

Selección de Resúmenes de Menopausia

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A review of estrogens used in menopausal hormone therapy

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Purpose of review: To provide an overview of endogenous and therapeutic estrogens, their receptor biology, clinical applications, and evolving safety considerations, with emphasis on how estrogen type, timing, and route of administration influence outcomes in menopausal hormone therapy (MHT). Recent findings: Emerging research shows that estrogen receptor (ER) α , ER β , and G protein-coupled estrogen receptor mediate distinct and sometimes opposing physiological effects. Updated analyses support the timing hypothesis, showing that starting MHT closer to menopause may yield cardiovascular and neurological benefits not observed with later initiation. Comparative studies demonstrate that estradiol has a more favorable thrombotic and metabolic profile than conjugated equine estrogens. Newer agents such as estetrol provide selective ER α activation with reduced hepatic stimulation and promising effects on vasomotor symptoms, bone turnover, and metabolic markers. Estriol has gained attention for its safety and effectiveness in treating genitourinary syndrome of menopause. Summary: Estrogen therapy reflects a nuanced approach informed by receptor selectivity, pharmacologic diversity, and timing of initiation. Estradiol-based and transdermal formulations remain preferred for systemic therapy, while low-dose vaginal estrogen is first line for urogenital symptoms. Novel estrogens and deeper mechanistic insights continue to refine therapeutic options, supporting more targeted and safer use of estrogen across the menopausal transition.

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Physical activity as an alternative or adjunct to menopausal hormone therapy for symptom management in women with primary ovarian insufficiency

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Background: Physical activity alleviates menopausal symptoms in women whose menopause occurs after the age of 45; however, its effect in primary ovarian insufficiency, which occurs before the age of 40, remains unknown. Objective: To examine the association between physical activity, menopausal symptoms, and the use of menopausal hormone therapy in women with primary ovarian insufficiency. Methods: We analysed data from 4708 participants from two studies conducted in 12 Latin American countries. After applying eligibility criteria, 564 women with primary ovarian insufficiency (351 idiopathic and 213 surgical) were included. Menopausal symptoms were assessed using a validated scale, and severe symptoms were defined according to established cut-offs. Physical activity was classified according to international recommendations for moderate-intensity activity. Logistic regression models were adjusted for sociodemographic, clinical, and lifestyle variables. Results: The prevalence of severe menopausal symptoms was 39.2%, with no significant difference between idiopathic and surgical primary ovarian insufficiency. Women with severe symptoms were less likely to meet recommended levels of physical activity or to be current users of menopausal hormone therapy. In adjusted models, regular physical activity (OR 0.65; 95% CI 0.45-0.94) and current use of menopausal hormone therapy (OR 0.27; 0.17-0.42) were associated with a lower likelihood of severe symptoms, whereas obesity and use of psychotropic medication were associated with a higher likelihood. Conclusions: Women with primary ovarian insufficiency who engage in regular physical activity or currently use menopausal hormone therapy report less severe menopausal symptoms. Regular exercise may be an important non-hormonal option for women who cannot or prefer not to use hormone therapy.

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Global Burden of Vertebral Fractures in Women by Menopausal Status, 1990-2021, With 2050 Projections: An Analysis of Global Burden of Disease 2021

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Study DesignEco-epidemiological study.ObjectivesVertebral fractures (VFs) are a major cause of morbidity, disability, and mortality in women, with risk increasing sharply after menopause due to accelerated bone loss. However, global patterns of VF burden by menopausal status and long-term projections remain poorly characterized.MethodsWe analyzed Global Burden of Disease (GBD) 2021 data on VF incidence, prevalence, and years lived with disability (YLDs) for 204 countries from 1990-2021. Women were categorized as premenopausal (15-49 years) or postmenopausal (≥50 years). Age-standardized rates (ASRs) were calculated per 100,000 population. Temporal trends were assessed using estimated annual percentage change and joinpoint regression. Socio-demographic disparities were examined with Slope Index of Inequality and Concentration Index. Decomposition analysis quantified contributions of population growth, aging, and epidemiologic change. Bayesian age-period-cohort models projected trends to 2050.ResultsIn 2021, 1.15 million VFs occurred in premenopausal women and 1.63 million in postmenopausal women, causing 50,060 and 206,652 YLDs, respectively. Absolute VF counts rose substantially since 1990, although ASRs declined in most regions. Postmenopausal women bore the highest burden, with marked geographic heterogeneity and persistent pro-poor inequality. Population growth and aging were the main drivers of increasing burden, and projections indicate that absolute VF cases will continue to rise globally through 2050 despite modest ASR declines.ConclusionsThe global burden of vertebral fractures in women is rising in absolute terms, especially among postmenopausal women. Targeted osteoporosis screening, fall-prevention programs, and equitable treatment access are needed to mitigate the projected growth.

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Global perspectives on perimenopause: a digital survey of knowledge and symptoms using the Flo application

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Objective: Perimenopause is the time leading up to a woman's last menstrual cycle and includes the 12 months afterward. Studies that systematically compare perimenopause symptoms across diverse cultural and geographic settings are lacking. This study, utilizing data from Flo, an international mobile health application, aimed to assess global knowledge and symptom experiences related to perimenopause. Methods: This cross-sectional survey was conducted via the Flo application, offered to users aged 18 years and above. The primary endpoints were knowledge of perimenopause symptoms from all survey participants, and self-reported perimenopause symptoms for survey participants aged 35 years and above. Secondary analyses compared knowledge scores and symptoms across geographic regions. Results: A total of 17,494 women from 158 countries were included. Commonly recognized perimenopause symptoms included hot flashes (71%), sleep problems (68%), and weight gain (65%). Of the participants, 12,681 were aged 35 years or above, with the most common self-reported symptoms being fatigue (83%), physical and mental exhaustion (83%), irritability (80%), depressive mood (77%), sleep problems (76%), digestive issues (76%), and anxiety (75%). This pattern of symptoms was similar among those who self-reported being in perimenopause, though higher than in those not in perimenopause. International variation in perimenopause symptom knowledge and symptoms experienced was noted ($P<0.001$). Conclusions: This survey highlights a discordance between perimenopause knowledge and actual symptoms experienced across diverse global populations. While hot flashes were the most widely recognized symptom, respondents aged 35 years or above most commonly reported experiencing fatigue, physical and mental exhaustion, and irritability.

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Knowledge, attitudes, and practices toward premature ovarian insufficiency: a cross-sectional study among women of childbearing age

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Background: Premature ovarian insufficiency (POI) is a significant public health concern, and its early identification in young women is paramount. This study investigated the knowledge, attitude, and practice (KAP) toward POI among women of childbearing age (WOCBA). Methods: This cross-sectional study was conducted among WOCBA in the primary communities of Chengdu, Sichuan Province, China, from December 2024 to March 2025. A self-designed

questionnaire was employed, and participants were selected using a stratified random sampling method. Results: A total of 459 valid questionnaires were collected, with respondents exhibiting a mean age of 32.44 ± 5.59 years. The majority of participants were married (69.28%), and residing in urban areas (46.19%). The knowledge, attitude, and practice scores were 11.35 ± 10.20 (possible range: 0-38), 37.91 ± 4.29 (possible range: 10-50), and 56.50 ± 15.97 (possible range: 18-90), respectively. Spearman correlation analysis revealed significant positive correlations between knowledge and attitude ($r = 0.185$, $P < 0.001$), between attitude and practice ($r = 0.474$, $P < 0.001$) and between knowledge and practice ($r = 0.356$, $P < 0.001$). Multivariable linear regression analyses showed that both knowledge and attitude were independent predictors of practice scores, and higher educational attainment was also associated with higher practice levels. Living environment contributed significantly to knowledge and attitude scores, while income and family history of early menopause were independently associated with attitude. Structural equation modeling showed that knowledge was associated with attitude ($\beta = 0.210$, $P = 0.015$) and with practice ($\beta = 0.301$, $P = 0.010$), and attitude was associated with practice ($\beta = 0.431$, $P = 0.005$). Knowledge was also indirectly associated with practice through attitude ($\beta = 0.091$, $P = 0.006$). Conclusion: WOCBA demonstrated a constrained understanding of POI, accompanied by moderate attitudes and practices related to it. Targeted educational strategies may help improve awareness of POI among WOCBA, which could be associated with more favorable attitudes and greater engagement in POI-related health-seeking behaviors.

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The Impact of the Menopausal Transition on Body Composition and Abdominal Fat Redistribution

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Objective: To evaluate the impact of the menopausal transition on body composition across different body mass categories and to identify menopause-related changes in lean and fat tissue distribution. **Methods:** This retrospective cross-sectional study included 325 women whose clinical and body composition data were extracted from existing records. Participants were classified as premenopausal (controls), perimenopausal, or postmenopausal and further stratified by body mass index (BMI) into normal-weight, overweight, and obesity groups. Body composition had been assessed using bioelectrical impedance analysis. **Results:** Across all BMI categories, postmenopausal women demonstrated significantly lower lean body mass, soft lean mass, skeletal muscle mass, total body water, protein, and mineral content compared with premenopausal and perimenopausal women ($p < 0.05$). Total and visceral fat area (VFA), body fat percentage (BF), and waist-to-hip ratio were significantly higher, indicating a shift toward central adiposity. These changes were most pronounced in normal-weight women (VFA: 36.4 ± 17.0 , 48.3 ± 22.3 , and 55.7 ± 23.5 cm²; BF: $24.8 \pm 5.3\%$, $27.2 \pm 5.2\%$, and $28.8 \pm 4.6\%$ in pre-, peri-, and postmenopause, respectively), and less marked among overweight women (VFA: 91.5 ± 36.3 , 106.1 ± 38.2 , and 111.7 ± 28.6 cm²; BF: $36.0 \pm 3.6\%$, $36.4 \pm 3.9\%$, and $37.2 \pm 3.2\%$) and with obesity (VFA: 180.3 ± 62.4 , 212.6 ± 96.2 , and 175.5 ± 54.4 cm²; BF: $44.5 \pm 4.5\%$, $44.5 \pm 5.7\%$, and $41.9 \pm 3.3\%$), suggesting a relative attenuation of muscle loss at higher BMI. **Conclusions:** Postmenopausal women showed a clear shift toward lower lean mass and greater central adiposity across BMI categories. These patterns indicate a consistent deterioration in body composition during the menopausal transition. Assessment of visceral fat in postmenopausal women is crucial, as its accumulation is closely linked to cardiometabolic risk. Menopause-related hormonal changes favor central adiposity, supporting the use of visceral fat as a key indicator for early risk stratification and preventive interventions in midlife women.

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Emotional and cognitive effects of menopause and hormone replacement therapy

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Background: Menopause is a natural physiological process, but its effects on the brain remain poorly understood. In England, approximately 15% of women use hormone-replacement therapy (HRT) to manage menopausal symptoms. However, the psychological benefits of HRT are not well established. This study aims to investigate the impact of menopause and HRT on mental health, cognitive function, and brain structure. **Methods:** We analyzed data from nearly 125,000 participants in the UK Biobank to assess associations between menopause, HRT use, and outcomes related to mental health, cognition, and brain morphology. Specifically, we focused on gray matter volumes in the medial temporal lobe (MTL) and anterior cingulate cortex (ACC). **Results:** Menopause was associated with increased levels of anxiety, depression, and sleep difficulties. Women using HRT reported greater mental health challenges than post-menopausal women not using HRT. Post-hoc analyses revealed that women prescribed HRT had higher levels of pre-existing mental health symptoms. In terms of brain structure, MTL and ACC volumes were smaller in post-menopausal women

compared to pre-menopausal women, with the lowest volumes observed in the HRT group. Conclusions: Our findings suggest that menopause is linked to adverse mental health outcomes and reductions in gray matter volume in key brain regions. The use of HRT does not appear to mitigate these effects and may be associated with more pronounced mental health challenges, potentially due to underlying baseline differences. These results have important implications for understanding the neurobiological effects of HRT and highlighting the unmet need for addressing mental health problems during menopause.