

Selección de Resúmenes de Menopausia

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REDLINC: two decades of collaborative insights into menopause and women's health in Latin America

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The Collaborative Group for Research of the Climacteric in Latin America (REDLINC) was established 20 years ago and comprises physicians who specialize in menopause medicine to acquire local information and understand the health needs of our population. Since then, 12 collaborative multinational studies have been conducted. Some of our most relevant results are the average age of menopause in Latin America (48.6 years), and the significant impact on quality of life, metabolic syndrome, sleep issues, sexual dysfunction, anxiety, depression, muscle pain, low muscle mass and mild cognitive decline. Also, we report variations in menopausal hormone therapy (MHT) prescriptions, noting that the tendency to prescribe is stronger among physicians themselves than toward patients. Finally, several factors contribute to the prevention, alleviation and treatment of menopausal changes in women, such as obesity control, exercise, higher education, utilization of MHT and seeking help from menopause practitioners. This article highlights the gathered information on Latin American women, which has been implemented for patients' better understanding. Physicians' awareness has grown, protocols have been adapted to accommodate our healthcare realities and patients are seeking menopause healthcare practitioners. International collaboration is key to the success of this project.

Endocr Rev. 2025 Jun 16:bnaf018. doi: 10.1210/endrev/bnaf018. Online ahead of print.

The impact of estrogen deficiency on liver metabolism; implications for hormone replacement therapy

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Metabolic dysfunction-associated steatotic liver disease (MASLD, previously NAFLD) is the most common chronic liver condition globally. It affects 1-in-3 individuals and is associated with increased liver and cardiovascular mortality. MASLD is a sexually dimorphic condition and in women the prevalence and severity of MASLD rises significantly following menopause. Preclinical data shows that lack of estrogen promotes multisystem metabolic dysfunction that is characteristic of MASLD. This not only includes hepatic lipid accumulation, insulin resistance and fibrosis, but also extra-hepatic metabolic processes in adipose and skeletal muscle. There are currently no available MASLD treatments tailored to women. The uptake of estrogen-based menopausal hormone replacement therapy (HRT) has seen a dramatic increase in recent years. Despite the changing attitudes to HRT and the strong evidence base implicating estrogen deficiency in the development of MASLD, the impact of HRT on MASLD in postmenopausal women is poorly studied. In this review, we discuss the burden of MASLD in women, the effect of estrogen deficiency on the processes that drive MASLD development and progression, and explore potential sex-specific therapeutic strategies that may prevent or limit MASLD development after menopause.

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Transdermal oestradiol and testosterone therapy for menopausal depression and mood symptoms: retrospective cohort study

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Background: Psychological symptoms in perimenopause and early menopause are common. The impact of menopausal hormone therapy (MHT) on menopausal mood symptoms is unclear. Aims: To assess the impact of 17 β -oestradiol $\pm$ micronised progesterone or the levonorgestrel-releasing intrauterine device, and/or transdermal testosterone, on depressive and anxiety symptoms in peri- and postmenopausal women. Method: A real-world retrospective cohort study set in the largest specialist menopause clinic in the UK. The Meno-D questionnaire measured mood-related symptoms. Results: The study included 920 women: 448 (48.7%) perimenopausal, and 435 (47.3%) postmenopausal.

Following initiation/optimisation of MHT, mean Meno-D scores decreased by 44.59% (95% CI -46.83% to -42.34%, $P < 0.001$) after average 107 days follow-up. Mood symptoms significantly improved ($P < 0.01$ per symptom). Improvement occurred in peri- and postmenopausal women. All MHT regimens improved mental health including both progestogen types (body-identical progesterone and levonorgestrel-releasing intrauterine device), MHT initiation strategy (oestradiol $\pm$ a progestogen versus oestradiol $\pm$ a progestogen and testosterone, 45.38 v. 48.53%, respectively, $P = 0.47$) and MHT optimisation strategy (MHT users treated with a higher oestradiol dose versus testosterone added versus both a higher oestradiol dose and testosterone, 34.70, 43.93 and 43.25%, respectively, $P = 0.38$). Conclusions: Use of menopausal hormone therapy was associated with significant improvement in mood in peri- and postmenopausal women. Prospective studies and randomised clinical trials are needed to assess the effects of different regimens in different patient populations over longer time periods.

Gynecol Oncol. 2025 Jun 10;198:130-136. doi: 10.1016/j.ygyno.2025.05.008. Online ahead of print.

Use of statins and risk of ovarian cancer: evidence on effect modification by parity, menopause and endometriosis from nationwide nested case-control studies

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Objective: Previous results on the association between statin use and risk of ovarian cancer (OC) are inconsistent, warranting further investigation. This study aims to examine the association between statin use and risk of OC in a large study population. **Methods:** Based on two nationwide nested case-control studies utilizing data from Danish and Swedish high-quality registries, we identified 11,874 OC cases who were individually matched on age to 474,960 controls using risk-set sampling. Conditional logistic regression was performed separately on the country-specific data to calculate odds ratios (ORs) and corresponding 95 % confidence intervals (CIs) for the association between statin use and risk of OC. Country-specific estimates were combined based on a fixed-effect assumption. Furthermore, we examined potential effect modifications by a priori selected OC risk factors on the association between statin use and OC risk. **Results:** We found no overall association between statin use and risk of OC (OR = 0.96; 95 % CI: 0.91-1.01); neither with duration nor intensity of use. However, statin use was associated with a decreased risk of OC in subsets of women with endometriosis (OR = 0.70; 95 % CI: 0.53-0.91), and nulliparous women (OR = 0.86; 95 % CI: 0.79-0.93). **Conclusion:** We found an effect modification of some known ovarian cancer risk factors on the association between statin use and risk of OC. In women with endometriosis, and in nulliparous women, respectively, statin use was associated with a decreased risk of OC, suggesting statins may have potential as a preventive measure.

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Association of cardiovascular health with reproductive lifespan and pregnancy loss: insights from NHANES 2005-2018

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Background: Altered reproductive timing of females has close relations to long-term health. Since the cardiovascular system delivers oxygen, nutrients, and hormones throughout the body, cardiovascular health (CVH) may significantly impact hormonally controlled events such as pregnancy, menarche, and menopause. This study sought to determine whether CVH is associated with reproductive lifespan and pregnancy loss, and the mediating role of inflammation. **Methods:** Female participants (3964) from the National Health and Nutrition Examination Survey (NHANES) 2005-2018 were employed in this cross-sectional investigation. The Life's Essential 8 (LE8) score was categorized into low (<50), moderate (50-79), and high (≥ 80) CVH. The years between menarche and menopause age was computed as the reproductive lifespan. Pregnancy loss was determined by the discrepancy between the total number of pregnancies and the number of live births. We conducted multivariable linear regression models and zero-inflated negative binomial regression models to investigate the prospective association of CVH with reproductive lifespan and pregnancy loss while accounting for various potential confounders. Mediation analysis was applied to explore the function of inflammation. **Results:** After multivariate adjustment, higher CVH levels were notably associated with lower reproductive lifespan ($\beta = -0.32$, 95% CI: -0.47, -0.17, $P < 0.001$) and lower number of pregnancy losses ($\beta = -0.04$, 95% CI: -0.07, -0.01, $P = 0.012$). Specifically, increased CVH levels were associated with increased age at menarche ($\beta = 0.14$, 95% CI: 0.10, 0.18, $P < 0.001$) and decreased age at menopause ($\beta = -0.18$, 95% CI: -0.33, -0.04, $P = 0.014$). Furthermore, a linear correlation was observed between CVH and reproductive lifespan ($P < 0.001$), while the number of pregnancy losses decreased as CVH levels increase within a certain range and approximately presented an L-shaped relationship.

($P=0.009$). Subgroup analyses proved a stronger inverse association between CVH and reproductive lifespan among never-married women (P for interaction <0.001), whereas no significant interaction existed between CVH and pregnancy loss. Inflammation biomarker alkaline phosphatase (ALP) mediated 9.4% of the association between CVH and reproductive lifespan ($P=0.048$). Conclusions: Higher CVH levels were associated with shorter reproductive lifespan and lower prevalence of pregnancy loss at population level, and inflammation may mediate the association of CVH with reproductive lifespan. Comprehensive management of CVH in women may be vital to safeguard their reproductive health.

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Sex differences in features of atherosclerotic plaques as revealed by various imaging techniques: historical review

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Numerous studies over several decades found that there are significant sex differences in the development and severity of atherosclerosis, which include plaque burden, composition and vulnerability to rupture. This review provides historical analysis of these studies starting with early histological analysis of post mortem samples to modern high-resolution imaging techniques. It is discussed that the abundance of evidence obtained by an array of approaches demonstrates that men are more prone to develop atherosclerosis, which manifests itself in earlier initiation of the plaques, while the occurrence of plaque is accelerated following menopause. These findings unequivocally show that men are more likely to develop plaques with larger lipid-rich necrotic cores, thinner fibrous caps, and stronger inflammatory responses, resulting in increased vulnerability at a younger age. However, the rapid escalation of plaque instability in postmenopausal women, which is caused by a significant reduction in smooth muscle cell density and changes in calcification patterns, results in comparable atherosclerotic burden in men and women in older adults. These findings highlight how differences in sex and age, influence the development and severity of atherosclerosis. Understanding these differences is essential for creating better ways to assess and treat heart disease in men and women.

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Menopause and Body Composition: A Complex Field

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Given that menopause affects about half of the world's midlife population, it is crucial to understand its impact beyond traditional menopausal symptomology. For instance, many women, while transitioning through menopause, experience profound changes in body composition. These changes may contribute to postmenopausal reductions in metabolic health. This narrative review explores the influence of menopause on skeletal muscle and adipose tissue, highlighting the decline in muscle mass and strength and the gain and redistribution of adipose tissue, particularly the increase in visceral adiposity. Although menopausal changes in body composition are seemingly extensively studied, the longitudinal studies are not that common, and the precise mechanisms driving body composition changes remain unclear, with uncertainties surrounding the roles of hormonal shifts compared with regular aging, energy balance, and lifestyle factors. Notably, it remains debated whether menopause or estrogen meaningfully influences resting energy expenditure. The review also considers the potential mitigating effects of menopausal hormone therapy and regular exercise. Understanding these changes is essential for developing effective strategies to support women's health during and after menopause.

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Association between premature ovarian insufficiency and biological aging

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Objective: This study aimed to analyze whether premature ovarian insufficiency (POI) is associated with accelerated biological aging, whether the degree of biological aging is exacerbated by an earlier age at menopause, and whether menopausal hormone therapy (MHT) in the POI population is associated with reduced biological aging. Design: This is a cross-sectional study. A total of 229 779 participants aged 40 years and older in the UK Biobank (2006-2010) and NHANES (1999-2018) were included in the study. Methods: Menopause information was collected through questionnaires. Biological age acceleration was defined by the Klemera-Doubal method, which is calculated through

biomarkers, in reference to chronological age. Biological age acceleration > 0 was defined as biological aging. Association between POI and biological aging analyzed using multivariate linear regression and logistic regression models. Results: The results showed that participants with POI had an increased risk of biological aging (UK Biobank: OR = 1.50 [95% CI: 1.24-1.82]; NHANES: OR = 1.20 [95% CI: 1.07-1.34]) and decrease in leukocyte telomere length compared with those without POI (UK Biobank: 0.0109 [95% CI: 0.0079-0.0109]). Participants with POI who underwent MHT had reduced risk of aging compared with those who did not (UK Biobank: OR = 0.63 [95% CI: 0.43-0.92]; NHANES: OR = 0.75 [95% CI: 0.61-0.92]). Conclusion: This study showed that participants with POI had a significantly increased risk of biological aging compared with those without POI. Participants with POI who received MHT had a reduced risk of aging compared with those who did not.

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Safety of menopause hormone therapy in postmenopausal women at higher risk of venous thromboembolism: a systematic review

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Objective: Studies have shown that oral estrogen with or without progestogen increases the risk of venous thromboembolism (VTE). Recent data suggest that transdermal estrogen confers little to no increased risk of VTE. There is no systematic review that examines menopause hormone therapy (MHT) use in women with risk factors for VTE. This systematic review therefore aims to summarize the evidence in this population. Method: The OVID Medline, Embase, PubMed and CENTRAL online databases were searched. A total of 762 studies were screened and 10 were included in the study. Results: Six studies were case-control studies, two were randomized controlled trials (RCTs), one was an RCT that contained a nested case-control study and one was a cohort study. Studies were heterogeneous in their definition of menopause, dose, form and route of administration of MHT, and the underlying VTE risk factor being assessed. In women with risk factors for VTE, transdermal estrogen conferred no increased risk of VTE. Oral estrogen alone has the next safest profile, and oral estrogen plus a progestogen conferred the highest increased risk of VTE. Conclusion: Transdermal MHT appears safe in women with risk factors for VTE. Oral MHT, notably oral estrogen plus a synthetic progestogen, does increase relative risk. More contemporary data are required to confirm these findings.