



## Selección de Resúmenes de Menopausia

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### **A pooled analysis of the association between sarcopenia and osteoporosis**

Xiaochao Yu 1 2, Shuo Sun 1, Shaoxiong Zhang 1, Qinggang Hao 3, Boheng Zhu 4, Yirong Teng 1, et al.

Background: Sarcopenia is a progressive generalized skeletal muscle disorder that causes the accelerated loss of muscle mass and function. Osteoporosis is a systemic condition of the skeleton that results in low bone mass and quality. Several studies have suggested that osteoporosis and sarcopenia are interrelated; however, a few studies indicate the lack of a significant association between sarcopenia and osteoporosis. We aimed to evaluate the association between sarcopenia and osteoporosis via a systematic review and pooled analysis. Methods: From the inception of the PubMed and Embase databases until September 2022, we conducted a systematic search for studies evaluating the relationship between sarcopenia and osteoporosis. Study appraisal and synthesis methods: We included observational studies that provided 95% confidence intervals (CIs) and risk estimates. Two reviewers independently extracted data and assessed the quality of the research. The random-effects model was applied to the pool analysis, and the odds ratios (ORs) and 95% CIs were finally calculated. Results: The primary statistic was the mutual risk between sarcopenia and osteoporosis. According to the inclusion criteria, 56 studies (796,914 participants) were finally included. Sarcopenia was significantly correlative to the risk of osteoporosis (OR, 3.06; 95% CI, 2.30-4.08), and each standard deviation increase in relative appendicular skeletal muscle mass was significantly related to a decreased risk of osteoporosis (OR, 0.65; 95% CI, 0.56-0.75). Osteoporosis observably referred to a higher risk of sarcopenia (OR, 2.63; 95% CI, 1.98-3.49). Conclusion: Our research indicated that sarcopenia and osteoporosis are highly positively correlated. Osteoporosis is closely associated with the risk of sarcopenia. Our finding highlights the importance of sarcopenia screening for those at risk of osteoporosis, and vice versa. However, heterogeneity was noted among the studies, and this might have influenced the accuracy of the results. Therefore, the results of our study should be interpreted with caution.

**J Womens Health (Larchmt). 2022 Nov 18. doi: 10.1089/jwh.2022.0153. Online ahead of print.**

### **Lifetime Smoking History and Prevalence of Osteoporosis and Low Bone Density in U.S. Adults, National Health and Nutrition Examination Survey 2005-2010**

Austin R Thompson 1 2, Molly Joyce 1, Kalera Stratton 1, Eric S Orwoll 3, Hans L Carlson 2, Nels L Carlson 2, et al.

Background: Osteoporosis is common among older adults. Women are more likely to have osteoporosis than men. The prevalence varies with race/ethnicity, with the highest prevalence observed among non-Hispanic, Asian women. Prior studies identified a negative association between smoking and bone mineral density (BMD). The association between smoking and osteoporosis has not been investigated according to race/ethnicity. Materials and Methods: We included 4,226 U.S. adults aged 50 years or older with complete information on smoking history, BMD, and other independent variables from the 2005-2010 National Health and Nutrition Examination Surveys. Design-based multinomial logistic regression was utilized to estimate prevalence odds ratios (POR) of osteoporosis (T-score  $\leq -2.5$ ) and of low bone density (T-score between -1.0 and -2.5) in relation to lifetime smoking pack-years, stratified by sex and race/ethnicity. Results: Participants were 61.5 (standard error 0.21) years old on average and 48% women (n = 2,027). Among women, a smoking history  $\geq 30$  pack-years was positively associated with osteoporosis (POR: 2.40; 95% confidence interval [CI]: 1.42-4.06). Similar POR were observed among non-Hispanic White, non-Hispanic Black, and Mexican American women. However, POR for  $\geq 30$  pack-years and low bone density were positive but not statistically significant. Among men, null associations of smoking history, osteoporosis, and low bone density were observed, except for a positive association of  $\geq 30$  pack-years and low bone density among non-Hispanic Black men. Conclusion: Osteoporosis was twice as prevalent among women who smoked  $\geq 30$  pack-years than among women who never smoked, regardless of race/ethnicity. Smoking history and osteoporosis were not associated among men.

**Climacteric. 2022 Nov 18;1-9. doi: 10.1080/13697137.2022.2139599. Online ahead of print.**

## **Impact of estetrol (E4) on hemostasis, metabolism and bone turnover in postmenopausal women**

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**Objective:** This study aimed to determine the effects of estetrol (E4) on hemostasis, lipids, carbohydrate metabolism and bone turnover in postmenopausal women. **Methods:** This study was a multicenter, randomized, double-blind placebo-controlled phase 2 trial. Participants (n = 180, age 43-64 years) received E4 2.5 mg, 5 mg, 10 mg and 15 mg or placebo once daily for 12 weeks. Changes from baseline at week 12 were evaluated versus placebo for hemostasis parameters, sex hormone binding globulin (SHBG), lipids, carbohydrate metabolism and bone markers. **Results:** Changes for hemostasis parameters were minimal with a small increase only in the normalized activated protein C sensitivity ratio in the E4 15 mg group versus placebo. SHBG increased in the E4 5 mg, 10 mg and 15 mg groups versus placebo. High-density lipoprotein cholesterol increased in all E4 groups; changes were not consistent for other lipids. Significant decreases versus placebo were seen for insulin resistance (E4 10 mg group), hemoglobin A1c (E4 15 mg group) and type 1 collagen C-terminal telopeptide (E4 10 mg and 15 mg groups). Small decreases in osteocalcin in the E4 5 mg, 10 mg and 15 mg groups were significant versus the increase observed in placebo. **Conclusion:** E4 had limited impact on hemostasis and potentially beneficial effects on lipids, carbohydrate metabolism and bone turnover.

**Front Immunol. 2022 Oct 27;13:997808. doi: 10.3389/fimmu.2022.997808. eCollection 2022.**

## **Bone marrow mesenchymal stem cells in premature ovarian failure: Mechanisms and prospects**

Yanjing Huang 1, Mengdi Zhu 1, Zhuo Liu 1, Runan Hu 1, Fan Li 1, Yufan Song 1, Yuli Geng 1, et al.

Premature ovarian failure (POF) is a common female reproductive disorder and characterized by menopause, increased gonadotropin levels and estrogen deficiency before the age of 40 years old. The etiologies and pathogenesis of POF are not fully clear. At present, hormone replacement therapy (HRT) is the main treatment options for POF. It helps to ameliorate perimenopausal symptoms and related health risks, but can't restore ovarian function and fertility fundamentally. With the development of regenerative medicine, bone marrow mesenchymal stem cells (BMSCs) have shown great potential for the recovery of ovarian function and fertility based on the advantages of abundant sources, high capacity for self-renewal and differentiation, low immunogenicity and less ethical considerations. This systematic review aims to summarize the possible therapeutic mechanisms of BMSCs for POF. A detailed search strategy of preclinical studies and clinical trials on BMSCs and POF was performed on PubMed, MEDLINE, Web of Science and Embase database. A total of 21 studies were included in this review. Although the standardization of BMSCs need more explorations, there is no doubt that BMSCs transplantation may represent a prospective therapy for POF. It is hope to provide a theoretical basis for further research and treatment for POF.

**Arch Endocrinol Metab. 2022 Nov 11;66(5):694-706. doi: 10.20945/2359-3997000000559.**

## **Update on trabecular bone score**

Telma Palomo 1, Patricia Muszkat 2, Fernanda G Weiler 2, Patricia Dreyer 2, Cynthia M A Brandão 2, et al

Trabecular bone score (TBS) is an indirect and noninvasive measure of bone quality. A low TBS indicates degraded bone microarchitecture, predicts osteoporotic fracture, and is partially independent of clinical risk factors and bone mineral density (BMD). There is substantial evidence supporting the use of TBS to assess vertebral, hip, and major osteoporotic fracture risk in postmenopausal women, as well as to assess hip and major osteoporotic fracture risk in men aged > 50 years. TBS complements BMD information and can be used to adjust the FRAX (Fracture Risk Assessment) score to improve risk stratification. While TBS should not be used to monitor antiresorptive therapy, it may be potentially useful for monitoring anabolic therapy. There is also a growing body of evidence indicating that TBS is particularly useful as an adjunct to BMD for fracture risk assessment in conditions associated with increased fracture risk, such as type-2 diabetes, chronic corticosteroid excess, and other conditions wherein BMD readings are often misleading. The interference of abdominal soft tissue thickness (STT) on TBS should also be considered when interpreting these findings because image noise can impact TBS evaluation. A new TBS software version based on an algorithm that accounts for STT rather than BMI seems to correct this technical limitation and is under development. In this paper, we review the current state of TBS, its technical aspects, and its evolving role in the assessment and management of several clinical conditions.

**Am J Physiol Heart Circ Physiol. 2022 Nov 11. doi: 10.1152/ajpheart.00477.2022. Online ahead of print.**

## **Vasomotor symptoms of menopause, autonomic dysfunction, and cardiovascular disease**

Emma Lee 1, Miguel Anselmo 1, Chowdhury Tasnova Tahsin 2, Marnie Vanden Noven 3, William Stokes 2, et al. Cardiovascular disease (CVD), the leading cause of death among United States adults, is more prevalent in menopausal females compared to age-matched males. Vasomotor symptoms of menopause (VMS; hot flashes/flushes and night sweats) are common among females undergoing menopausal transition and have been associated with elevated blood pressure (BP) and increased CVD risk. Autonomic dysregulation of BP has been posited as a contributing factor to the elevated CVD risk in menopausal females with VMS. This review includes: 1) a brief overview of the relationship between VMS and CVD; 2) mechanisms of hot flashes and their potential impact on short- and long-term BP regulation; and 3) how the disruption of autonomic function associated with VMS might provide a mechanistic pathway to CVD development. Lastly, this review will highlight knowledge gaps and future directions towards better understanding hot flush physiology and VMS contributions to CVD.

**Healthcare (Basel). 2022 Oct 24;10(11):2121. doi: 10.3390/healthcare10112121.**

## **Association between Menopausal Hormone Therapy and Frailty: Cross-Sectional Study Using National Survey Data in Korea**

Hyunjoo Kim 1, Euni Lee 1

Frailty is a multidimensional clinical syndrome that increases the risk of adverse health outcomes. Previous studies have reported a close link between menopause and frailty. Combined estrogen-progestin therapy (or estrogen-only therapy in women who have undergone a hysterectomy) is currently approved as a menopausal hormone therapy (MHT) to treat menopausal symptoms. Despite increasing evidence of the importance of sex hormones in the development of frailty, very few studies have investigated the association between MHT and frailty. A cross-sectional evaluation was conducted using population-based survey data known as the Korea National Health and Nutrition Examination Survey (KNHANES IV-V, 2008-2012). The KNHANES data provided variables that were used to construct a 51-item frailty index (FI). The number of study population, only including postmenopausal women, was 7823 women, and their mean age was 62.51 years (range 32-80 years). Approximately 40% of them had graduated from middle school or higher, 45% lived in metropolitan statistical areas, and 5% were recipients of the national Medical Aid. The mean age at menopause was 48.66 years (range 30-62 years). Overall, the mean FI value was 0.15, and the prevalence of MHT was 13.23%. Findings from multiple regression analysis using the inverse probability of treatment weighting showed that a treatment duration of more than 2 years and up to 5 years, age at first treatment between 50 and 59 years, and MHT initiation 3 to 6 years after menopause were all negatively associated with frailty ( $p < 0.05$ ). Further studies are needed to confirm these findings using prospective data.

**Sleep Med Rev. 2022 Oct 27;66:101710. doi: 10.1016/j.smrv.2022.101710. Online ahead of print.**

## **The role of ovarian hormones in the pathophysiology of perimenopausal sleep disturbances: A systematic review**

Annika Haufe 1, Fiona C Baker 2, Brigitte Leeners 3

Sleep disturbance is a common clinical concern throughout the menopausal transition. However, the pathophysiology and causes of these sleep disturbances remain poorly understood, making it challenging to provide appropriate therapy. Our goal was to i) review the literature about the influence of ovarian hormones on sleep in perimenopausal women, ii) summarize the potential underlying pathophysiology of menopausal sleep disturbances and iii) evaluate the implications of these findings for the therapeutic approach to sleep disturbances in the context of menopause. A systematic literature search using the databases Embase, MEDLINE and Cochrane Library was conducted. Keywords relating to ovarian hormones, sleep disturbances and menopause were used. Ultimately, 86 studies were included. Study Quality Assessment Tools of the National Institutes of Health were used for quality assessment. Results from good-quality studies demonstrated that the postmenopausal decline in estrogen and progesterone contributes to sleep disturbances in women and that timely treatment with estrogen and/or progesterone therapy improved overall sleep quality. Direct and indirect effects of both hormones acting in the central nervous system and periphery, as well as via secondary effects (e.g. reduction in vasomotor symptoms), can contribute to improvements in sleep. To strengthen external validity, studies examining neurobiological pathways are needed.

**BMC Womens Health. 2022 Nov 8;22(1):438. doi: 10.1186/s12905-022-02021-4.**

## **Risk factors for natural menopause before the age of 45: evidence from two British population-based birth cohort studies**

Darina Peycheva 1 2, Alice Sullivan 3, Rebecca Hardy, Alex Bryson 3, Gabriella Conti 3 5, George Ploubidis 3, et al. Background: Menopause that occurs before the age of 45 and is not medically induced (referred to here as 'early natural menopause') affects around one in 10 women and has serious health consequences. These consequences include increased risk of all-cause mortality, cardiovascular disease, osteoporosis, and type 2 diabetes. Methods: We investigate risk factors for the onset of natural menopause before the age of 45 in two population-based prospective cohort studies in Britain: the 1958 cohort following 8959 women and the 1970 cohort following 8655 women. These studies follow women from birth to adulthood, and we use harmonized data on birth and early life characteristics, reproductive health, health behaviour, and socioeconomic characteristics for 6805 women who were pre-menopausal, peri-menopausal or had undergone natural menopause. Of these 6805 women, 3614 participated in the 1958 cohort (of which 368 had early menopause) and 3191 participated in the 1970 cohort (of which 206 had early menopause). Taking a life course approach, we focus on three distinct life stages - birth/early life, childhood, and early adulthood - to understand when risk factors are most harmful. Respecting the temporal sequence of exposures, we use a series of multivariable logistic regression models to estimate associations between early menopause and each potential risk factor adjusted for confounders. Results: We find that early menopause is influenced by circumstances at birth. Women born in lower social class families, whose mother smoked during the pregnancy or who were breastfed 1 month or less were more likely to undergo early menopause. Early menopause is also associated with poorer cognitive ability and smoking in childhood. Adult health behaviour also matters. Smoking is positively correlated with early menopause, while regular exercise and moderate frequency of alcohol drinking in women's early thirties are associated with reduced risk of early menopause. The occurrence of gynaecological problems by women's early thirties is also linked to early menopause. Conclusions: We demonstrate that characteristics at different periods of life are associated with early menopause. Some of these associations relate to modifiable behaviours and thus the risks of early menopause and the adverse health outcomes associated with it may be preventable.

**Rev Int Androl. 2022 Nov 5;S1698-031X(22)00079-6. doi: 10.1016/j.androl.2021.09.002. Online ahead of print.**

## **Efficacy and safety of testosterone in the treatment of hypoactive sexual desire in women: what does the evidence say?**

Franklin José Espitia De La Hoz 1

Objective: To determine the efficacy and safety of testosterone in the treatment of hypoactive sexual desire in women. Materials and methods: A systematic review of the literature was carried out in different electronic databases (CINAHL, DynaMed, EMBASE, Lilacs, Medline, Scopus, among others), between January 1990 and May 2021; through standardized search terms. The outcomes evaluated included the efficacy and safety of testosterone in increasing sexual desire, the total number of satisfactory sexual activity, the number of orgasms and the level of distress in patients with hypoactive sexual desire and the proportion of adverse reactions. Results: 72 articles were included. The use of testosterone, in postmenopausal women, with hypoactive sexual desire, reports a positive effect on sexual function, with significant increases in satisfactory sexual activity, as well as improvement in all domains of sexual function (desire, arousal and orgasmic response) and a decrease in personal anguish, with an increase in the Female Sexual Function Index score. In women of childbearing age, testosterone is formulated for "off-label" use, in such a way that compounds and doses designed for treatments in men or magisterial formulas are used (which are not approved by consensus groups or endorsed by research), but has not shown any effect on sexual function. The most frequent adverse reactions are usually hirsutism and acne, although in general testosterone, at physiological doses, has a favorable safety profile. Conclusions: Testosterone is an effective and safe therapy in the treatment of hypoactive sexual desire disorder in women after menopause. Currently there are no studies available to support the use of testosterone therapy in women of reproductive age, therefore, its use is not approved.