

Selección de Resúmenes de Menopausia

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María Soledad Vallejo. Obstetricia y Ginecología. Hospital Clínico. Universidad de Chile

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Elimination of the Black Box Warning on Menopausal Hormone Therapy

Intira Sriprasert 1, Howard N Hodis, Wendy J Mack, Mary Rosser, Megan L Evans, Xiao Xu, Jason D Wright

In 2003, the U.S. Food and Drug Administration (FDA) issued a black box warning on menopausal hormone therapy (MHT) products based on putative harm of secondary outcomes and incompletely collected and adjudicated data from the Women's Health Initiative (WHI) oral conjugated equine estrogens and medroxyprogesterone acetate study. Despite the specific parameters and limitations of the WHI study, these warnings were inappropriately generalized across all doses, formulations, and routes of administration, including local vaginal therapies, under the mandate to prescribe the "lowest effective dose for the shortest duration." After 22 years of clinical controversy, the U.S. Department of Health and Human Services and the FDA announced removal of the boxed warning on November 10, 2025. This decision was based on the FDA's independent and comprehensive review of the scientific literature, deliberations from an expert panel on July 17, 2025, and a 60-day public comment period. The FDA's transition to product-specific labeling, the removal of the mandate for the lowest effective dose for the shortest duration, and the inclusion of guidance on the optimal timing of MHT initiation within 10 years of menopause or before age 60 years, represent critical steps toward evidence-based menopause management. By replacing misleading information with accurate data, this regulatory shift facilitates individualized benefit-risk assessments and empowers shared decision making. Ultimately, these updates ensure that MHT use is optimized for the specific needs of each patient, integrating modern risk assessment with the latest clinical evidence to improve long-term health outcomes.

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Assessing the Roles of Aging, Estrogen, Nutrition, and Neuroinflammation in Women and Their Involvement in Alzheimer's Disease-A Narrative Overview

Edwin D Lephart 1, K Scott Weber 2, Dawson W Hedges 3

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The purpose of this narrative review is to examine women's cognitive health and to highlight its association with four major pillars: (1) aging, (2) estrogen decline and loss, (3) diet, and (4) neuroinflammation, and their contribution to cognitive decline, with a focus on this combination to increase awareness and address the progression and potential amelioration of Alzheimer's disease (AD). Often overlooked, estrogen decline during perimenopause and loss of estrogen production from the ovaries after menopause negatively influences almost every tissue and organ in the body, including the brain. This estrogen loss leads to inflammation, as can poor nutritional choices, both of which have a profound impact on short- and long-term health and can increase the risk of dementia, including AD. Thus, this overview covers the following four pillars (1) a brief background on cognitive decline and AD with aging, (2) the importance of and changes in estrogen with aging, (3) influence of dietary choices on overall well-being and brain health, and (4) the biochemical and molecular mechanisms by which this combination of factors may lead to neuroinflammation, resulting in cognitive decline and AD. Finally, this review briefly presents a hypothesis on whether women during perimenopause should be administered estrogen to span the transition into menopause to protect against cognitive decline and possibly ameliorate the risk of AD. This article is based on previously conducted studies and does not contain new data/results (studies) of human participants or animals performed by the authors.

medRxiv [Preprint]. 2026 Feb 5:2026.02.04.26345605. doi: 10.64898/2026.02.04.26345605.

Reproductive lifespan and hormonal therapy in relation to later-life neurovascular health: A population-based study of women in the Gothenburg H70-1944 Birth Cohort

Giulia Lorenzon, Gemma García-Lluch, Gillian Coughlan, Shireen Sindi, Silvia Maioli, Konstantinos Poulakis, et al.

Background: Women face greater vulnerability to dementia and Alzheimer's disease (AD), potentially due to estrogen fluctuations across the lifespan. However, its role in vascular brain health is unclear. We investigated associations between lifelong estrogen exposure-endogenous (reproductive span) and exogenous (oral contraceptives [OC], menopausal hormone therapy [MHT])-and late-life vascular brain injury, AD-related atrophy, and APOE -ε4 modification. **Methods and findings:** We included 352 cognitively unimpaired 70-years-old women from the Gothenburg H70-1944 Birth Cohort with brain MRI and 5-year follow-up. Reproductive lifespan was calculated as age at menopause or oophorectomy minus age at menarche. OC and MHT use were self-reported. Outcomes included cerebral small vessel disease (SVD), AD-related cortical thickness, and white-matter integrity (fractional anisotropy). Linear and multinomial regression and mixed-effects models were adjusted for confounders and stratified by APOE -ε4. Longer reproductive span (OR=0.90 [95%CI 0.83-0.98]) and MHT use (OR=0.43 [95% CI 0.20-0.92]) were linked to lower SVD burden, particularly fewer perivascular spaces and microbleeds. OC and MHT were associated with greater white matter integrity, with additive use throughout life showing the highest fractional anisotropy (OR=0.45 [95% CI 0.12-0.78]). MHT use was associated with greater thickness in areas often affected in AD among APOE -ε4 carriers (β =0.38 [95% CI 0.01-0.76]) but not in non-carriers. Longer estrogen exposure was linked to stable cortical thickness and WMH trajectories over time. **Conclusions:** Extended estrogen exposure throughout life-both endogenous and exogenous-appear to support late-life cerebrovascular health in women, with potential genotype-specific neuroprotective effects. Given the current absence of sex-specific prevention guidelines for cognitive disorders, future research should clarify estrogen's long-term impact on brain health and cognition to inform personalized medicine.

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Efficacy of nonablative radiofrequency on sexual function in postmenopausal women: a randomized clinical trial

Claudia Quezada-Bascuñán, Asunción Ferri-Morales, Vicente Martínez-Vizcaíno, Cristina Gallego-Gómez, et al.

3Objective: To evaluate the efficacy of nonablative capacitive-resistive monopolar radiofrequency on sexual function and vaginal health in postmenopausal women with genitourinary syndrome of menopause. **Methods:** This was a single-blind, randomized, controlled clinical trial. The participants were randomly assigned to receive six weekly sessions of capacitive-resistive monopolar radiofrequency (n=32) or sham treatment (n=30). Sexual function was assessed using the Female Sexual Function Index (FSFI) and vaginal health was assessed using the Vaginal Health Index (VHI). The estrogenic status was determined by vaginal cytology, which involves calculating the proportions of basal, intermediate, and superficial cells. Assessments were conducted at baseline, post-treatment, and 12-week follow-up. **Results:** Compared with the control group, the intervention group showed significantly greater improvements in the Female Sexual Function Index and Vaginal Health Index at post-treatment and at the 12-week follow-up. FSFI mean changes were 5.86 versus 1.33 at posttreatment ($P<0.001$) and 4.41 versus -0.41 at 12-week follow-up ($P=0.011$). VHI mean changes were 4.75 versus -0.03 at post-treatment ($P<0.001$) and 6.90 versus -0.66 at follow-up ($P<0.001$). The effect sizes were moderate to large for the FSFI (Cohen's $d >0.77$, 95% CI, 0.25-1.29) and large for the VHI ($d >3.49$, 95% CI, 2.68-4.28). No significant changes were observed in estrogenic status, and no adverse events were reported. **Conclusion:** Capacitive-resistive monopolar radiofrequency significantly improved sexual function and vaginal health in women with genitourinary syndrome of menopause, thereby supporting its use as a safe, nonhormone treatment option.

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Effectiveness of Medical Management in Heavy Menstrual Bleeding: A Prospective Cohort Study

Vasudha Vani Lanka 1, Medha Davile 2, Avantika Gupta 3, Deepika Yadav 2, Shuchita Mundle 2

Introduction: Heavy menstrual bleeding (HMB) is a prevalent gynecological condition among women in the reproductive and perimenopausal age groups, significantly impairing quality of life. While several medical treatment options are available, their comparative effectiveness and patient adherence vary. This study aimed to evaluate the effectiveness of medical management in HMB. **Methods:** This prospective cohort study was carried out at a tertiary care institute in Central India from February 2023 to July 2024. The study included 240 women between 13 and 50 years of age presenting with HMB who opted for medical management. HMB was defined by a Pictorial Blood Loss Assessment Chart (PBAC) score of > 100 . Women with HMB secondary to pregnancy complications, women needing surgical management, and women with postmenopausal bleeding were excluded from the study. Medical management was

selected based on patient preference and clinical suitability. Outcome parameters like change in PBAC score and hemoglobin level were noted at baseline and reassessed at three and six months. Results: The mean age of participants was 41.03 ± 7.23 years. Baseline median PBAC scores (IQR) were: levonorgestrel intrauterine system (LNG-IUS) 475 (360-690), tranexamic acid 400 (255-600), norethisterone 645 (350-775), injectable depot medroxyprogesterone acetate (inj DMPA) 690 (355-956), and combined oral contraceptive pills (COCP) 380 (259-580). All five groups showed a significant reduction in PBAC scores at three and six months ($p < 0.001$). The greatest reduction at three months was seen with inj DMPA (78%), while LNG-IUS showed the highest reduction at six months (93%). A statistically significant improvement in hemoglobin levels was also observed over six months in all groups. Conclusion: Medical management of HMB was effective in reducing menstrual blood loss and improving hemoglobin levels. LNG-IUS offered the most significant benefit with high compliance, but treatment choice should be individualized based on patient needs and clinical profile.

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Association between physical activity and mortality in postmenopausal women: evidence from NHANES 2007-2018

Baixiang Zhang 1, Mu Yang 2 3, Gareth Ambler 4, Shuangfang Fang, Qilin Yuan 2 3, Yixian Zhang 5, Nan Liu, et al. Background: Whether physical activity (PA) levels relate to mortality in postmenopausal women remains not well understood. Methods: We analyzed 5,880 postmenopausal women from NHANES 2007-2018 (median follow-up: 77 months). PA-including total PA (TPA), leisure-time PA (LTPA), and occupational PA (OPA)-was assessed using the Global Physical Activity Questionnaire and expressed as metabolic equivalent of task (MET)-minutes/week. TPA was classified as no, insufficiently active (< 600), or sufficiently active (≥ 600), while LTPA and OPA were classified as no, low (< 600), or high (≥ 600). Weighted proportional hazards Cox models and restricted cubic spline (RCS) analyses examined associations with all-cause, cardiovascular disease (CVD), and non-CVD mortality. Results: During follow-up, 718 deaths occurred (215 CVD, 503 non-CVD). Compared with no PA, insufficiently and sufficiently active TPA were associated with reduced risks of all-cause, CVD, and non-CVD mortality; both low and high LTPA with reduced risks of all-cause and non-CVD mortality; and low OPA with reduced risks of all-cause and non-CVD mortality. RCS analyses showed linear inverse associations for TPA and non-linear inverse associations for LTPA with all-cause and non-CVD mortality, while OPA showed no significant associations. Tests for trend were significant for TPA in relation to all-cause and non-CVD mortality, and for LTPA across all three outcomes. Sensitivity analyses excluding early deaths yielded similar results. Conclusions: Higher TPA and LTPA were associated with reduced risks of all-cause and non-CVD mortality among postmenopausal women. Promoting adequate PA, particularly moving from inactivity to modest levels, may be an effective strategy to support healthy aging in this population.