

### Selección de Resúmenes de Menopausia

Semana del 6 a 12 de agosto, 2025 María Soledad Vallejo. Obstetricia Ginecología. Hospital Clínico. Universidad de Chile

# J Epidemiol Community Health. 2025 Aug 10:jech-2025-223994. doi: 10.1136/jech-2025-223994. Online ahead Reproductive history, menopause and cardiometabolic health in women: a multicountry analysis

Wilhemina Quarpong 1, Suchitra Chandrasekaran 2 3, K M Venkat Narayan 4 3 5, Usha Ramakrishnan 4 5, et al. Background: We investigated the association of reproductive history with cardiometabolic health in ethnically diverse women across five continents. M ethods: We pooled cross-sectional survey data on non-pregnant women aged 30-49 years from 15 countries. Multilevel models were used to examine associations between menopausal status, age at first birth (≥20 vs <20 years), parity (1, 2, 3, 4+ vs 0 births) and cardiometabolic indicators: body mass index (BMI), systolic blood pressure (SBP) and fasting blood glucose (FBG), adjusting for age and socioeconomic status, Results: We included 413 802 women (median age 38 years; 14% postmenopausal). Being in a postmenopausal state was associated with lower BMI (-0.22, 95% CI -0.27 to -0.17 kg/m2) and higher SBP (0.35, 95% CI 0.18, 0.52 mm Hg). In parous premenopausal women (n=332 569), later age at first birth was associated with lower BMI (-0.33, 95% CI -0.36 to -0.30 kg/m<sup>2</sup>) and lower SBP (-0.59, 95% CI -0.69 to -0.48 mm Hg); higher parity was associated with higher BMI (0.11-0.14 kg/m<sup>2</sup> for 1-3 births) and lower SBP (-0.77 to -2.04 mm Hg for 1-4+ births). Among parous postmenopausal women (n=55 788), later age at first birth was associated with lower BMI (-0.15, 95% CI -0.23 to -0.07 kg/m<sup>2</sup>), lower SBP (-0.38, 95% CI -0.67 to -0.08 mm Hg) and higher FBG (2.08, 95% CI 0.08 to 4.11 mg/dL); higher parity was associated with lower SBP (-1.60 to -3.06 mm Hg for 1-4+ births). Conclusions: Irrespective of menopausal status, later age at first birth was associated with lower BMI and SBP, while higher parity was associated with lower SBP. Reproductive history has implications for cardiometabolic risk in women across diverse settings.

# Maturitas. 2025 Aug 6:201:108688. doi: 10.1016/j.maturitas.2025.108688. Online ahead of print. The impact of exercise on cardiovascular parameters in postmenopausal women: A narrative review

Vitor E Valenti 1, Bruno M Candeloro 2, Rodrigo D Raimundo 3, Luana A Gonzaga 4, Luiz O C Jaloto 5, et al. Introduction: Several studies indicate that regular physical activity can reduce systolic and diastolic blood pressure, improve endothelial function, and enhance overall cardiovascular fitness in postmenopausal women. To gain a deeper understanding, we conducted a narrative review of systematic reviews to assess the impact of exercise on cardiovascular parameters in postmenopausal women. Method: The literature search was conducted using the Excerpta Medica, Medical Literature Analysis and Retrieval System Online, Scopus, and Web of Science databases. We included systematic reviews investigating the effects of exercise on cardiovascular parameters in postmenopausal women, with publications considered up until December 2024. Results: Following the exclusion of 187 publications, three systematic reviews were selected. These reported significant exercise-induced improvements in vasomotor symptoms, systolic blood pressure, diastolic blood pressure and heart rate. Conclusion: This narrative review revealed that exercise benefits cardiovascular health in postmenopausal women. Still, methodological limitations emphasize the need for better systematic reviews. Clinicians ought to interpret findings carefully when recommending physical exercise.

Maturitas. 2025 Jul 1:200:108646. doi: 10.1016/j.maturitas.2025.108646. Online ahead of print. Are health-related, lifestyle, work-related, and socio-demographic factors associated with work productivity among menopausal women? A systematic review

Michelle G A Clevis 1, Karen Nieuwenhuijsen 2, Irene G M van Valkengoed 3, Teddy Oosterhuis 4; et al.

An increasing number of women of menopausal age, many of whom experience menopausal symptoms, are participating in the workforce. Understanding the factors that influence work productivity in this life stage can inform the development of targeted interventions. This systematic review explores which health-related, lifestyle, workrelated, and socio-demographic factors are associated with work productivity among menopausal women. A systematic search was conducted for observational studies in PubMed, PsycINFO, and Embase up to July 2024. The risk of bias was assessed using an adapted Newcastle-Ottawa scale. The GRADE framework for prognostic research was applied to evaluate the quality of evidence. A total of 29 studies were included. Menopausal symptoms in general, as well as psychological and vasomotor symptoms, and lower sleep quality were associated with lower at-work productivity, with moderate to high quality of evidence. Additionally, there was moderate quality of evidence that better (perceived) health was associated with higher at-work productivity. Regarding absenteeism, moderate evidence was found for an association with vasomotor symptoms. Inconclusive evidence was found for socio-demographic, work-related factors and remaining health-related and lifestyle factors in relation to both at-work productivity and absenteeism. This review highlights the association of menopausal symptoms and poor sleep quality with decreased work productivity in menopausal women. The evidence for other associations was limited due to the low quality of available evidence or a lack of studies. Further research on modifiable lifestyle and work-related factors is needed to improve the work functioning of women during menopause.

# Curr Probl Cancer. 2025 Aug 7:58:101239. doi: 10.1016/j.currproblcancer.2025.101239. Online ahead of print. Hormone replacement therapy in endometrial cancer survivors: A retrospective cohort study on recurrence, survival, and quality of life

Jiali Xing 1, Qi Liu 2, Li Qiao 1

Background: Endometrial cancer is the most common gynecologic malignancy in developed countries, often affecting postmenopausal women but also seen in younger patients. Standard treatment includes hysterectomy with bilateral salpingo-oophorectomy, which may lead to menopausal symptoms, especially in premenopausal women. The use of hormone replacement therapy (HRT) in survivors remains controversial due to concerns about stimulating cancer cells. This study aims to evaluate the impact of postoperative HRT on cancer recurrence, survival outcomes, and quality of life in endometrial cancer survivors. Methods: This retrospective cohort study analyzed 176 women -between August 2024 and May 2025- with histologically confirmed endometrial adenocarcinoma. Participants were categorized into HRT users (n = 91) and non-users (n = 85) with a median age of 58 and 62 years respectively. Demographic, clinical, and treatment data were compared. Survival analyses were conducted using Kaplan-Meier and Cox regression models. Quality of life was assessed using the MENQOL questionnaire. Results: HRT use was associated with lower recurrence (HR=0.379, p = 0.002) and death hazard (HR=0.248, p = 0.039) rates. Mean recurrence-free survival was longer in the HRT group (53.14 vs 46.28 months, p < 0.001). Improvement in menopausal symptom scores was significantly higher in HRT users (MD= -2.03) compared to the control group (MD= -0.89). No significant increase in adverse cardiovascular or thromboembolic events was observed. Conclusion: Postoperative HRT appears safe and beneficial for selected endometrial cancer survivors, offering improved recurrence-free survival and better menopausal symptom control without increasing serious adverse events. Individualized assessment remains crucial, and further prospective trials are needed to confirm these findings.

## Prz Menopauzalny. 2025 Jun;24(2):131-136. doi: 10.5114/pm.2025.152241. Epub 2025 Jun 23. Position paper of the expert panel of the Polish Society of Menopause and Andropause on the use of Oestrogel® in menopausal hormone therapy

Małgorzata Bińkowska 1, Tomasz Paszkowski 2, Violetta Skrzypulec-Plinta 3, Wojciech Zgliczyński 4
This position paper of the expert panel presents a comprehensive review of the efficacy, safety, and clinical application of bioidentical hormone replacement therapy (HRT), with particular focus on transdermal 17β-oestradiol gel (Oestrogel®). Bioidentical hormones - chemically identical to endogenous human hormones - are increasingly recognised as the preferred option in modern HRT, consistent with current international guidelines. Based on a review of randomised clinical trials and observational studies (sourced primarily from PubMed and Medline), transdermal oestradiol demonstrates a superior safety profile compared to oral formulations. Benefits include stable serum oestradiol levels without supraphysiological fluctuations; minimal impact on hepatic synthesis of procoagulant factors, triglycerides, hormone-binding proteins (SHBG, TBG, CBG), and inflammatory mediators (e.g. C-reactive protein); no increased risk of venous thromboembolism or ischaemic stroke; and the ability to use lower doses while maintaining

efficacy. Additional advantages are a more physiological E2/E1 ratio, reduced inter-individual variability, and the option to monitor serum oestradiol levels. Oestrogel® supports dose flexibility and personalisation, allowing treatment to be tailored according to patient needs and guideline-based therapeutic schemes. When combined with micronised progesterone - the gold-standard progestogen for endometrial protection and the preferred option due to its favourable overall safety profile - this form of HRT offers a modern, well-tolerated, and individualised approach to the management of menopausal symptoms and osteoporosis prevention.

### Climacteric. 2025 Aug 7:1-11. doi: 10.1080/13697137.2025.2509850. Online ahead of print.

Major adverse cardiovascular events risk in menopausal women treated with oral estradiol/micronized progesterone versus conjugated estrogens/medroxy-progesterone: a claims data analysis in the USA

John C Stevenson 1, Rodney Baber 2, Risa Kagan 3 4, Rossella E Nappi 5 6, Santiago Palacios 7, Nick Panay, et al. 80bjective: Using real-world data, the current study compared the risk of major adverse cardiovascular events (MACE) between two regulated combined oral hormonal products that are currently available to women in the USA: body-identical oral 17β-estradiol/micronized progesterone (E2/P4) and conjugated equine estrogens/medroxyprogesterone acetate (CEE/MPA). Methods: Women aged ≥40 years treated with E2/P4 or CEE/MPA were selected from a US claims database (April 2019-June 2021). The E2/P4 or CEE/MPA cohorts were defined based on the first dispensation of E2/P4 or CEE/MPA (index) as prescribed in the real world. Women with pre-index MACE hospitalization were excluded. Confounding was controlled via inverse probability of treatment (IPT) weighting. MACE risk was compared between the IPT-weighted cohorts using Cox and Poisson/negative binomial regression models. Results: The E2/P4 and CEE/MPA cohorts included 6520 and 29,426 women respectively (mean follow-up 1.2 and 1.4 years). In the IPT-weighted analyses, MACE rates were 23.5 versus 85.4 per 10,000 women-years among women treated with E2/P4 and CEE/MPA (IPT-weighted incidence rate ratio [IRR] 0.28, 95% confidence interval [CI] 0.17 - 0.45; IPT-weighted hazard ratio [HR] 0.37, 95% CI 0.27 - 0.50). Conclusions: Real-world evidence suggests that the MACE risk is significantly lower among women treated with E2/P4 compared to CEE/MPA.

# Front Endocrinol (Lausanne). 2025 Jul 23:16:1628612. doi: 10.3389/fendo.2025.1628612. eCollection 2025. Association between menopause-related symptoms and muscle mass index among perimenopausal and postmenopausal women and the mediating role of estrogen levels

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Background: The decline in muscle mass is a common concern among perimenopausal women. However, the association between menopause-related symptoms and muscle mass remains inconclusive, and the mechanistic role of estrogen is still unclear. Methods: The study included 407 peri- and postmenopausal women aged 40-60 years who visited the International Peace Maternity and Child Health Hospital. Menopausal symptoms were assessed using the modified Kupperman Index (KMI). Muscle mass was evaluated using the InBody 270 analyzer, and sex hormone levels were determined by chemiluminescent immunoassay. Multiple linear regression and Mediation analysis were conducted to examine the association of KMI with MMI and the mediation of estrogen. Results: A total of 407 valid cases were collected. The mean age of the patients was  $49.96 \pm 3.25$  years, with an average body weight of  $58.02 \pm$ 7.36 kg and an average BMI of  $22.50 \pm 2.61$  kg/m<sup>2</sup>. The findings showed that advanced age, lower education level, and reduced muscle mass index (MMI) were linked to elevated KMI scores (p<0.05). Patients with hypertension had higher KMI scores (p<0.05). Additionally, decreased estradiol (E2) levels correlated with heightened menopausal symptoms (p<0.05). After controlling for confounding factors such as age, educational level, menopausal stage, history of hypertension, follicle-stimulating hormone (FSH), and E2, KMI was negatively correlated with MMI ( $\beta$ =-1.612, 95% CI: -2.677 to -0.546, p=0.003). Specifically, for each unit increase in MMI, KMI decreased by 1.612 points (R<sup>2</sup>=0.186, p=0.003). Stratified analysis showed that the negative correlation between KMI and MMI was significant only in premenopausal women. Both the direct and indirect effects of MMI and E2 on KMI were statistically significant (p<0.01). The mediating effect of MMI on KMI through E2 accounted for 26.9% (p=0.001). Conclusions: Lower muscle mass is associated with severe menopausal symptoms, partially mediated by estrogen. Maintaining muscle mass may alleviate symptoms, highlighting the importance of resistance training and hormone regulation in perimenopausal women. However, due to the cross-sectional nature of the study, causality cannot be inferred.

Longitudinal or interventional studies are warranted to further validate these associations and explore underlying mechanisms.

#### BMC Med. 2025 Aug 6;23(1):461. doi: 10.1186/s12916-025-04223-7.

## Menopausal status, transition, and age at menopause with accelerated biological aging across multiple organ systems: findings from two cohort studies

Yi Xiang # 1, Qiong Meng # 2, Zitong Huang 1, Ning Zhang 1, Yuan Zhang 1, Xianbin Ding 3, et al. Background: Biological aging is a heterogeneous process that varies across organs and systems. The dynamic hormonal changes during the menopausal transition may have profound and organ-specific impacts on biological aging. However, the relationship between the menopausal transition and both comprehensive and organ-specific biological aging remains poorly understood. This study aimed to investigate the associations between menopausal factors and both comprehensive and organ-specific biological aging, as well as the modifying role of reproductive history. Methods: This study included 37,244 women from the China Multi-Ethnic Cohort (CMEC) and 140,479 from the UK Biobank (UKB). Menopausal factors included menopausal status, menopausal transition, and age at menopause. Comprehensive and organ-specific biological ages (BAs) were calculated using the Klemera-Doubal method and clinical biomarkers and have been shown to predict age-related health outcomes. Multiple linear regression and change-to-change models were applied, with stratified analyses based on reproductive history. Results: Compared with pre-menopausal women, those who were peri- or post-menopausal or had undergone hysterectomy or oophorectomy exhibited greater acceleration in comprehensive, liver, metabolic, and kidney BA. In longitudinal change-to-change models, women undergoing menopausal transition showed greater increases in comprehensive BA (CMEC:  $\beta = 1.33$ , 95% CI = 0.89, 1.76; UKB:  $\beta$  = 2.60, 95% CI = 1.91, 3.30), as well as liver, metabolic, and kidney BAs compared to those remaining pre-menopausal. Earlier age at menopause was associated with accelerated comprehensive BA in UKB (< 40 years:  $\beta = 0.69$ , 95% CI = 0.39, 0.98; 40-44 years:  $\beta = 0.24$ , 95% CI = 0.09, 0.40). Across organ-specific BAs, liver BA showed the strongest associations with menopausal factors. Reproductive history like age at live birth and number of live births emerged as potential modifiers of these associations. Conclusions: Menopause, particularly the menopausal transition, was associated with accelerated comprehensive and organ-specific biological aging, with liver aging being most affected. These findings underscore the menopausal transition as a critical window for interventions to enhance women's health and longevity.

### Menopause. 2025 Aug 5. doi: 10.1097/GME.00000000002620. Online ahead of print.

### Unraveling the association between obesity and climacteric symptoms: a generalized structural equation modeling approach

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Objective: To assess the direct and indirect associations between obesity and the severity of menopausal symptoms in postmenopausal women, considering related conditions such as chronic diseases and physical activity. Methods: This observational subanalysis utilized data from the REDLINC XII multinational study, which included 722 postmenopausal women aged 70 or younger from 9 Latin American countries. Menopausal symptoms were measured using the Menopause Rating Scale (MRS). Clinical, behavioral, and sociodemographic data were obtained through physician-administered surveys. Generalized Structural Equation Modeling was employed to examine the direct and indirect relationships between obesity, chronic cardiovascular and respiratory diseases, chronic hypertension, diabetes mellitus, and physical activity, and MRS scores. Odds ratios (ORs) were calculated to enhance interpretability. Results: A total of 722 participants were included. Obesity was directly associated with higher MRS scores (OR = 1.75). In addition, obesity exhibited indirect associations with MRS scores, with an odds ratio of 19.07, through chronic arterial hypertension, diabetes mellitus, physical inactivity, and chronic cardiovascular or respiratory diseases. The total association between obesity and MRS scores was reflected in an OR of 33.45. Furthermore, physical inactivity and the use of antidepressants were associated with greater symptom severity, whereas higher educational attainment, regular physical activity, and menopausal hormone therapy were associated with lower MRS scores. Conclusions: Obesity is strongly associated with more severe menopausal symptoms, both directly and through related chronic conditions and behavioral factors. Longitudinal studies are needed to establish temporal and causal inferences.