Selección de Resúmenes de Menopausia

Semana del 9 al 15 de julio 2025

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Blood-detected mitochondrial biomarker NSUN4: a potential indicator of ovarian aging

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Background: Mitochondrial dysfunction is a key hallmark of aging, and blood-based biomarkers related to mitochondrial genes provide an effective means to assess ovarian aging progression. In this study, we aimed to explore the role of mitochondrial dysfunction-related genetic variations in determining the natural age at menopause (ANM) by applying both Mendelian randomization (MR) and summary data-based Mendelian randomization (SMR) approaches, complemented by experimental validation in animal models. Methods: Summary statistics on ANM, gene expression, DNA methylation, and protein abundance quantitative trait loci (eQTL, mQTL, pQTL) were obtained from public databases. Genetic variations associated with mitochondrial dysfunction were selected as instrumental variables, and SMR analysis was performed to investigate causal relationships with ANM. MR methods were also used to evaluate the causal effect of mitochondrial DNA copy number (mtDNA-CN) on ANM, with preliminary validation through animal experiments. Results: SMR and meta-analysis results identified NSUN4 as a critical regulator of ANM at both the gene expression and DNA methylation levels. A preliminary causal relationship between reduced mtDNA-CN and increased ANM risk was found, though further validation with larger datasets is needed. Animal experiments indicated that NSUN4 levels in blood reflect ovarian function decline and may correlate with its expression in ovarian tissue. Conclusions: The findings suggest that NUSN4 levels detected in the blood could serve as a potential biomarker for ovarian aging. This provides new insights into the role of mitochondrial dysfunction in reproductive age-related traits and may inform future targeted interventions to slow ovarian aging.

Patient. 2025 Jul 12. doi: 10.1007/s40271-025-00748-4. Online ahead of print.

Exit Interviews Examining Changes to Mood and Work/Productivity Impacts Related to Vasomotor Symptoms: Perspectives of Postmenopausal Women Receiving Elinzanetant in Phase III Clinical Trials

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Background: Vasomotor symptoms (VMS; hot flashes) significantly impact women's health-related quality of life during the menopausal transition. Two phase III trials (OASIS 1 and 2) were conducted to investigate the efficacy and safety of elinzanetant for the treatment of moderate-to-severe VMS associated with menopause. This exit interview study explored the impact of VMS on women's mood and work/productivity before and since treatment. Methods: A total of 40 postmenopausal women from the USA who participated in OASIS 1 and 2 (receiving elinzanetant for 26 weeks or placebo for 12 weeks followed by elinzanetant for 14 weeks) took part in a 60-min exit interview. Interviews were conducted via telephone by trained qualitative interviewers using a semi-structured interview guide; concept-elicitation techniques, followed by focused questioning, were used to explore concepts of interest. Interview transcripts were analyzed using thematic analysis methods in Atlas.ti. Saturation analysis was conducted to determine the appropriateness of the sample size. Results: Twelve mood concepts and seven work/productivity concepts were reported to be associated with VMS before taking the study medication. Most commonly reported mood concepts included reduced happiness (60.0%), embarrassment (50.0%), and mood swings (45.0%). Most commonly reported work/productivity concepts included reduced concentration (77.5%) and reduced productivity (67.5%). Most participants reported improvements since taking the study medication (mood: ≥ 82.4%; work/productivity: ≥ 80.0%), which contributed to other positive changes (e.g., in social wellbeing). Improvements were considered meaningful (≥ 72.2%) and highly satisfying (≥ 71.4%). Conclusion: This study provides novel insights into women's experiences of VMS-associated impacts on mood and work/productivity, highlighting the emotional and economic burdens of VMS. Data support and contextualize the treatment benefits of elinzanetant on mood and work/productivity that are meaningful to women.

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Magnesium: Exploring Gender Differences in Its Health Impact and Dietary Intake

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Background: Magnesium (Mg2+) plays a fundamental role in various physiological processes, including neuromuscular function, glucose metabolism, cardiovascular regulation, and bone health. Despite its significance, the influence of sex on magnesium metabolism, requirements, and health outcomes remains unexplored. The aim of this review is to analyze sex-based differences in magnesium homeostasis, with a particular focus on hormonal regulation, body composition, and disease susceptibility. Methods: This narrative review, based on a non-systematic MEDLINE search conducted in January 2025, prioritized clinical trials from the past 15 years on human subjects and explored gender-specific aspects of magnesium intake, status, metabolism, and supplementation. Results: Hormonal fluctuations, particularly variations in estrogen levels, affect magnesium absorption, distribution, and retention, thereby influencing magnesium balance across different life stages such as puberty, pregnancy, and menopause. Additionally, dietary intake and lifestyle factors often differ between men and women, further impacting magnesium status. Emerging evidence suggests that suboptimal magnesium levels may differentially contribute to conditions such as osteoporosis, cardiovascular disease, and metabolic disorders in each sex. Conclusions: In conclusion, acknowledging sex-specific differences in magnesium metabolism is essential for developing personalized dietary guidelines and therapeutic strategies. Tailored nutritional approaches could significantly improve magnesium status, enhance overall health, and reduce the burden of chronic diseases linked to magnesium imbalance.

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Divergent mechanisms of cardiovascular remodeling between men and women

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Free article

Cardiovascular diseases (CVD) remain the leading cause of morbidity and mortality. Notably, there are significant differences between men and women in the manifestation, progression and outcome of CVD, as well as in therapeutic responses. Overall, premenopausal women show greater protection against adverse remodeling. However, following menopause, women lose this advantage. It is, therefore, widely expected that sex hormones, particularly estrogen, play a major role, conferring females with protection, which might not necessarily be the case for males. In the present article, we elucidate pathways and biological processes affected by biological sex, i.e. the renin-angiotensin-aldosterone system, oxidative stress responses, inflammation, endothelial function, microRNA regulation, as well as cell death. We conclude that more research on sex-biased mechanisms and interventions in CVD is necessary. Ultimately, these efforts will lead to the development of sex- and gender-informed guidelines for CVD prevention and treatment, thereby contributing to more equitable and effective cardiovascular care for all patients.

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Hormonal modulation, mitochondria and Alzheimer's prevention: the role of GLP-1 agonists and estrogens

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Alzheimer's disease (AD) is the most prevalent cause of dementia worldwide, disproportionately affecting women and lacking effective disease-modifying therapies. While traditional approaches have focused on amyloid β (Aβ) plaques and tau pathology, emerging evidence highlights the role of metabolic dysfunction, mitochondrial impairment, and hormonal signaling in the pathogenesis of AD. Estrogens exert neuroprotective effects by modulating synaptic plasticity, enhancing mitochondrial bioenergetics, and reducing oxidative stress and inflammation. Similarly, glucagon-like peptide-1 receptor agonists (GLP-1RAs), initially developed for the treatment of type 2 diabetes, have demonstrated promising cognitive benefits, potentially mediated through improved insulin signaling, neuronal survival, and reduced β-amyloid (Aβ) and tau burden. This review explores the converging mechanisms through which estrogens and GLP-1RAs may act synergistically to prevent or delay the onset of AD. We examine the influence of sex differences in mitochondrial dynamics, estrogen receptor distribution, and GLP-1 signaling pathways, particularly within central nervous system regions implicated in AD. Preclinical studies using GLP-1-estrogen conjugates have shown enhanced metabolic and neuroprotective outcomes, accompanied by reduced systemic hormonal exposure, suggesting a viable therapeutic strategy. As the global prevalence of AD continues to rise, especially among

postmenopausal women, dual agonism targeting estrogen and GLP-1 receptors may represent a novel, physiologically informed approach to prevention and intervention. Ongoing clinical trials and future research must consider sex-specific factors, receptor polymorphisms, and brain-region selectivity to optimize the translational potential of this combined strategy.

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Dietary Inflammatory Index: is it really associated with postmenopausal symptoms?

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Objective: Diet significantly modulates immunological responses and can impact climacteric symptoms. This study evaluated the association between Dietary Inflammatory Index (DII) scores and climacteric symptoms in postmenopausal women. Method: The study was conducted with postmenopausal women between May and July 2024. A face-to-face questionnaire including demographic characteristics, the Menopause Rating Scale (MRS) and the Kupperman Menopausal Index (KMI) was administered. The DII score was computed based on dietary data. Anthropometric measurements were based on participants' self-reports. The data were analyzed using SPSS 24.0. Result: s: In total, 193 postmenopausal women were recruited. Participants in T3, who had the highest DII scores and thus followed the most pro-inflammatory diets, had higher MRS and KMI scores, with significant differences between the groups ($p < 0.001$ and $p = 0.033$, respectively). T3 had higher intakes of energy and total fat ($p = 0.018$ and $p = 0.030$, respectively) but lower intakes of n-3 fatty acids ($p = 0.038$). Multivariate linear regression analysis revealed that moderate to high DII scores correlated with elevated MRS scores (odds ratio 1.100, $p < 0.001$ and 1.106, $p < 0.001$, respectively). After adjusting for age, marital status, education, employment, physical activity, year of menopause, supplement use and socioeconomic status, the results remained consistent. Conclusion: A pro-inflammatory diet might be associated with higher symptoms. Further studies are needed to confirm these findings.

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Frequency of Sleep Disorders and Their Association with Neurocognitive, Psychological, or Physical Alterations in Postmenopausal Women

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Objective: The objective of the study was to determine the frequency of sleep disorders and their association with neurocognitive, psychological, or physical alterations in postmenopausal Colombian women. Materials and methods: A cross-sectional study carried out on postmenopausal women (50-75 years). Participants were surveyed on a general questionnaire, the Jenkins Sleep Scale, the Mini-Mental State Examination tool, the Menopause Rating Scale (MRS), and the Strength, Assistance with walking, Rising from a chair, Climbing stairs, and Falling scale. Crude and adjusted logistic regression analyses were performed to determine the association between sleep problems (dependent variable) with the neurocognitive, psychological, and physical established impairments (independent variables). The covariates were age, age at menopause, years of being postmenopausal, coffee consumption, smoking habit, and nutritional status. Results: Among 601 participants, 53 (8.8%) had sleep problems. Bivariate analysis found that overall impairment of quality of life and its domains (somato-vegetative, psychological, and urogenital), and cognitive impairment and its various aspects (memory, language, fixation, and temporal fixation) were found at a higher rate among women with sleep problems. The risk of sarcopenia was similar among those with and without sleep problems. Adjusted logistic regression determined that sleep problems were associated with somato-vegetative (odds ratio [OR]: 3.44, 95% confidence interval [CI]: 1.56-7.59), urogenital (OR: 2.35, 95% CI: 1.00-5.51) and cognitive impairment (OR: 2.20, 95% CI: 1.02-4.71). Conclusion: 8.8% of this sample of postmenopausal women had sleep problems, which were significantly associated with impairment of quality-of-life aspects and cognition.

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Oral contraceptive use increases bone density and reduces the risk of osteoporosis

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Osteoporotic fractures, largely resulting from reduced estrogen levels after menopause and subsequent bone loss, are a leading cause of disability among older women. Although oral contraceptive pills (OCPs) contain estrogen, their

long-term impact on bone health and osteoporosis risk remain uncertain. Here, we assessed the effect of OCP use on bone mineral density (BMD) and osteoporosis using data from 257,185 women from the UK Biobank, born 1936-1970. Time-dependent Cox regression was used to estimate adjusted hazard ratios (HRs) and 95% confidence intervals (CI) for osteoporosis, while multivariable linear regression was used to assess the effect of OCP use on BMD, measured as T-scores in standard deviation units based on quantitative ultrasound of the calcaneus. By the end of follow-up in 2020, 7.6% of the participants had received an osteoporosis diagnosis. The rate of osteoporosis was lower among ever OCP users (HR = 0.86; 95% CI 0.83-0.89; P = 2.8 × 10-17). OCP use was also associated with a higher BMD T-score (0.052; 0.038-0.067; P = 2.1 × 10-12) with an increasing effect with longer use. Use of OCPs for 0-1 years had no significant effect on BMD (P = 0.081). However, longer durations were associated with increased BMD T-scores compared to never users: 2-5 years (0.046; 0.027-0.065, P = 2.2 × 10-6), 6-10 years (0.062; 0.043-0.080; P = 3.5 × 10-12), 11-15 years (0.062; 0.042-0.081; P = 3.2 × 10-12) and 16 + years (0.064; 0.044-0.083; P = 1.2 × 10-10). We found prior OCP use to be associated with higher BMD and a reduced risk of osteoporosis, potentially offering long-term benefits and suggesting that OCP use could reduce osteoporotic complications in older women.