

## Selección de Resúmenes de Menopausia

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### **The association between chronic pain and the clustering of menopausal symptoms: Evidence from a British birth cohort study**

Catherine Borra 1, Rebecca Hardy 2

**Background:** Cross-sectional studies have demonstrated an association between menopausal symptoms and chronic pain, but the direction of the association remains unknown. We assessed whether chronic pain is associated with subsequent clusters of menopausal symptoms. **Methods:** We used data from the National Child Development Study, a birth cohort of people born in 1958 in England, Scotland and Wales, which has included a biomedical sweep at age 44 when chronic pain was assessed and a 20-item menopause symptom questionnaire at age 50. Chronic pain was defined as lasting longer than 3 months, and chronic widespread pain was defined as chronic contralateral upper and lower quadrant pain and spinal pain. Latent class analysis was used to define menopause symptom classes ( $n = 4897$ ) and structural equation models ( $n = 3308$ ) to relate chronic pain and chronic widespread pain to these classes, adjusting for confounding variables. **Results:** We found four latent classes of menopause symptom experience at 50 years. These were a low symptom burden class, one defined by vasomotor symptoms, one by psychological symptoms and one with high symptom burden. Chronic pain and chronic widespread pain at 44 years were related to greater odds of being in the higher symptom burden classes compared with the low burden group. For example, the odds ratio (95 % confidence interval) for the high symptom burden class was 2.90 (2.21, 3.81) for chronic pain and 3.50 (2.23, 5.49) for chronic widespread pain, and for the vasomotor symptom class 1.50 (1.16, 1.94) for chronic pain and 1.93 (1.19, 3.13) for chronic widespread pain. **Conclusion:** Women with chronic pain and chronic widespread pain earlier in life may experience greater burden of menopausal symptoms and this should be considered in their clinical management.

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### **Association of the dietary index for gut microbiota with osteoporosis in postmenopausal women over 50**

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This study aimed to investigate the association between the dietary index for gut microbiota (DI-GM) and the risk of osteoporosis in postmenopausal women aged 50 years and older in the United States. A total of 3520 postmenopausal women aged 50 years and older were selected from the National Health and Nutrition Examination Survey conducted from 2007 to 2018. Participants' DI-GM scores were obtained via a dietary questionnaire, and femoral bone mineral density was measured using dual-energy x-ray absorptiometry (DXA). Weighted logistic regression was used to analyze the association between DI-GM and osteoporosis risk. Subgroup analyses were performed to examine the association between DI-GM and osteoporosis risk in different subgroups. Participants were categorized into 4 groups based on DI-GM quartiles, with the lowest quartile (0-4) serving as the reference. After adjusting for covariates, compared with the reference group, participants in the second highest (DI-GM score of 6) and highest (DI-GM score  $\geq 7$ ) quartiles exhibited a 41% (OR: 0.59, 95% CI: 0.42-0.84) and 44% (OR: 0.56, 95% CI: 0.38-0.84), respectively, reduced risk of osteoporosis. Subgroup analysis revealed that this association was consistent across different age groups of postmenopausal women but was statistically significant only among White women. This study of postmenopausal women aged 50 and older in the United States demonstrated that those with higher DI-GM scores had a lower risk of osteoporosis compared to those with lower scores. This finding suggests that dietary intake increasing beneficial components of the gut microbiota may have a positive role in the prevention of postmenopausal osteoporosis.

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### **Relationship between monocyte-to-HDL-cholesterol ratio, estradiol levels, and coronary atherosclerosis severity in postmenopausal women**

Xiang Sha 1, Wei Wang 1, Jie Qiu 1, Li Ling 2, Ruzhu Wang 3

**Background:** Coronary atherosclerosis is a leading cause of coronary heart disease (CHD), particularly among postmenopausal women who experience significant hormonal changes that influence lipid metabolism and inflammatory processes. We aimed to investigate the correlation between monocyte-to-HDL-cholesterol ratio (MHR), estradiol and the severity of coronary lesions in postmenopausal patients with CHD. **Methods:** This study included 360 postmenopausal women diagnosed with CHD. The Gensini score (GS) was obtained from coronary angiography, and patients were divided into three groups according to the severity of coronary lesions assessed by GS - patients with mild coronary lesions (Gensini score < 20), patients with moderate coronary lesions ( $20 \leq$  Gensini score < 40) and patients with severe coronary lesions (Gensini score  $\geq$  40). We used ordinal logistic regression to estimate the odds ratios (ORs) and 95% confidence intervals (CIs) for the association between estradiol, MHR, and coronary lesion severity. For assessing the value of estradiol and MHR in predicting the severity of CHD, we adopted the generalized area under the receiver operating characteristic (ROC) curve method. **Results:** The severe lesion group had the lowest estradiol levels and the highest MHR (all  $p < 0.001$ ). MHR showed a weaker negative correlation with estradiol levels. After adjusting for confounding factors, estradiol was significantly negatively correlated with the severity of CHD (OR = 0.93, 95%CI = 0.91-0.96), while MHR was significantly positively correlated with the severity of CHD (OR = 1.15, 95%CI = 1.01-1.29). Interaction analysis showed significant interaction between estradiol levels and MHR ( $p < 0.001$ ). The area under the curve (AUC) of MHR and estradiol in predicting the severity of CHD in postmenopausal women for the ROC analysis was 0.806 (95%CI = 0.745-0.866) and 0.661 (95%CI = 0.592-0.730), respectively. The AUC of MHR combined with estradiol was 0.826 (95%CI = 0.774-0.877). **Conclusion:** Both estradiol and MHR are independently correlated with and can be used to predict the severity of CHD in postmenopausal women. The combination of estradiol and MHR has a higher predictive value for the severity of CHD.

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### **Efficacy and Safety of 48-Week Low-Dose Dienogest Treatment in Patients with Endometriosis-Associated Dysmenorrhea: A Randomized, Open-Label, Parallel-Group Trial**

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**Introduction:** Dienogest (DNG) is widely used to manage endometriosis-associated pain; however, long-term data comparing low and standard doses are limited. Therefore, this study aimed to evaluate the efficacy and safety of 48-week DNG treatment (1 mg/day vs. 2 mg/day) in patients with endometriosis-related dysmenorrhea (composite score). **Methods:** In this randomized, open-label, parallel-group, trial, 88 patients with endometriosis were enrolled, all of whom had at least one ovarian endometriotic cyst confirmed by imaging. Other phenotypes of endometriosis, such as deep infiltrating or peritoneal lesions, were not systematically assessed and may have been present. Patients were randomized to receive either 1-mg/day or 2-mg/day DNG. The primary endpoint was the change in menstrual pain measured using a visual analog scale (VAS). Secondary endpoints included changes in the dysmenorrhea score, ovarian endometrioma volume, serum estradiol levels, bone mineral density (BMD), and menopausal symptoms. **Results:** Both groups demonstrated a significant reduction in menstrual pain (VAS). The mean VAS scores decreased by 44.63 and 54.19 mm in the 1-mg and 2-mg groups, respectively. However, the between-group difference (- 9.57 mm; 95% confidence interval: - 22.7 to 3.56) was not above the predefined non-inferiority margin of - 15 mm; thus, non-inferiority of the 1-mg dose could not be confirmed. Improvements in dysmenorrhea scores and endometrioma volume were also observed in both groups, although greater effects were noted in the 2-mg group than in the 1-mg group. Serum estradiol suppression was comparable between the groups, whereas BMD loss was less pronounced in the 1-mg group than in the 2-mg group. **Conclusions:** This study did not demonstrate statistical non-inferiority of 1-mg/day DNG treatment over 2-mg/day DNG treatment for pain relief. These results suggest that the 2-mg/day dose may offer more robust analgesic effects, particularly during the early treatment phase. However, 1-mg/day DNG still showed meaningful symptom improvement with fewer adverse events than 2-mg/day DNG, supporting its potential use in selected patients requiring long-term therapy.

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### **Associations of life's essential 8 and life's crucial 9 scores with all-cause and cardiovascular mortality: A population-based cohort study of postmenopausal women**

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**Objectives:** This study examines the associations of scores on the Life's Essential 8 (LE8) and Life's Crucial 9 (LC9) scales with all-cause and cardiovascular mortality among postmenopausal women in the United States. **Methods:** We analyzed data from 5499 postmenopausal women aged  $\geq 20$  years from the 2005-2014 National Health and Nutrition Examination Survey (NHANES), linked to mortality data through December 31, 2019. LE8 includes four behavioral and four clinical metrics; LC9 adds psychological well-being. Cox proportional hazards models were used to estimate hazard ratios (HRs) for all-cause mortality. Generalized additive models explored dose-response relationships. Kaplan-Meier curves and log-rank tests assessed survival differences across score tertiles. **Results:** During a median follow-up of 64 months, 1154 deaths occurred (20.99 %), including 358 (31.0 %) from cardiovascular causes. Mean LC9 score was 63.7 (SD = 14.2). Each 1-SD increase in LE8 and LC9 scores was associated with a 27 % (HR = 0.73, 95 % CI: 0.68-0.78) and 30 % (HR = 0.70, 95 % CI: 0.66-0.76) lower risk of all-cause mortality, respectively. Compared with the lowest tertiles, the highest tertiles of LE8 and LC9 were associated with 50 % (HR = 0.50, 95 % CI: 0.43-0.59) and 51 % (HR = 0.49, 95 % CI: 0.41-0.57) lower risks. Dose-response curves showed inverse, approximately linear associations. Kaplan-Meier survival curves showed significantly higher survival probabilities among participants with higher LE8 and LC9 scores (log-rank  $P < 0.0001$ ). **Conclusions:** Higher LE8 and LC9 scores were associated with lower all-cause and cardiovascular mortality among postmenopausal women.

*PD. Los LE8 y LC9 son scores o puntuaciones compuestas que reflejan el estado de salud cardiovascular según los criterios de la American Heart Association (AHA). Que sean más altos implica mejor salud cardiovascular global y, por lo general, menor riesgo de enfermedad cardiovascular, deterioro cognitivo y mortalidad por todas las causas.*

**Cochrane Database Syst Rev. 2025 Oct 23;10(10):CD000402. doi: 10.1002/14651858.CD000402.pub5.**

## **Hormone therapy in postmenopausal women and risk of endometrial hyperplasia or endometrial cancer**

Dongah Kim 1, Vanessa Jordan 2, Francesca Casciola 3, Mackenzie Ferguson 3, Aimee Humphries 3, et al.

**Rationale:** Reduced circulating estrogen levels around the time of menopause can induce symptoms that affect health and well-being. Estrogen therapy is the most effective treatment, but may be associated with some adverse health outcomes, including endometrial pathology. This is an update of a review first published in 1999 and last updated in 2012. **Objectives:** • To assess the effects of hormone therapy regimens for protecting postmenopausal women against endometrial hyperplasia and endometrial cancer. • To define the lowest effective dose(s) of progestogen used in combination with estrogen therapy for protecting the endometrium. **Included studies:** This update included 72 studies (involving 40,652 women) conducted worldwide. There were 42 multicenter trials. **Synthesis of results:** There were too few studies with events to draw conclusions about endometrial cancer. The results for endometrial hyperplasia are presented below. Unopposed estrogen versus placebo Unopposed estrogen probably increases the risk of endometrial hyperplasia at one year compared with placebo (22-43 events/1000 women versus 5 events/1000 women; OR 5.86, 95% CI 4.09 to 8.40;  $I^2 = 0\%$ ; 6 RCTs, 2493 women; moderate-certainty-evidence). Unopposed estrogen probably increases the risk of endometrial hyperplasia after one year (40-68 events/1000 women versus 6 events/1000 women; OR 8.97, 95% CI 6.78 to 11.87;  $I^2 = 49\%$ ; 9 RCTs, 2539 women; moderate-certainty-evidence). Continuous combined estrogen plus progestogen versus placebo Continuous combined therapy may have little to no effect on the risk of endometrial hyperplasia at one year compared with placebo (0-16 events/1000 women versus 5 events/1000 women; OR 0.51, 95% CI 0.08 to 3.38;  $I^2 = 48\%$ ; 4 RCTs, 3893 women; low-certainty-evidence). We are unsure about the effect of continuous combined therapy after one year (OR 0.25, 95% CI 0.04 to 1.40;  $I^2 = 47\%$ ; 4 RCTs, 789 women; very low-certainty evidence). Sequential combined estrogen plus progestogen versus placebo Sequential combined therapy may increase the risk of endometrial hyperplasia at one year compared with placebo (6-27 events/1000 women versus 2 events/1000 women; OR 5.53, 95% CI 2.60 to 11.76;  $I^2 = 0\%$ ; 4 RCTs, 1030 women; low-certainty-evidence). Sequential combined therapy may result in little to no difference in the risk of endometrial hyperplasia after one year (16-97 events/1000 women versus 20 events/1000 women; OR 2.30, 95% CI 0.76 to 6.99;  $I^2 = 0\%$ ; 3 RCTs, 534 women; low-certainty-evidence). Unopposed estrogen versus continuous combined estrogen plus progestogen Unopposed estrogen probably increases the risk of endometrial hyperplasia at one year compared with continuous combined therapy (46-75 events/1000 women versus 3 events /1000 women; OR 21.90, 95% CI 16.76 to 28.62;  $I^2 = 53\%$ ; 11 RCTs, 7856 women; moderate-certainty-evidence). Unopposed estrogen probably increases the risk of endometrial hyperplasia after one year compared with continuous combined therapy (33-73 events/1000 women versus 3 events/1000 women; OR 16.78, 95% CI 11.01 to 25.55;  $I^2 = 69\%$ ; 3 RCTs, 1191 women; moderate-certainty-evidence). Unopposed estrogen versus sequential combined estrogen plus progestogen Unopposed estrogen may increase the risk of endometrial hyperplasia at one year compared with sequential combined therapy (156-301 events/1000 women versus 16 events/1000 women; OR 17.19, 95% CI 11.27 to 26.22;  $I^2 = 70\%$ ; 5 RCTs, 2354 women;

low-certainty-evidence). Unopposed estrogen may increase the risk of endometrial hyperplasia after one year compared with sequential combined treatment (379-612 events/1000 women versus 49 events/1000 women; OR 19.21, 95% CI 11.95 to 30.90;  $I^2 = 15\%$ ; 2 RCTs, 417 women; low-certainty-evidence). Continuous combined estrogen plus progestogen versus sequential combined estrogen plus progestogen All analyses had insufficient events to draw conclusions. Continuous combined estrogen plus progestogen - dose comparisons We are unsure about the effect of moderate-dose estrogen plus low-dose progestogen compared with moderate-dose estrogen plus moderate-dose progestogen on the risk of endometrial hyperplasia at one year (OR 1.18, 95% CI 0.24 to 5.84;  $I^2 = 36\%$ ; 2 RCTs, 2363 women; very low-certainty-evidence). The remaining dose comparisons had insufficient events to draw conclusions. Sequential combined estrogen plus progestogen - dose comparisons Moderate-dose estrogen plus low-dose progestogen may result in little to no difference in the risk of endometrial hyperplasia at one year compared with moderate-dose estrogen plus moderate-dose progestogen (3-32 events/1000 women versus 6 events/1000 women; OR 1.66, 95% CI 0.49 to 5.65;  $I^2 = 0\%$ ; 4 RCTs, 1072 women; low-certainty-evidence). The remaining dose comparisons had insufficient events to draw conclusions. Authors' conclusions: Unopposed estrogen probably increases the risk of endometrial hyperplasia versus placebo and continuous combined therapy at one year and later. Sequential combined therapy may increase the risk of endometrial hyperplasia at one year versus placebo. The evidence is less certain for continuous versus sequential combined regimens and dose comparisons of continuous and sequential combined regimens. The trials had few events, and long-term follow-up was challenging. For endometrial cancer, events were rare and trials were underpowered to draw meaningful conclusions.

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## **From obesity to oncology; bariatric surgery and the impact on breast cancer-what is the link? - A systematic review and meta-analysis**

Julie-Therese Clifford 1, Odhrán K Ryan 2, Mark Donnelly 2, Matthew Davey 2, Talal Al-Mukhlifi 3, et al.

Background: Obesity is a complex, progressive and relapsing chronic disease associated with significant medical complications, such as breast cancer. Bariatric surgery is currently the most effective treatment modality for obesity. This systematic review and meta-analysis examined the incidence of breast cancer in those who underwent bariatric surgery, as well subgroup analysis focusing on the effect of menopausal status in this cohort. Methods: This systematic review and meta-analysis was conducted in accordance with PRISMA guidelines, involving the search of databases including Cochrane Library, Embase, Scopus, Pubmed and Google Scholar. The quality of the studies was assessed using the Newcastle-Ottawa scale (NOS). Statistical analysis was performed using Review Manager (Revman) Version 5.4. Results: A total of 2,288,003 patients with obesity were included in the analysis. There was a statistically significant risk reduction in breast cancer incidence in those who underwent bariatric surgery compared to those who did not (RR 0.58 95 % confidence interval (CI) 0.46, 0.72,  $p < 0.001$ ) across all fourteen studies. There was significant heterogeneity across the studies ( $\text{Chi}^2 = 358$   $p < 0.00001$ ,  $I^2 = 96\%$ ). Further subgroup analysis was performed on four of the included studies regarding the impact of menopausal status on breast cancer incidence. There was no statistically significant reduction in premenopausal breast cancer risk (RR 0.88 95 % CI 0.74, 1.04). The result was similar in the postmenopausal cohort (RR 0.46 CI 95 % 0.18, 1.19). Conclusion: This systematic review and meta-analysis demonstrates that bariatric surgery is associated with a statistically significant reduction in breast cancer incidence by pathways alluded to in this review and likely by a number of mechanisms yet to be fully elucidated. The role of menopausal status on breast cancer incidence in those who undergo bariatric surgery remains unclear.