



## Selección de Resúmenes de Menopausia

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### **Role of estrogen in the regulation of central and peripheral energy homeostasis: from a menopausal perspective**

Jing Zhu 1, Yier Zhou 1, Bihui Jin 1, Jing Shu 2

Estrogen plays a prominent role in regulating and coordinating energy homeostasis throughout the growth, development, reproduction, and aging of women. Estrogen receptors (ERs) are widely expressed in the brain and nearly all tissues of the body. Within the brain, central estrogen via ER regulates appetite and energy expenditure and maintains cell glucose metabolism, including glucose transport, aerobic glycolysis, and mitochondrial function. In the whole body, estrogen has shown beneficial effects on weight control, fat distribution, glucose and insulin resistance, and adipokine secretion. As demonstrated by multiple in vitro and in vivo studies, menopause-related decline of circulating estrogen may induce the disturbance of metabolic signals and a significant decrease in bioenergetics, which could trigger an increased incidence of late-onset Alzheimer's disease, type 2 diabetes mellitus, hypertension, and cardiovascular diseases in postmenopausal women. In this article, we have systematically reviewed the role of estrogen and ERs in body composition and lipid/glucose profile variation occurring with menopause, which may provide a better insight into the efficacy of hormone therapy in maintaining energy metabolic homeostasis and hold a clue for development of novel therapeutic approaches for target tissue diseases.

**Maturitas. 2023 Sep 7;178:107844. doi: 10.1016/j.maturitas.2023.107844. Online ahead of print.**

### **The role of estrogen in female skeletal muscle aging: A systematic review**

Annabel J Critchlow 1, Danielle Hiam 2, Ross Williams 3, David Scott 4, Séverine Lamou 5

Aging is associated with a loss of skeletal muscle mass and function that negatively impacts the independence and quality of life of older individuals. Females demonstrate a distinct pattern of muscle aging compared to males, potentially due to menopause, when the production of endogenous sex hormones declines. This systematic review aims to investigate the current knowledge about the role of estrogen in female skeletal muscle aging. A systematic search of MEDLINE Complete, Global Health, Embase, PubMed, SPORTDiscus, and CINAHL was conducted. Studies were considered eligible if they compared a state of estrogen deficiency (e.g. postmenopausal females) or supplementation (e.g. estrogen therapy) to normal estrogen conditions (e.g. premenopausal females or no supplementation). Outcome variables of interest included measures of skeletal muscle mass, function, damage/repair, and energy metabolism. Quality assessment was completed with the relevant Johanna Briggs critical appraisal tool, and data were synthesized in a narrative manner. Thirty-two studies were included in the review. Compared to premenopausal women, postmenopausal women had reduced muscle mass and strength, but the effect of menopause on markers of muscle damage and expression of the genes involved in metabolic signaling pathways remains unclear. Some studies suggest a beneficial effect of estrogen therapy on muscle size and strength, but evidence is largely conflicting and inconclusive, potentially due to large variations in the reporting and status of exposure and outcomes. The findings from this review point toward a potential negative effect of estrogen deficiency on aging skeletal muscle, but further mechanistic evidence is needed to clarify its role.

**J Transl Med. 2023 Sep 16;21(1):629. doi: 10.1186/s12967-023-04413-y.**

### **Association of serum 25-hydroxyvitamin D levels with all-cause and cause-specific mortality among postmenopausal females: results from NHANES**

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Background: Vitamin D deficiency is common among the population, but its relationship with mortality of postmenopausal females is unclear. The aim of this study is to explore the association between serum 25-Hydroxyvitamin D (25(OH)D) and all-cause and cause-specific mortality among postmenopausal women in the United States. Methods: 6812 participants of postmenopausal females from the National Health and Nutrition Examination Survey (2001-2018) were included in this study. The mortality status of the follow-up was ascertained by linkage to

National Death Index (NDI) records through 31 December 2019. We used cox proportional hazards models to estimate the association of serum 25(OH)D concentrations and mortality of postmenopausal females. Results: The mean level of serum 25(OH)D was  $72.57 \pm 29.93$  nmol/L, and 65.34% had insufficient vitamin D. In postmenopausal females, low serum 25(OH)D concentrations were significantly associated with higher levels of glycohemoglobin, glucose, and lower levels of HDL. During follow-up, 1448 all-cause deaths occurred, including 393 cardiovascular disease (CVD)-related deaths and 263 cancer deaths. After multivariate adjustment, higher serum 25(OH)D levels were significantly related with lower all-cause and CVD mortality. In addition, serum 25(OH)D presented a L-shaped relationship with all-cause mortality, while appeared a U-shaped with CVD mortality, and the cut-off value is 73.89 nmol/L and 46.75 nmol/L respectively. Conclusions: Low serum 25(OH)D levels are associated with the higher risk of all-cause and CVD mortality in postmenopausal females. These findings provide new ideas and targets for the health management of postmenopausal women.

**Medicine (Baltimore). 2023 Sep 15;102(37):e35218. doi: 10.1097/MD.00000000000035218.**

## **Reproductive health factors in relation to risk of hypertension in postmenopausal women: Results from NHANES 2011-2014**

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Few studies have systematically assessed the relationship between multiple reproductive factors and hypertension, and these limited studies paid more attention to age at menarche and menopause, abortion, or the number of live births, and yielded controversial results. This study aimed to explore the relationship between reproductive health factors and hypertension from 5 aspects: history of menstruation, pregnancy, delivery, gynecological surgery, and reproductive-related medication use. We analyzed data from the National Health and Nutrition Examination Survey 2011 to 2014. Data on reproductive factors were collected using a questionnaire survey. The associations between multiple reproductive factors and the risk of hypertension were assessed using multivariable logistic regression models. There were significant inverse associations between age at menopause (odds ratio [OR] = 0.984, 95% confidence interval [CI]: 0.971-0.998,  $P = .0234$  per 1-year increase), age at first live birth (OR = 0.970, 95% CI: 0.944-0.998,  $P = .0346$  per 1-year increase), age at last live birth (OR = 0.982, 95% CI: 0.964-0.999,  $P = .0488$  per 1-year increase), and the risk of hypertension. In contrast, a positive association was found between the risk of hypertension and a history of gestational diabetes (OR = 1.693, 95% CI: 1.042-2.751,  $P = .0333$ ), hysterectomy (OR = 1.398, 95% CI: 1.139-1.717,  $P = .0014$ ), ovariectomy (OR = 1.374, 95% CI: 1.074-1.758,  $P = .0115$ ), and birth control pill use (OR = 1.293, 95% CI: 1.035-1.616,  $P = .0236$ ). Age at menopause but not menarche, is inversely associated with hypertension. A history of gestational diabetes, hysterectomy, ovariectomy, or birth control pills was associated with a higher risk of hypertension.

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## **Real-World Effectiveness of Osteoporosis Medications in France: A Nationwide Cohort Study**

Pauline Bosco-Lévy 1, Karine Briot 2, Nadia Mehsen-Cetre 3, James O'Kelly 4, Gaëlle Désaméricq 5, et al.

Although drugs for osteoporosis have been demonstrated to be effective in reducing fracture risk in placebo-controlled clinical trials, data on effectiveness in real-world practice is limited. Data from the French national health insurance claims database (SNDS) were used to follow five cohorts of women aged  $\geq 55$  years after initiating treatment for  $\geq 6$  months with either denosumab, zoledronic acid, oral bisphosphonates, raloxifene, or teriparatide in 2014-2016. Fracture incidence was compared within each cohort between the 3 months following initiation (baseline fracture risk) and the 12month, 18month, and 24 month postinitiation periods. Data are presented as incidence rate ratios (IRRs) with their 95% confidence intervals (CIs). Overall, 67,046 women were included in the denosumab cohort, 52,914 in the oral bisphosphonate cohort, 41,700 in the zoledronic acid cohort, 11,600 in the raloxifene cohort, and 7510 in the teriparatide cohort. The baseline vertebral fracture rate ranged from 1.74 per 1000 person years (%PY) in the raloxifene cohort to 34.75%PY in the teriparatide cohort, and the baseline hip fracture rate from 0.70%PY in the raloxifene cohort to 10.52%PY in the zoledronic acid cohort. Compared with the baseline fracture rate, vertebral fractures involving hospitalization were significantly reduced in the 3-24-month postinitiation period with denosumab (IRR 0.6; 95% CI, 0.5-0.7), zoledronic acid (IRR 0.4; 95% CI, 0.3-0.4), teriparatide (IRR 0.3; 95% CI, 0.2-0.5), and oral bisphosphonates (IRR 0.6; 95% CI, 0.4-0.8). Hip fracture incidence was reduced with denosumab (IRR 0.8; 95% CI, 0.6-0.9), but higher for oral bisphosphonates (IRR 1.7; 95% CI, 1.2-2.3); no significant change in hip fracture rate was

observed for zoledronic acid, teriparatide, or raloxifene. A reduction in nonvertebral, non-hip fracture incidence was observed only in the denosumab cohort (IRR 0.8; 95% CI, 0.7-0.9). These findings indicate that treatment with osteoporosis drugs is effective in the real-world setting.

**Menopause. 2023 Sep 12. doi: 10.1097/GME.0000000000002254. Online ahead of print.**

### **Long-term effects of premenopausal bilateral oophorectomy with or without hysterectomy on physical aging and chronic medical conditions**

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**Objective:** We examined the long-term effects of premenopausal bilateral oophorectomy (PBO) with or without concurrent or preceding hysterectomy on physical and cognitive function and on odds of chronic conditions. **Methods:** We enrolled 274 women with PBO with or without concurrent or preceding hysterectomy and 240 referents aged 55 years and older who were residents of Olmsted County, MN as of the PBO or index date. Chronic conditions were assessed via medical record abstraction. Cognitive diagnoses were based on neurocognitive testing. A physical function assessment included measures of strength and mobility. Multivariable regression models compared characteristics for women with PBO <46 years, PBO 46-49 years, and referent women with adjustments for age and other confounders. **Results:** The clinical visits (median age, 67 years) were a median of 22 years after the PBO or index date. Of 274 women with PBO, 161 (59%) were <46 years at PBO and 113 (41%) were 46-49 years. Compared with referents, women with a history of PBO <46 years had increased odds of arthritis (odds ratio [OR], 1.64; 95% confidence interval [CI], 1.06-2.55), asthma (OR, 1.74; 95% CI, 1.03-2.93), obstructive sleep apnea (OR, 2.00; 95% CI, 1.23-3.26), and bone fractures (OR, 2.86; 95% CI, 1.17-6.98), and walked a shorter mean distance on a 6-minute walk test ( $b = -18.43$ ;  $P = 0.034$ ). Compared with referents, women with a history of PBO at age 46-49 years had increased odds of arthritis (OR, 1.92; 95% CI, 1.16-3.18) and obstructive sleep apnea (OR, 2.21; 95% CI, 1.33-3.66). There were no significant differences in cognitive status in women with PBO compared with referents. **Conclusions:** Women with a history of PBO with or without concurrent or preceding hysterectomy, especially at age <46 years, have more chronic conditions in late mid-life compared with referents.

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### **Nutritional interventions in treating menopause-related sleep disturbances: a systematic review**

Dominik Polasek, Nayantara Santhi, Pamela Alfonso-Miller, Ian H Walshe, Crystal F Haskell-Ramsay, Greg J Elder. **Context:** Sleep disturbances are a core symptom of menopause, which refers to the permanent cessation of menstrual periods. Nutritional interventions may alleviate menopause-related sleep disturbances, as studies have shown that certain interventions (eg, tart cherry juice, or tryptophan-rich foods) can improve relevant aspects of sleep. **Objective:** The aim of this systematic review was to examine the effect of nutritional interventions for menopause-related sleep disturbances, in order to inform the subsequent development of specific interventional trials and assess their potential as a treatment for menopause-related sleep disturbances. **Data sources:** Published studies in English were located by searching PubMed and PsycArticles databases (until September 15, 2022). **Data extraction:** Following full-text review, a final total of 59 articles were included. The search protocol was performed in accordance with PRISMA guidelines. **Data analysis:** A total of 37 studies reported that a nutritional intervention improved some aspect of sleep, and 22 studies observed no benefit. Most ( $n = 24$ ) studies recruited postmenopausal women, 18 recruited menopausal women, 3 recruited perimenopausal women, and 14 recruited women from multiple groups. The majority of the studies were of low methodological quality. Due to the heterogeneity of the studies, a narrative synthesis without meta-analysis is reported. **Conclusion:** Despite the large heterogeneity in the studies and choice of intervention, the majority of the identified studies reported that a nutritional intervention did benefit sleep, and that it is mainly subjective sleep that is improved. More high-quality, adequately powered, randomized controlled trials of the identified nutritional interventions are necessary.