



## Selección de Resúmenes de Menopausia

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### Impact of estrogens on resting energy expenditure: A systematic review

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The fear of weight gain is one of the main reasons for women not to initiate or to early discontinue hormonal contraception or menopausal hormone therapy. Resting energy expenditure is by far the largest component and the most important determinant of total energy expenditure. Given that low resting energy expenditure is a confirmed predictive factor for weight gain and consecutively for the development of obesity, research into the influence of sex steroids on resting energy expenditure is a particularly exciting area. The objective of this systematic review was to evaluate the effects of medication with natural and synthetic estrogens on resting energy expenditure in healthy normal weight and overweight women. Through complex systematic literature searches, a total of 10 studies were identified that investigated the effects of medication with estrogens on resting energy expenditure. Our results demonstrate that estrogen administration increases resting energy expenditure by up to +208 kcal per day in the context of contraception and by up to +222 kcal per day in the context of menopausal hormone therapy, suggesting a preventive effect of circulating estrogen levels and estrogen administration on weight gain and obesity development.

**Bone. 2023 Aug 4;116867. doi: 10.1016/j.bone.2023.116867. Online ahead of print.**

### The association of vitamin D with bone microarchitecture, muscle strength, and mobility performance in older women in long-term care

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Background: Osteoporosis and sarcopenia are prevalent in older adults. Trabecular bone score (TBS) is a novel method to evaluate bone microarchitecture, whereas grip strength and gait speed are simple methods to assess muscle strength and function. Few studies have linked the relationship between vitamin D levels (25OHD) with TBS, grip strength, and gait speed in healthy community dwelling adults. We sought to investigate this relationship in older women with osteoporosis and multiple comorbid conditions residing in long-term care (LTC) facilities. Methods: We analyzed baseline 25OHD, spine TBS, grip strength, and gait speed in 246 women with osteoporosis who were residents of LTC and enrolled in a randomized controlled clinical trial. Results: On average, participants were 81.6 years old and had a BMI of 26.8 kg/m<sup>2</sup>. The correlation (r) of 25OHD with spine TBS, grip strength, and gait speed were (r = 0.15; p = 0.0208), (r = - 0.05; p = 0.4686), and (r = 0.19; p = 0.0041), respectively. Each 5 ng/dl increase in 25OHD was associated with an increase of 0.006 in spine TBS and 0.014 m/s in gait speed. After adjusting for covariates, each 5 ng/dl increase in 25OHD was associated with an increase of 0.004 in spine TBS (p = 0.0599) and 0.012 m/s in gait speed (p = 0.0144). Conclusion: In older women residing in LTC facilities, 25OHD was associated with spine TBS and gait speed. The strengths of the associations suggest there may be other factors with a more prominent role in bone microarchitecture, muscle strength, and physical function in this population.

**Nutrition. 2023 Jul 6;116:112151. doi: 10.1016/j.nut.2023.112151. Online ahead of print.**

### Supplementation of vitamin D isolated or calcium-associated with bone remodeling and fracture risk in postmenopausal women without osteoporosis: A systematic review of randomized clinical trials

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Menopause and vitamin D deficiency increase bone reabsorption and bone fracture risk in women in postmenopause, and vitamin D supplementation may improve bone health and decrease bone fracture risk. This study aims to discuss the effect of vitamin D supplementation, isolated or calcium-associated, on remodeling and fracture risk bone in women in postmenopause without osteoporosis. This study was conducted according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines (PROSPERO database registration: CRD42022359796). A search was conducted in four databases and gray literature using MeSH and similar terms related to supplements, vitamin D, calcium, remodeling, and fracture bone, without the restriction of language and year of publication. A total of 3460

studies were identified, and nine were selected. Vitamin D supplementation increased 25-hydroxyvitamin D levels  $\geq 10$  ng/mL and decreased parathyroid hormone secretion dependent on baseline levels. The doses of 400 IU of vitamin D improved the percentage of carboxylated osteocalcin, whereas 800 to 1000 IU combined with calcium resulted in reduced, improved, or maintained bone mineral density and reduced alkaline phosphatase levels. However, 4000 IU alone or combined with calcium for 6 mo did not improve C-telopeptide and procollagen type 1 peptide levels. Additionally, 15 000 IU/wk increased the cortical area of metacarpal bone, whereas 500 000 IU of vitamin D annually for 5 y did not contribute to reducing the fracture risk and falls. Only one study found a reduction in fracture risk (dose of 800 IU of vitamin D plus 1200 mg of calcium). Thus, the vitamin D supplementation, alone or calcium-associated, improved the status of 25-hydroxyvitamin D and bone remodeling, but it was not possible to assert that it reduced fracture bone risk in postmenopausal women.

**Obstet Gynecol. 2023 Aug 4. doi: 10.1097/AOG.0000000000005288. Online ahead of print.**

## **Nonestrogen Therapies for Treatment of Genitourinary Syndrome of Menopause: A Systematic Review**

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Objective: To systematically review the literature and provide clinical practice guidelines regarding various nonestrogen therapies for treatment of genitourinary syndrome of menopause (GSM). Data sources: MEDLINE, EMBASE, ClinicalTrials.gov, and Cochrane databases were searched from inception to July 2021. We included comparative and noncomparative studies. Interventions and comparators were limited to seven products that are commercially available and currently in use (vaginal dehydroepiandrosterone [DHEA], ospemifene, laser or energy-based therapies, polycarbophil-based vaginal moisturizer, Tibolone, vaginal hyaluronic acid, testosterone). Topical estrogen, placebo, other nonestrogen products, as well as no treatment were considered as comparators. Methods of study selection: We double-screened 9,131 abstracts and identified 136 studies that met our criteria. Studies were assessed for quality and strength of evidence by the systematic review group. Tabulation, integration, and results: Information regarding the participants, details on the intervention and comparator and outcomes were extracted from the eligible studies. Alternative therapies were similar or superior to estrogen or placebo with minimal increase in adverse events. Dose response was noted with vaginal DHEA and testosterone. Vaginal DHEA, ospemifene, erbium and fractional carbon dioxide (CO<sub>2</sub>) laser, polycarbophil-based vaginal moisturizer, tibolone, hyaluronic acid, and testosterone all improved subjective and objective signs of atrophy. Vaginal DHEA, ospemifene, tibolone, fractional CO<sub>2</sub> laser, polycarbophil-based vaginal moisturizer, and testosterone improved sexual function. Conclusion: Most nonestrogen therapies are effective treatments for the various symptoms of GSM. There are insufficient data to compare nonestrogen options to each other.

**Occup Med (Lond). 2023 Aug 5;kqad078. doi: 10.1093/ocmed/kqad078. Online ahead of print.**

## **Impact of menopausal symptoms on work and careers: a cross-sectional study**

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Background: Women over 50 years are one of the fastest-growing employment groups. Menopausal symptoms can adversely impact quality of life, work performance and attendance; however, few studies look at the impact of individual menopausal symptoms on work and career development. Aims: To measure the prevalence of menopausal symptoms in employees in a healthcare setting, to assess the impact of individual symptoms on work, attendance and career development and to explore perceptions about workplace supports. Methods: In this cross-sectional study of Irish hospital workers, menopausal employees were asked about the frequency of 10 menopausal symptoms and the extent to which each symptom impacted them at work. Impacts on performance, attendance and career development were assessed, along with the benefits of workplace support. Results: Responses from 407 women showed that the most common menopausal symptoms affecting employees greater than 50% of the time while at work were fatigue (54%), difficulty sleeping (47%), poor concentration (44%) and poor memory (40%). Work performance was impacted for 65% of respondents and 18% had taken sick leave. There was a significant association between symptom severity at work and reduced work performance, career development decisions and attendance. Manager awareness about menopause (29%) and flexible working times (29%) were selected as the most important workplace supports. Conclusions: Female employees are negatively impacted by menopausal symptoms while at work, particularly by psychological and neurocognitive symptoms which were associated with reduced work performance, attendance and career decisions. Manager awareness and flexible schedules were considered the most beneficial workplace supports.

**Psychoneuroendocrinology. 2023 Jul 20;156:106339. doi: 10.1016/j.psyneuen.2023.106339.**

## **Hormone sensitivity predicts the beneficial effects of transdermal estradiol on reward-seeking behaviors in perimenopausal women: A randomized controlled trial**

Danielle A Swales 1, Serena Lozza-Fiacco 2, Elizabeth Helen Andersen 3, Jessica A Cooper 4, et al.

Depression is highly prevalent during the menopause transition (perimenopause), and often presents with anxious and anhedonic features. This increased vulnerability for mood symptoms is likely driven in part by the dramatic hormonal changes that are characteristic of the menopause transition, as prior research has linked fluctuations in estradiol (E2) to emergence of depressed mood in at risk perimenopausal women. Transdermal estradiol (TE2) has been shown to reduce the severity of depression in clinically symptomatic women, particularly in those with recent stressful life events. This research extends prior work by examining the relation between E2 and reward seeking behaviors, a precise behavioral indicator of depression. Specifically, the current study utilizes a randomized, double blind, placebo-controlled design to investigate whether mood sensitivity to E2 flux ("hormone sensitivity") predicts the beneficial effects of TE2 interventions on reward seeking behaviors in perimenopausal women, and whether recent stressful life events moderate any observed associations. Method: Participants were 66 women who met standardized criteria for being early or late perimenopausal based on bleeding patterns. Participants were recruited from a community sample; therefore, mood symptoms varied across the continuum and the majority of participants did not meet diagnostic criteria for a depressive or anxiety disorder at the time of enrollment. Hormone sensitivity was quantified over an 8-week baseline period, using within-subjects correlations between repeated weekly measures of E2 serum concentrations and weekly anxiety (State Trait Anxiety Inventory) and anhedonia ratings (Snaith-Hamilton Pleasure Scale). Women were then randomized to receive 8 weeks of TE2 (0.1 mg) or transdermal placebo, and reward-seeking behaviors were assessed using the Effort-Expenditure for Rewards Task (EEfRT). Results: Participants who were randomized to receive transdermal estradiol and who demonstrated greater anxiety sensitivity to E2 fluctuations at baseline, demonstrated more reward seeking behaviors on the EEfRT task. Notably, the strength of the association between E2-anxiety sensitivity and post-randomization EEfRT for TE2 participants increased when women experienced more recent stressful life events and rated those events as more stressful. E2-anhedonia sensitivity was not associated with reward-seeking behaviors. Conclusion: Perimenopausal women who are more sensitive to E2 fluctuations and experienced more recent life stress may experience a greater benefit of TE2 as evidenced by an increase in reward seeking behaviors.

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## **Safety of Vaginal Estrogen Therapy for Genitourinary Syndrome of Menopause in Women With a History of Breast Cancer**

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Objective: To assess the risk of recurrence of breast cancer associated with vaginal estrogen therapy in women diagnosed with genitourinary syndrome of menopause with a history of breast cancer using a large U.S. claims database. Methods: A U.S. health research network (TriNetX Diamond Network) was queried from January 2009 to June 2022. Our cohort consisted of women diagnosed with breast cancer within 5 years before the initial genitourinary syndrome of menopause diagnosis. Patients with active disease, defined as those undergoing mastectomy, radiation treatment, or chemotherapy within 3 months before diagnosis of genitourinary syndrome of menopause, were excluded. Recurrence was defined as mastectomy, radiation, chemotherapy, or secondary malignancy within 3 months to 5 years after the initiation of vaginal estrogen therapy for genitourinary syndrome of menopause. The study cohort included those with three or more vaginal estrogen prescriptions. The control cohort included women with breast cancer without any vaginal estrogen prescriptions after genitourinary syndrome of menopause diagnosis. Propensity matching was performed. A subanalysis by positive estrogen receptor status, when available, was performed. Results: We identified 42,113 women with a diagnosis of genitourinary syndrome of menopause after breast cancer diagnosis with any estrogen receptor status, 5.0% of whom received vaginal estrogen. Of the initial cohort, 10,584 patients had a history of positive estrogen receptor breast cancer, and 3.9% of this group received vaginal estrogen. Risk of breast cancer recurrence was comparable between those who received vaginal estrogen and those who did not in both the any estrogen receptor (risk ratio 1.03, 95% CI 0.91-1.18) and positive estrogen receptor (risk ratio 0.94, 95% CI 0.77-1.15) status analyses. Conclusion: In a large, claims-based analysis, we did not find an increased risk of breast cancer recurrence within 5 years in women with a personal history of breast cancer who were using vaginal estrogen for genitourinary syndrome of menopause.