

### Selección de Resúmenes de Menopausia

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Front Oncol. 2025 Feb 11:15:1541585. doi: 10.3389/fonc.2025.1541585. eCollection 2025.

## The influence of menopause age on gynecologic cancer risk: a comprehensive analysis using NHANES data

Background: Menopause, a natural transition, affects women's health risks, including gynecologic cancers. Early menopause, linked to lower estrogen, may increase cancer susceptibility. This study analyzed NHANES data from 1999 to 2020 for 8,219 postmenopausal women to explore the relationship between menopausal age and gynecologic cancers. We used regression models and RCS models to assess the risk. Methods: This study utilized data from the NHANES spanning 1999 to 2020, focusing on 8,219 postmenopausal women selected through stratified sampling. Variables including socioeconomic factors, health behaviors, nutritional status, and medical history were assessed in relation to participants' menopausal age and gynecologic cancer prevalence. We analyzed the relationship between menopausal age and gynecologic cancers (cervical, ovarian, and uterine) using multiple regression models. Additionally, we employed RCS models to evaluate nonlinear relationships between menopausal age and gynecologic cancer risk. Results: Our findings indicate a significant inverse association between menopausal age and the risk of gynecologic cancers. After controlling for confounding factors such as age, race, BMI, and lifestyle variables, a later age at menopause was associated with a reduced risk of cervical, ovarian, and uterine cancers. The RCS model revealed a non-linear, low-L-shaped relationship, particularly highlighting increased cancer risks at younger menopausal ages. Subgroup analyses demonstrated consistent results across demographic and lifestyle factors, confirming the robustness of the observed associations. Conclusion: This study reveals the link between menopausal age and gynecologic cancer prevalence. Early menopause is a significant risk factor for cervical, ovarian, and uterine cancers. Our findings support tailored cancer screening based on menopausal age, potentially improving preventive care for postmenopausal women.

#### Clin Endocrinol (Oxf). 2025 Feb 24. doi: 10.1111/cen.15218. Online ahead of print.

### Lifestyle Management in Menopause: A Systematic Review of Women With Premature Ovarian Insufficiency

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Objective: Premature ovarian insufficiency (POI), the loss of ovarian function before age 40, increases the risk of cardiovascular disease, low bone mineral density, dementia and psychological distress. Lifestyle interventions reduce chronic disease risk in other populations and, with hormone therapy, may improve health outcomes in POI. This review aims to identify the role of lifestyle, including diet and physical activity, in managing symptoms, improving quality of life (QoL) and preventing chronic disease in women with POI. The findings of this review informed the 2024 update of the ESHRE Evidence-Based POI Guideline. Design: A systematic search was conducted in PubMed and Medline databases from January 2014 to February 2024. The review included randomized controlled trials and quasiexperimental trials that examined the impact of lifestyle interventions on women with POI. Outcomes included menopause symptoms, QoL, cardiovascular health and bone health. Risk of bias was assessed using Joanna Briggs Institute critical appraisal tool, Results: The literature search yielded 890 citations, with one study meeting the inclusion criteria. Two additional studies from other guideline chapter searches were included, totalling three articles. Two studies involved cancer survivors and one included those with Turner syndrome. Limited evidence suggests lifestyle interventions, particularly physical activity, improve cardiovascular health and bone mineral density in women with POI. The effect of dietary supplementation was mixed. Conclusions: While a healthy lifestyle is proven to prevent chronic diseases and improve QoL in postmenopausal women, there is limited evidence specific to women with POI. Targeted studies are needed to determine the most effective interventions for addressing their heightened risks and unmet needs.

#### Maturitas. 2025 Feb 21:195:108220. doi: 10.1016/j.maturitas.2025.108220. Online ahead of print.

## Efficacy and safety of fezolinetant and elinzanetant for vasomotor symptoms in postmenopausal women: A systematic review and meta-analysis

Helen Michaela de Oliveira, Camilo André Viana Diaz, Lucas Mendes Barbosa, Victor H Palhares Flávio-Reis, et al. Objective(s): Menopause, marked by a decline in estrogen, leads to disruptive vasomotor symptoms like hot flashes and night sweats, significantly affecting quality of life. This meta-analysis evaluated the efficacy and safety of fezolinetant and elinzanetant, two neurokinin 3 receptor antagonists, in managing vasomotor symptoms in postmenopausal women. Methods: Data sources were identified by searches in PubMed, Embase, and the Cochrane Central Register of Controlled Trials up to September 2024. The study followed Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines, with the risk of bias assessed using the version 2 of the Cochrane Risk of Bias Tool for Randomized Trials and evidence quality was evaluated using the Grading of Recommendations Assessment, Development and Evaluation approach. Data were pooled using a random-effects model, and statistical analysis was performed using R version 4.4.1. Results: Ten studies involving 4663 patients were included in the analysis. Elinzanetant >100 mg and fezolinetant ≤45 mg were the most effective doses for reducing vasomotor symptom frequency and severity. Fezolinetant (MD = -1.38) and elinzanetant (MD = -2.04) achieved  $\ge 50 \%$  reductions in vasomotor symptom frequency, with a greater effect in the elinzanetant group. Additionally, elinzanetant improved menopause-specific quality of life. However, higher doses of both drugs were associated with increased adverse effects, with elinzanetant demonstrating a more favorable side-effect profile than fezolinetant. Conclusions: Fezolinetant and elinzanetant are effective options for managing vasomotor symptoms. However, further research is needed to compare these treatments directly and evaluate their long-term safety profiles across different patient populations.

## Maturitas. 2025 Feb 20:195:108221. doi: 10.1016/j.maturitas.2025.108221. Online ahead of print. Relationship between menopausal status and suicidal behavior among the Korean population

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Objective: We investigated whether, in the Korean population, the risk of suicidal behavior is associated with menopausal status and especially age at menopause. For a deeper understanding of suicidal behavior, participants were asked about suicidal ideation and plans, and actual suicide attempts. Methods: This cross-sectional, population-based study involved 27,524 women for analyzing suicidal ideation, 26,893 women for suicidal plans, 28,682 women for suicide attempts, registered in the Korea National Health and Nutrition Examination Survey (2010-2022). Data on menopausal status, including age at menopause, and suicidal behavior were obtained from a self-reported questionnaire. A logistic regression model was applied to examine whether premature ovarian insufficiency, early menopause, and normal menopause significantly impact rates of suicidal behavior, which was further stratified by depression. Weighted prevalence of suicidal behavior according to age at menopause was also analyzed. Results: Compared with premenopausal status, the risk of suicidal ideation was increased in women with premature ovarian insufficiency by an odds ratio (95 % confidence interval) of 1.53 (1.17-2.01), in women with early menopause by 1.57 (1.28-1.92), and in women with clinically normal menopause by 1.17 (1.00-1.37). The risk of suicidal planning was also increased in women in each of these three respective menopausal groups: 1.92 (1.06-3.47), 1.55 (0.96-2.51), and 1.61 (1.13-2.30). The risk of suicide attempt was also increased in women with premature ovarian insufficiency, by an odds ratio of 2.01 (0.91-4.44), and in women with a clinically normal menopause, by 1.97 (1.22-3.18). The weighted prevalence of suicidal ideation decreased with age at menopause, grouped as ≤30 (21.5 %), 31-40 (14.8 %), 41-50 (11.1 %), and ≥50 (9.4 %). Conclusion: The risks of suicidal ideation and planning were higher in women with premature ovarian insufficiency, early menopause, and clinically normal menopause. The risk of suicide attempt was also higher in women with premature ovarian insufficiency and normal menopause, compared with premenopausal women. Younger age at menopause led to a higher risk of suicidal ideation and planning in general. Due to the limitations of this study's cross-sectional design, longitudinal studies must be conducted to establish more strongly this relationship between menopause and suicidal behavior.

Clin Epigenetics. 2025 Feb 21;17(1):31. doi: 10.1186/s13148-025-01827-x.

## Timing of menarche and menopause and epigenetic aging among U.S. adults: results from the National Health and Nutrition Examination Survey 1999-2002

Saher Daredia 1, Dennis Khodasevich 2, Nicole Gladish 2, Hanyang Shen 2, Jamaji C Nwanaji-Enwerem 3 4, et al. Reproductive aging, including timing of menarche and menopause, influences long-term morbidity and mortality in women, yet underlying biological mechanisms remain poorly understood. Using DNA methylation-based biomarkers, we assessed associations of age at menarche (N = 1,033) and menopause (N = 658) with epigenetic aging in a nationally representative sample of women  $\geq$  50 years. Later age at menopause was associated with lower GrimAge epigenetic age deviation B = -0.10 years, 95% CI: -0.19, -0.02). No associations were observed for menarche timing. This suggests a connection between earlier menopause and biological aging, with potential clinical implications for identifying those at high risk for age-related disease.

## J Affect Disord. 2025 Feb 19:377:45-52. doi: 10.1016/j.jad.2025.02.068. Online ahead of print. The effects of estradiol on subcortical brain volumes in perimenopausal-onset depression

Kathryn Gibson 1, Melissa Walsh 2, Megan Hynd 3, Tory Eisenlohr-Moul 4, Erin Walsh 4, Erin Bondy 2, et al. Background: Perimenopause is associated with increases in depressive and vasomotor symptoms (VMS), which can be alleviated with transdermal estradiol (TE2) administration. Subcortical brain regions are commonly implicated in depression, are dense with E2 receptors and are susceptible to volumetric changes resulting from E2 regulation of synaptic density. No studies have examined linkages among TE2 administration, perimenopausal-onset major depression (PO-MDD) and subcortical brain volumes. Methods: This is an exploratory data analysis of change in subcortical brain volumes measured via 3 T MRI before and after three-weeks of TE2 administration in 14 women with PO-MDD and 17 euthymic controls. Regions of interest were the hippocampus, amygdala, putamen, thalamus, and caudate nucleus. Multilevel models examined relations between baseline volumes and volumetric changes with symptom trajectories in the PO-MDD group. Results: In the PO-MDD group, anhedonia (p < 0.004) and VMS (p <0.001) significantly reduced following TE2 administration. There was a significant Group X Time interaction in the right hippocampus (p < 0.01), driven by volume increases in the control group (p < 0.001). In the PO-MDD group, change in right hippocampal volumes significantly predicted decreases in anhedonia trajectories from baseline to week 2 and week 3 (p's < 0.001) and decreases in VMS across all timepoints (p's < 0.001). Discussion: Women with PO-MDD, who presented with more severe baseline anhedonia and VMS, experienced greater reductions in anhedonia, VMS, and hippocampal volumes, demonstrating a greater response to E2. Hippocampal volume change may be a candidate for predicting treatment response to E2 for anhedonia and vasomotor symptoms in women with PO-MDD. These findings should be validated with a placebo-controlled trial.

# Eur J Endocrinol. 2025 Feb 21:lvaf032. doi: 10.1093/ejendo/lvaf032. Online ahead of print. Sex Steroid Hormones and Subclinical Atherosclerosis Progression in Postmenopausal Women

Irene J Chen 1, Frank Z Stanczyk 2, Intira Sriprasert 2 3, Roksana Karim 1 3, Donna Shoupe 2, Naoko Kono 1, et al. Objective: The Early versus Late Intervention Trial with Estradiol demonstrated that hormone therapy (HT) reduces subclinical atherosclerosis progression in healthy postmenopausal women who initiated HT in proximity to menopause (<6 years) but not in those distant from menopause, ( $\ge10$  years). This analysis explores the role of serum sex steroid hormones and sex hormone-binding globulin (SHBG) in atherosclerosis progression, examining differences based on time since menopause. Design: Post-trial analysis. Methods: The study included 535 healthy postmenopausal women; nearly half received HT. Serum levels of estradiol, estrone, testosterone, and SHBG were measured at baseline, 12 months, and 36 months. Carotid intima-media thickness (CIMT) was assessed every six months. Mixed-effects linear models evaluate the relationship between sex steroid hormones, SHBG, and CIMT progression, with time since menopause included as an interaction term, after adjusting for age, hysterectomy, baseline CIMT, systolic blood pressure, and body mass index. Results: Late postmenopausal women were older with higher baseline CIMT. Associations between estradiol, estrone, and SHBG levels with CIMT progression differed significantly by time since menopause (interaction p < 0.01). In early postmenopause, CIMT progression was significantly inversely associated with SHBG (p = 0.024) and nonsignificantly inversely with estradiol and estrone. In late postmenopause, CIMT progression was significantly positively associated with estradiol (p = 0.005), estrone (p < 0.001), and SHBG (p =

0.037). Conclusion: Serum sex steroid hormones and SHBG relate differently to CIMT progression based on time since menopause. Estradiol, estrone, and SHBG levels show opposite associations with CIMT progression in early versus late postmenopause, highlighting the importance of HT timing in cardiovascular disease.

#### Obesity (Silver Spring). 2025 Feb 20. doi: 10.1002/oby.24219. Online ahead of print.

## Global cancer burden attributable to excess body weight, 1990 to 2021, decomposed by population size, aging, and epidemiological change

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Objective: The objective of this study was to estimate cancer burden attributable to excess body weight (EBW) and identify its main source. Methods: We obtained relative risks from meta-analyses, cancer and population data from the Global Burden of Disease Study (GBD) 2021, and BMI prevalence data from the NCD Risk Factor Collaboration (NCD-RisC). We calculated the incidence of 11 cancers attributable to high BMI from 1990 to 2021, analyzed trends using joinpoint regression, and assessed cohort effects with the age-period-cohort model. Decomposition analysis was conducted by cancer-specific risk factors and by population size, aging, and epidemiological changes. Results: The incidence of 11 EBW-related cancers has increased from 1990 to 2021. Later-born cohorts and older age groups had higher cancer incidence rates. High BMI was the top contributor to changes in cancer burden (15.96% of all disability-adjusted life years [DALYs]), particularly in high Sociodemographic Index (SDI) regions. Colorectal, esophageal, and liver cancer had the highest burden due to high BMI (1,349,622; 1,284,385; and 944,616 DALYs, respectively). Epidemiological changes in BMI contributed to the rising DALY burden, ranging from 7.88% for postmenopausal breast cancer to 49.20% for liver cancer. Conclusions: The rising prevalence of EBW contributed to the global cancer burden, showing a significant birth cohort effect. High BMI was the top contributing factor to obesity-related cancers, surpassing other epidemiological risk factors.