989 to 2011. PARTICIPANTS/MATERIALS, SETTING, METHODS: Our analysis included 107 275 women who were premenopausal at baseline. Menopause status was self-reported biennially. Time per week participating in specific activities was reported approximately every 4 years and used to calculate metabolic task hours per week (MET h/week). We used Cox proportional hazards model to evaluate the association between physical activity and incidence of natural menopause before age 45 years while controlling for potential confounding factors. MAIN RESULTS AND THE ROLE OF CHANCE: There were 2 786 study members who experienced menopause before the age of 45. After adjustment for age, smoking and other factors, we observed no association between adulthood physical activity and early menopause. For example, compared to women reporting <3 MET h/week, the hazard ratio for women in the highest category (≥42 MET h/week) of cumulatively-averaged total physical activity was 0.89 (95% confidence interval: 0.76-1.04; P-trend: 0.26). Neither moderate nor strenuous activity in adolescence and young adulthood were related to risk. The relation of physical activity and early menopause did not vary across strata of body mass index or smoking status. LIMITATIONS, REASONS FOR CAUTION: Physical activity and menopausal status were self-reported, but repeated assessment of physical activity and prospective report of menopause status likely reduce the potential for non-differential misclassification. While the majority of our study participants were white, it is unlikely that the physiological relation of activity and early menopause varies by ethnicity. WIDER IMPLICATIONS OF THE FINDINGS: Findings from our large prospective study do not support an important association between physical activity and early menopause.

**Int J Cancer. 2018 Sep 5. doi: 10.1002/ijc.31851. [Epub ahead of print]**

## Estrogen metabolism in menopausal hormone users in the Women's Health Initiative Observational Study: Does it differ between estrogen plus progestin and estrogen alone?

Falk RT, Manson JE, Barnabei VM, Anderson GL, Brinton LA, Rohan TE, Cauley JA, Chen C, Coburn SB, et al.
The WHI found an unexpected reduced breast cancer risk in women using CEE alone. We hypothesized CEE alone induces estrogen hydroxylation along the 2-pathway rather than the competing 16-pathway, a pattern linked to reduced postmenopausal breast cancer risk. 1864 women in a WHIOS case-control study of estrogen metabolism and ovarian and endometrial cancer were studied of whom 609 were current E+P users (351 used CEE+MPA), while 272 used E alone (162 used CEE). Fifteen EM were measured, and analyses conducted for each metabolite, hydroxylation pathway (2-, 4-, or 16-pathway), and ratios of pathway concentrations using inverse probability weighted linear regression. Compared to E+P users, all EM were higher in E alone users (significant for unconjugated estrone, total/conjugated estradiol, total/unconjugated 2-methoxyestrone, 4-methoxyestrone and unconjugated estriol). The relative concentrations of 2- and 4-pathway EM did not differ between the MHT users (2-pathway EM comprised 15% and 4-pathway EM <2% of the total), but 16-pathway EM were lower in E alone users (p=0.036). Ratios of 2- and 4-pathway EM compared to 16-pathway EM were significantly higher in E alone compared to E+P users. Similar but not significant patterns were observed in CEE-alone and CEE+MPA users. Our data suggest that compared to E+P users, women using E alone have more extensive metabolism via the 2- versus the competing 16-pathway. This is consistent with epidemiologic evidence of reduced postmenopausal breast cancer risk associated with this metabolic profile and may provide a clue to the breast cancer risk reduction in CEE alone users during the WHI. 

**Clin Endocrinol (Oxf). 2018 Sep 4. doi: 10.1111/cen.13848. [Epub ahead of print]**

## Safety of Calcium and Vitamin D Supplements, a Randomized Controlled Trial.

Aloia JF, Katumuluwa S, Stolberg A, Usera G, Mikhail M, Hoofnagle AN, Islam S.
OBJECTIVE: It is anticipated that an intake of vitamin D found acceptable by Endocrine Society Guidelines (10,000 IU/day) with co-administered calcium supplements may result in frequent hypercalciuria and hypercalcemia. This

combination may be associated with kidney stones. The objective of this study was to compare the episodes of hypercalciuria and hypercalcemia from calcium supplements co-administered with 10,000 IU or 600 IU vitamin D daily. This design allows a comparison of the Institute of Medicine recommendation for the RDA of vitamin D along with the Upper Limit of calcium intake with the high intake of vitamin D suggested by the Endocrine Society. CONTEXT: Harms of currently recommended high intake of vitamin D have not been studied. DESIGN: The design was a randomized controlled trial with 2 groups with evaluation every 3 months for one year: (1) CaCO3 1,200 mg/day with 10,000 IU vitamin D3 /day or (2) CaCO3 1,200 mg/day with 600 IU vitamin D3. PATIENTS: This study was conducted in an ambulatory research center in healthy, white postmenopausal women. MEASUREMENTS: Serum and 24-hour urine calcium were measured. RESULTS: Hypercalcemia and hypercalciuria occurred in both groups. At the final visit, 19/48 in the high dose D group had hypercalciuria. The odds of developing hypercalciuria was 3.6 [OR=3.6(1.39, 9.3)] times higher in the high dose D group. The odds of developing hypercalcemia did not differ between groups. CONCLUSIONS: The safe upper level of vitamin D recommended by the Endocrine Society when accompanied by calcium supplements results in frequent hypercalciuria. The risk of kidney stones at these levels should be investigated.

**Menopause. 2018 Sep 4. doi: 10.1097/GME.0000000000001174. [Epub ahead of print]**

## Guidelines for the evaluation and treatment of perimenopausal depression: summary and recommendations.

Maki PM, Kornstein SG, Joffe H, Bromberger JT, Freeman EW, Athappilly G, Bobo WV, Rubin LH, Koleva HK, Cohen LS, Soares CN; Board of Trustees for The North American Menopause Society (NAMS) and the Women and Mood Disorders Task Force of the National Network of Depression Centers.

There is a new appreciation of the perimenopause - defined as the early and late menopause transition stages as well as the early postmenopause - as a window of vulnerability for the development of both depressive symptoms and major depressive episodes. However, clinical recommendations on how to identify, characterize and treat clinical depression are lacking. To address this gap, an expert panel was convened to systematically review the published literature and develop guidelines on the evaluation and management of perimenopausal depression. The areas addressed included: 1) epidemiology; 2) clinical presentation; 3) therapeutic effects of antidepressants; 4) effects of hormone therapy; and 5) efficacy of other therapies (eg, psychotherapy, exercise, and natural health products). Overall, evidence generally suggests that most midlife women who experience a major depressive episode during the perimenopause have experienced a prior episode of depression. Midlife depression presents with classic depressive symptoms commonly in combination with menopause symptoms (ie, vasomotor symptoms, sleep disturbance), and psychosocial challenges. Menopause symptoms complicate, co-occur, and overlap with the presentation of depression. Diagnosis involves identification of menopausal stage, assessment of co-occurring psychiatric and menopause symptoms, appreciation of the psychosocial factors common in midlife, differential diagnoses, and the use of validated screening instruments. Proven therapeutic options for depression (ie, antidepressants, psychotherapy) are the front-line treatments for perimenopausal depression. Although estrogen therapy is not approved to treat perimenopausal depression, there is evidence that it has antidepressant effects in perimenopausal women, particularly those with concomitant vasomotor symptoms. Data on estrogen plus progestin are sparse and inconclusive.