

## Selección de Resúmenes de Menopausia

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### **The association between testosterone and depression in postmenopausal women: A systematic review of observational studies**

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**Objective:** The contribution of testosterone to depression in older women is uncertain. This review was conducted to investigate the association between endogenous testosterone blood concentrations and depression in postmenopausal women. **Methods:** We searched Ovid MEDLINE, EMBASE, PsycINFO, and Web of Science databases for observational studies with at least 100 community-dwelling participants. The results were categorised by study design, and the reporting of total, bioavailable and free testosterone findings is narrative. **Results:** The search strategy retrieved 28 articles for full-text review, of which eight met the criteria for inclusion; these described 6 cross-sectional and 2 longitudinal studies. Testosterone was measured by immunoassay in all of the included studies. No association was seen between total testosterone or free testosterone and depression in either the cross-sectional or the longitudinal studies. A significant association between bioavailable testosterone and incident depressive symptoms was limited to women at least 21 years postmenopause in one study. Most of the cross-sectional studies were not representative of national populations and lacked random selection. **Conclusions:** This systematic review does not support an association between testosterone and depression in postmenopausal women. However, as the included studies had substantial methodological limitations, studies of community-based samples, employing validated instruments for depression and precise measurement of blood testosterone, are needed to address this knowledge gap.

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### **Cognitive decline and dementia in women after menopause: Prevention strategies**

Bogdan Stefanowski 1, Marek Kucharski, Anna Szeliga, Milena Snopek, Anna Kostrzak, Roman Smolarczyk, et al.

Worldwide, cognitive decline and dementia are becoming one of the biggest challenges for public health. The decline in cognition and the development of dementia may be caused by predisposing or trigger factors. There is no consensus over whether the drop in estrogen levels after menopause is a risk factor for cognitive decline and dementia. This article discusses the prevention of cognitive decline and dementia in women after menopause, both primary prevention (essentially pharmacological intervention) and secondary prevention (chiefly diet and weight reduction). Further study is required to clarify whether menopausal hormone therapy (MHT) has a role in dementia.

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### **The risk between thyrotropin suppression and bone mineral density in differentiated thyroid cancer**

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**Background:** The effect of thyroid stimulating endocrine (TSH) suppression medical aid on bone mineral density (BMD) of patients with differentiated thyroid carcinoma (DTC) or differentiated thyroid malignant neoplastic disease is still controversial. Our aim was to investigate the effect of TSH suppression therapy on BMD of patients with DTC. **Methods:** A total of 1651 DTC patients with TSH-suppression medical care were analyzed by RevMan 5.3 software (<https://training.cochrane.org/online-learning/core-software/revman/revman-5-download>) in the present study. The PubMed and Embase databases were consistently hunted for works revealed through July 29, 2022. **Results:** The results indicated that a significant association between femoral bone mineral density (FN-BMD) ( $P = .02$ ) or lumbar spine bone mineral density (L-BMD) ( $P = .04$ ) and DTC patients with TSH-suppression therapy. However, the total hip bone mineral density (TH-BMD) was not significantly related to DTC patients with TSH-suppression therapy ( $P = .11$ ). For premenopausal women, it was shown that TH-BMD ( $P = .02$ ) or L-BMD ( $P = .01$ ) were closely related to DTC patients with TSH-suppression therapy. However, there was no relationship between FN-BMD and DTC patients with TSH-suppression therapy ( $P = .06$ ). For postmenopausal women, TH-BMD was closely related to DTC patients with TSH-suppression therapy ( $P = .02$ ). It was revealed that there was no significant difference between L-BMD ( $P = .16$ ) or

FN-BMD ( $P = .26$ ) and DTC patients with TSH-suppression therapy. For men, there was no relationship between FN-BMD ( $P = .94$ ) or L-BMD ( $P = .29$ ) and DTC patients with TSH-suppression therapy. Conclusion: Our systematic review has demonstrated that TSH inhibition treatment mainly influence the TH-BMD or L-BMD of the DTC patients who were premenopausal women; the TH-BMD of the DTC patients who were postmenopausal women. In addition, there was no influence on the FN-BMD or L-BMD of the DTC patients who were men.

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## **Ovarian removal and subsequent breast cancer prognosis: a nationwide cohort study**

Mathilde Gottschau 1, Susanne K Kjær 2 3, Jakob Hansen Viuff 1, Allan Jensen 4, Christian Munk 2, et al.

Purpose: To evaluate whether previous ovarian removal concomitant with benign hysterectomy improves prognosis in a cohort of women with breast cancer. Methods: In this nationwide register-based cohort study, risk of recurrence and mortality were examined in 4563 women with invasive breast cancer and previous bilateral salpingo-oophorectomy (BSO) concomitant with benign hysterectomy, during 1977-2018. Comparing with benign hysterectomy alone, hazard ratios (HRs) and 95% confidence intervals (CIs) were evaluated by Cox-proportional hazards regression models. Analyses were stratified on age at hysterectomy as a proxy for menopausal status ( $< 45$ , 45-54 and  $\geq 55$  years); tumor characteristics, estrogen receptor (ER)-status, and use of hormone therapy (HT) were included in multivariable models. Results: Compared with hysterectomy alone, premenopausal ( $< 45$  years) BSO at benign hysterectomy was associated with an age and calendar period adjusted HR of 1.48 (95% CI 0.83-2.65) for breast cancer recurrence within 10 years of follow-up, a HR of 1.07 (95% CI 0.66-1.72) for overall mortality after breast cancer, and a HR of 0.59 (95% CI 0.26-1.32) for breast cancer-specific mortality. The corresponding HRs for postmenopausal ( $\geq 55$  years) BSO at benign hysterectomy were 1.51 (95% CI 0.73-3.12) for recurrences, 1.34 (95% CI 0.74-2.44) for overall mortality, and 1.78 (95% CI 0.74-4.30) for breast cancer mortality. Adjusting for tumor characteristics, ER-status and HT did not alter the results. Conclusion: Results from this cohort study did not indicate an improvement in breast cancer prognosis when removing the ovaries at benign hysterectomy prior to the cancer diagnosis.

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## **Post-COVID-19 syndrome in a sample of climacteric women living in Latin America**

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Objective: The aim of this study was to assess resilience, fear of COVID-19, sleep disorders, and menopause-related symptoms after the acute phase of COVID-19 in middle-aged women with positive reverse transcription-polymerase chain reaction and noninfected women. Methods: This is a cross-sectional, analytical study of climacteric women from 9 Latin American countries, aged 40-64 years, attending a routine health checkup. We evaluated clinical characteristics and used the Connor-Davidson Resilience Scale, the Fear of COVID-19 Scale, the Jenkins Sleep Scale, and the Menopause Rating Scale to evaluate their health. Results: A total of 1,238 women were studied, including 304 who were positive for COVID-19 reverse transcription-polymerase chain reaction. The median (interquartile range) age was 53 (12) years; years of studies, 16 (6); body mass index, 25.6 (5.1) kg/m<sup>2</sup>; and time since first COVID-19 symptom, 8 (6) months. COVID-19 patients reported fatigability (18.8%), joint and muscular discomfort (14.1%), and anosmia (9.5%). They had a significantly lower resilience score ( $26.87 \pm 8.94$  vs  $29.94 \pm 6.65$ ), higher Fear of COVID-19 score ( $17.55 \pm 7.44$  vs  $15.61 \pm 6.34$ ), and a higher Jenkins Scale score ( $6.10 \pm 5.70$  vs  $5.09 \pm 5.32$ ) compared with control women. A logistic regression model confirmed these results. There was not a significant difference in the total Menopause Rating Scale score, although the odds ratios for both severe menopausal symptoms (1.34; 95% confidence interval, 1.02-1.76) and the use of hypnotics were higher in women with COVID-19 (1.80; 95% confidence interval, 1.29-2.50) compared with those without infection. We found no decrease in studied outcomes between the initial 7 months versus those reported after 8 to 18 months since first COVID-19 symptoms. Conclusions: COVID-19 climacteric women have sleep disorders, lower resilience and higher fear of COVID-19.

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## **Consensus and Controversial Aspects of Vitamin D and COVID-19**

John P Bilezikian 1, Neil Binkley 2, Hector F De Luca 3, Angelo Fassio 4, Anna Maria Formenti 5, et al,

**Objectives:** This work aims to review and discuss controversial topics in the field of vitamin D, SARS-CoV-2 infection, and COVID-19. **Participants:** The International Conferences "Controversies in Vitamin D" are a series of workshops that started in 2017 featuring international experts and leaders in vitamin D research and clinical practice. The 5th annual conference was held in Stresa, Italy, from 15 to 18 September 2021. **Evidence:** Before the event, participants reviewed available studies on their assigned topic, drafted a related abstract, and presented their findings at the time of the conference. Relevant literature that became available since was also discussed within the panel and updated accordingly. **Consensus:** Before the event, the drafted abstracts had been merged to prepare a preliminary document. After the conference presentations, in-depth discussions in open sessions led to consensus. The document was subsequently modified according to discussions and up-to-date literature inclusion. **Conclusions:** There is quite consistent evidence for an association between low 25 OH vitamin D (25(OH)D) levels and poor COVID-19 outcomes, despite heterogeneous publications of variable quality. However, the low vitamin D status in COVID-19 patients might also reflect reverse causality. Vitamin D supplementation might have a positive role in COVID-19 prevention. The evidence supporting a beneficial effect of vitamin D treatment in decreasing the risk of COVID-19 complications is conflicting. Conclusive statement regarding the beneficial effect of vitamin D in this context await high-quality randomized controlled trials.

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### **Bone-Targeted delivery of senolytics to eliminate senescent cells increases bone formation in senile osteoporosis**

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Systemic elimination of senescent cells using senolytic drugs presents therapeutic effects on age-related diseases, including senile osteoporosis. However, low bioavailability and potential side effects of senolytics restrict clinical application. Therefore, we developed a bone-targeted delivery system for senolytics to effective treatment of senile osteoporosis. In this study, quercetin was screened out as the ideal senolytics for eliminating senescent BMSCs. Treatment of quercetin efficiently decreased the senescence markers in senescent BMSCs models. After treatment with quercetin in vitro, cell mitosis and calcification staining assay confirmed that the proliferation and osteogenesis of the senescent BMSCS populations were enhanced. To enhance the effectiveness and minimize the side effect of treatment, liposomes decorated with bone affinity peptide (DSS)6 were constructed for bone-targeted delivery of quercetin. After administration of liposomes loading quercetin in two aged mice models, histological and cellular analysis confirmed that bone-targeted treatment with quercetin efficiently eliminated senescent cells in bone, restored the function of BMCSs, and promoted bone formation in aged mice models when compared to non-targeted treatment. Taken together, the bone-targeted delivery of senolytics efficiently eliminates senescent cells to recover bone mass and microarchitecture, showing an effective treatment for senile osteoporosis. **STATEMENT OF SIGNIFICANCE:** Senile osteoporosis, a common and hazardous chronic disease, has been still lacking effective therapy. How to effectively eliminate the hazards of senescent cells in skeleton to bone formation remains challenge. In this study, quercetin was screened out as the ideal senolytic drug for senescent BMSCs and could effectively eliminated senescent BMSCs to restore the cellular functions of senescent BMSCs models in vitro. Then, the bone-targeted liposomes were designed to encapsulate and deliver senolytics efficiently to senile bone tissue. Based on two aged mice models, we confirmed that bone-targeted delivery of quercetin efficiently eliminated senescent cells in skeleton and enhanced bone formation in vivo, suggesting the bone-targeted elimination of senescent cells is an effective treatment for senile osteoporosis.