



## Selección de Resúmenes de Menopausia

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### Trajectories of Sleep Over Midlife and Incident Cardiovascular Disease Events in the Study of Women's Health Across the Nation

Rebecca C Thurston 1 2, Yuefang Chang 3, Christopher E Kline 4, Leslie M Swanson 5, Samar R El Khoudary, et al. Background: Up to 50% of women report sleep problems in midlife, and cardiovascular disease (CVD) is the leading cause of death in women. How chronic poor sleep exposure over decades of midlife is related to CVD risk in women is poorly understood. We tested whether trajectories of insomnia symptoms or sleep duration over midlife were related to subsequent CVD events among SWAN (Study of Women's Health Across the Nation) participants, whose sleep was assessed up to 16 times over 22 years. Methods: At baseline, SWAN participants (n=2964) were 42 to 52 years of age, premenopausal or early perimenopausal, not using hormone therapy, and free of CVD. They completed up to 16 visits, including questionnaires assessing insomnia symptoms (trouble falling asleep, waking up several times a night, or waking earlier than planned  $\geq 3$  times/week classified as insomnia), typical daily sleep duration, vasomotor symptoms, and depressive symptoms; anthropometric measurements; phlebotomy; and CVD event ascertainment (ie, fatal or nonfatal myocardial infarction, stroke, heart failure, revascularization). Sleep trajectories (ie, insomnia, sleep duration) were determined by means of group-based trajectory modeling. Sleep trajectories were tested in relation to CVD in Cox proportional hazards models (multivariable models: site, age, race and ethnicity, education, CVD risk factors averaged over visits; additional covariates: vasomotor symptoms, snoring, depression). Results: Four trajectories of insomnia symptoms emerged: low insomnia symptoms (n=1142 [39% of women]), moderate insomnia symptoms decreasing over time (n=564 [19%]), low insomnia symptoms increasing over time (n=590 [20%]), and high insomnia symptoms that persisted (n=668 [23%]). Women with persistently high insomnia symptoms had higher CVD risk (hazard ratio, 1.71 [95% CI, 1.19, 2.46], P=0.004, versus low insomnia; multivariable). Three trajectories of sleep duration emerged: persistently short (~5 hours: n=363 [15%]), moderate (~6 hours: n=1394 [55%]), and moderate to long (~8 hours: n=760 [30%]). Women with persistent short sleep had marginally higher CVD risk (hazard ratio, 1.51 [95% CI, 0.98, 2.33], P=0.06, versus moderate; multivariable). Women who had both persistent high insomnia and short sleep had significantly elevated CVD risk (hazard ratio, 1.75 [95% CI, 1.03, 2.98], P=0.04, versus low insomnia and moderate or moderate to long sleep duration; multivariable). Relations of insomnia to CVD persisted when adjusting for vasomotor symptoms, snoring, or depression. Conclusions: Insomnia symptoms, when persistent over midlife or occurring with short sleep, are associated with higher CVD risk among women.

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### Previous cancers in women diagnosed with premature ovarian insufficiency: A nationwide population-based case-control study

Heidi Silvén 1 2 3, Susanna M Savukoski 1 2 3, Paula Pesonen 4, Riitta Niinimäki 2 3 5, Eero Pukkala 6 7, et al. Introduction: To investigate the occurrence of previous cancer diagnoses in women suffering from premature ovarian insufficiency (POI) and compare it with the general population, shedding light on the association between cancer, cancer treatments, and POI. Material and methods: We conducted a nationwide case-control study based on registry data from various sources, including the Social Insurance Institution, Finnish Population Information System, and Finnish Cancer Registry spanning from 1953 to 2018. Our subjects comprised all women in Finland who, between 1988 and 2017, received hormone replacement therapy reimbursement for ovarian insufficiency before the age of 40 years (n = 5221). Controls, matched in terms of age and municipality of residence, were selected from the Finnish Population Information System (n = 20 822). Our main exposure variable was a history of cancer diagnosis preceding the diagnosis of POI. We analyzed odds ratios (OR) to compare the prevalence of previous cancers in women with POI with that in controls, stratifying results based on cancer type, age at cancer diagnosis, and the time interval between cancer diagnosis and POI. We also assessed changes in OR for previous cancer diagnoses over the follow-up period. Results: Out of the women diagnosed with POI, 21.9% had previously been diagnosed with cancer, resulting in an elevated OR of 36.5 (95% confidence interval [CI] 30.9 to 43.3) compared with 0.8% of the controls. The risk of developing POI was most pronounced during the first 2 years following a cancer diagnosis, with an OR of 103 (95%

CI 74.1 to 144). Importantly, this risk remained elevated even when the time interval between cancer and POI exceeded 10 years, with an OR of 5.40 (95% CI 3.54 to 8.23). Conclusions: This study reveals that 21.9% of women with POI have a history of cancer, making the prevalence of cancer among these women 27.5 times higher than age-matched controls in the Finnish population. The risk of developing POI is most substantial in the first 2 years following a cancer diagnosis. These findings underscore the role of cancer treatments as an etiological factor for POI and emphasize the importance of recognizing the risk of POI in cancer survivors for early diagnosis and intervention.

**Front Aging Neurosci. 2024 Jan 11:15:1326747. doi: 10.3389/fnagi.2023.1326747. eCollection 2023.**

### **Effect of hormone replacement therapy on amyloid beta (A $\beta$ ) plaque density in the rhesus macaque amygdala**

Maria-Luisa Appleman 1, Jeremy L Thomas 1, Alison R Weiss 1, Benjamin I Nilaver, Rita Cervera-Juanes, et al.

Background: Amyloid beta (A $\beta$ ) plaque density was examined in the amygdala of rhesus macaques, to elucidate the influence of age, diet and hormonal environment. Methods: Luminex technology was used to measure cerebrospinal fluid (CSF) concentrations of A $\beta$ 40 and A $\beta$ 42 across three decades, while immunohistochemistry was used to examine A $\beta$  plaque density in the amygdala. Results: A $\beta$ 40 was found to be the predominant isoform of A $\beta$  in the CSF, but neither A $\beta$ 40 or A $\beta$ 42 concentrations showed an age-related change, and the ratio of A $\beta$ 42 to A $\beta$ 40 showed only a marginal increase. Significantly fewer A $\beta$  plaques were detected in the amygdala of old ovariectomized animals if they received estradiol HRT ( $p < 0.001$ ); similar results were obtained regardless of whether they had been maintained on a regular monkey chow for ~48 months or on a high-fat, high-sugar, Western-style diet for ~30 months. Conclusion: The results demonstrate that HRT involving estrogen can reduce A $\beta$  plaque load in a cognitive brain region of aged non-human primates. The results from this translational animal model may therefore have clinical relevance to the treatment of AD in post-menopausal women, whether used alone, or as a supplement to current pharmacological and monoclonal antibody-based interventions.

**Post Reprod Health. 2024 Jan 25:20533691241227100. doi: 10.1177/20533691241227100.**

### **How do women feel cold water swimming affects their menstrual and perimenopausal symptoms?**

Megan Pound 1, Heather Massey 2, Sasha Roseneil 3, Ruth Williamson 4, C Mark Harper 5 6, Mike Tipton 2, et al.

Objective: This study aimed to determine how women felt cold water swimming affected their menstrual and perimenopausal symptoms. Study design: An online survey that asked women who regularly swim in cold water about their experiences. The survey was advertised for 2 months on social media. Questions related to cold water swimming habits and menstrual and perimenopausal symptoms were analysed. Main outcome measures: Quantitative and qualitative data including; frequency of menstrual and menopause symptoms, the effect of cold water swimming on these symptoms. Results: 1114 women completed the survey. Women reported that cold water swimming reduced their menstrual symptoms, notably psychological symptoms such as anxiety (46.7%), mood swings (37.7%) and irritability (37.6%). Perimenopausal women reported a significant improvement in anxiety (46.9%), mood swings (34.5%), low mood (31.1%) and hot flushes (30.3%). The majority of women with symptoms swam specifically to reduce these symptoms (56.4% for period and 63.3% for perimenopause symptoms). Women said they felt it was the physical and mental effects of the cold water that helped their symptoms. For the free text question, five themes were identified: the calming and mood-boosting effect of the water, companionship and community, period improvements, an improvement in hot flushes and an overall health improvement. Conclusion: Women felt that cold water swimming had a positive overall effect on menstrual and perimenopause symptoms. Studies on other forms of exercise to relieve menstrual and perimenopause symptoms may show similar findings.

**Menopause. 2024 Feb 1;31(2):123-129. doi: 10.1097/GME.0000000000002305.**

### **Does hormone therapy exacerbate other venous thromboembolism risk factors?**

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Objective: Postmenopausal symptoms in women at higher risk for venous thromboembolism (VTE) due to comorbidities are often undertreated because of concerns that hormone therapy (HT) may increase VTE risk; however, it is unclear how much HT impacts risk of VTE when compared with other risk factors. Methods: This is a case-control study in a commercial claims database from 2007 to 2019. Women aged 50 to 64 years ( $n = 223,949$ ) were classified

as cases if they had an International Classification of Diseases code indicating an acute VTE plus a filled prescription for an anticoagulant, placement of intravascular vena cava filter, or death within 30 days of diagnosis. Controls were matched 10:1 to each case by index date and age. Risk factors and comorbidities present within the year before index were examined. Exposure was defined as a HT prescription within 60 days before index. Results: There were 20,359 VTE cases and 203,590 matched controls. A conditional logistic regression indicated that the greatest risks for VTE were from metastatic cancer (odds ratio [OR], 13.66; 95% CI, 12.64-14.75), hospitalization/surgery (OR, 8.51; 95% CI, 8.09-8.96), trauma (OR, 3.52; 95% CI, 3.32-3.73), comorbidity burden (OR, 3.51; 95% CI, 3.34-3.69), history of hypercoagulable condition (OR, 3.10; 95% CI, 2.87-3.36), and varicose veins (OR, 2.87; 95% CI, 2.56-3.22). Regarding hormone exposure, we observed ORs of 1.51 (95% CI, 1.43-1.60) for any recent hormone exposure; 1.13 (95% CI, 1.04-1.23; number needed to harm, 4,274) for unopposed estrogen menopausal HT; 1.23 (95% CI, 1.10-1.38; number needed to harm, 2,440) for combined menopausal HT; and 5.22 (95% CI, 4.67-5.84) for combined hormonal contraceptives compared with no recent HT exposure. Conclusions: Hormone therapy exposure did not appear to adversely influence other risk factors, and exposure generally played a minor role in VTE risk. Contraceptives, however, were a strong risk factor.

**Osteoporos Int. 2024 Jan 24. doi: 10.1007/s00198-024-07023-6. Online ahead of print.**

### **Average daily glucocorticoid dose, number of prescription days, and cumulative dose in the initial 90 days of glucocorticoid therapy are associated with subsequent hip and clinical vertebral fracture risk: a retrospective cohort study using a nationwide health insurance claims database in Japan**

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Purpose: Fracture risk assessment is recommended at three months after glucocorticoid (GC) therapy initiation. This study aimed to assess whether GC exposure in the initial 90 days of GC therapy is associated with subsequent hip and clinical vertebral fracture risk using the nationwide health insurance claims database of Japan (NDBJ). Methods: Patients aged [Formula: see text] 50 years who were prescribed GC ( $\geq 70$  mg prednisolone or equivalent; PSL) in the initial 90 days of GC therapy and were followed for hip and clinical vertebral fracture incidences for the subsequent 1080 days were selected from NDBJ. Associations of GC exposure with hip or clinical vertebral fracture risk were evaluated by Cox regression analysis adjusted for potential confounders. Results: We selected 316,396 women and 299,871 men for the GC-exposed group and 43,164 women and 33,702 men for the reference group. Higher GC doses and longer prescription days in the initial 90 days of GC therapy were significantly and dose-dependently associated with increased fracture risk relative to the reference group. Patients receiving GC [Formula: see text] 5 mg PSL/day had a significantly increased fracture risk in the stratum of 30-59 days of GC prescription. In addition, female patients who received GC ( $\geq 1$  and  $< 2.5$  mg PSL/day) for 90 days in the initial 90 days of GC therapy had a significantly increased fracture risk. Conclusions: GC exposure in the initial 90 days of GC therapy was dose-dependently associated with hip and clinical vertebral fracture risk. GC may increase fracture risk with lower doses for shorter durations than previously reported. Fracture risk assessment three months after glucocorticoid (GC) therapy initiation is recommended. We found that GC exposure in the initial 90 days of GC therapy at lower daily doses for shorter durations than previously reported were significantly and dose-dependently associated with fracture risk using a nationwide health insurance claims database.