

Selección de Resúmenes de Menopausia

Semana del 12 a 18 de abril, 2023 María Soledad Vallejo. Clínica Quilín. Universidad de Chile

J Hum Hypertens. 2023 Apr 15. doi: 10.1038/s41371-023-00826-w. Online ahead of print. Vascular function in hypertension: does gender dimension matter?

Rosa-Maria Bruno 1 2, Szabolcs Varbiro 3 4, Giacomo Pucci 5, János Nemcsik 6, Mai Tone Lønnebakken, et al. Blood pressure and vascular ageing trajectories differ between men and women. These differences develop due to sexrelated factors, attributable to sex chromosomes or sex hormones, and due to gender-related factors, mainly related to different sociocultural behaviors. The present review summarizes the relevant facts regarding gender-related differences in vascular function in hypertension. Among sex-related factors, endogenous 17ß-estradiol plays a key role in protecting pre-menopausal women from vascular ageing. However, as vascular ageing (preceding and inducing hypertension) has a steeper increase in women than in men starting already from the third decade, it is likely that gender-related factors play a prominent role, especially in the young. Among gender-related factors, psychological stress (including that one related to gender-based violence and discrimination), depression, some psychological traits, but also low socioeconomic status, are more common in women than men, and their impact on vascular ageing is likely to be greater in women. Men, on the contrary, are more exposed to the vascular adverse consequences of alcohol consumption, as well as of social deprivation, while "toxic masculinity" traits may result in lower adherence to lifestyle and preventive strategies. Unhealthy diet habits are more prevalent in men and smoking is equally prevalent in the two sexes, but have a disproportional negative effect on women's vascular health. In conclusion, given the major and complex role of genderrelated factors in driving vascular alterations and blood pressure patterns, gender dimension should be systematically integrated into future research on vascular function and hypertension and to tailor cardiovascular prevention strategies.

Am J Obstet Gynecol. 2023 Apr 12;S0002-9378(23)00239-9. doi: 10.1016/j.ajog.2023.04.009. Is there a link between infertility, miscarriage, stillbirth, and premature or early menopause? Results from pooled analyses of nine cohort studies

Chen Liang, Hsin-Fang Chung, Annette J Dobson, Janet E Cade, Darren C Greenwood, Kunihiko Hayashi, et al. Background: Some reproductive factors (such as age at menarche and parity) have been shown to be associated with age at natural menopause, but there has been little quantitative analysis of the association between infertility, miscarriage, stillbirth, and premature (<40 years of age) or early menopause (40-44 years). Additionally, it was unknown whether the association would be different between Asian and non-Asian women, even though the age at natural menopause was younger among Asian women. Objective: This study aimed to investigate the association of infertility, miscarriage, and stillbirth with age at natural menopause, and whether the association differed by race (Asian and non-Asian). Study design: This was a pooled individual participant data analysis from nine observational studies, contributing to the InterLACE consortium. Naturally postmenopausal women with data on at least one of the reproductive factors (i.e., infertility, miscarriage, and stillbirth), age at menopause, and confounders (i.e., race, education level, age at menarche, body-mass index, and smoking status) were included. Multinominal logistic regression model was used to estimate relative risk ratios (RRRs) and 95% confidence intervals (CIs) for the association of infertility, miscarriage, and stillbirth with premature or early menopause, adjusting for confounders. Between study difference and within-study correlation were taken into account by including study as a fixed effect and indicating study as a cluster variable. We also examined the association with number of miscarriages $(0, 1, 2, \ge 3)$ and stillbirths $(0, 1, \ge 2)$ and tested whether the strength of association differed between Asian and non-Asian women. Results: A total of 303,594 postmenopausal women were included. Their median age at natural menopause was 50.0 years (interquartile range: 47.0 - 52.0). The percentages of women with premature and early menopause were 2.1% and 8.4%, respectively. The RRRs (95%CIs) of premature and early menopause were 2.72 (1.77, 4.17) and 1.42 (1.15, 1.74) for women with infertility; 1.31 (1.08, 1.59) and 1.37 (1.14, 1.65) for women with recurrent miscarriages; and 1.54 (1.52, 1.56) and 1.39 (1.35, 1.43) for women with recurrent stillbirths. Asian women with infertility, recurrent miscarriages (\geq 3), or recurrent stillbirths (≥2) had higher risk of premature and early menopause compared to non-Asian women with the same reproductive history. Conclusion: The histories of infertility, recurrent miscarriages and stillbirths were associated with higher risk of premature and early menopause, and the associations differed by race, with stronger associations for Asian women with such reproductive history.

J Sex Med. 2022 Jul 1;19(7):1098-1115. doi: 10.1016/j.jsxm.2022.03.614.

Sexual Function and Mood Disorders Among Menopausal Women: A Systematic Scoping Review

Azam Rahmani 1, Elahe Afsharnia 2, Julia Fedotova 3, Shirin Shahbazi 4, Arezoo Fallahi 7, Leila Allahqoli, et al Background: Changes in sex hormones during menopause may have detrimental effects on a woman's sexual function and cause mood disorders. The treatment of both conditions is a challenge in gynecology. Aim: To review the published literature on sexual function and mood disorders among peri- and postmenopausal women. Methods: The review is based on the methodological framework of scoping reviews. We searched electronic databases including Medline (PubMed), Scopus, Embase, and Web of Science (WoS). Publications that reported data about the relationship between sexual function and mood disorders among menopausal women were included in the review. The search was not subject to any limitation in terms of time or method. Outcomes: The main outcome measures used for the review were sexual dysfunction and mood disorders. Results: We found 106 total records. After a full-text screening we included 19 studies from 1986 to 2020 based on various methodologies; the majority of the studies16 were cross-sectional. Investigations that addressed the symptoms of mood disorders and some domains of sexual function showed a close relationship between sexual dysfunction and mood disorders among menopausal women. Clinical implications: In clinical practice, it would be appropriate to screen women for at least one mood disorder or sexual dysfunction. If a woman suffers from either, it will be necessary to assess for a further disorder as well. Strengths & limitations: The review was based on a detailed search of the published literature concerning mood disorders and sexual dysfunction among menopausal women compared to women of reproductive age. Despite the clinical importance of the subject, the number of studies eligible for inclusion in the review are rather small. Further investigation of the topic is clearly warranted. Conclusions: While the association between sexual dysfunction and mood disorders appears to be bidirectional, future studies will have to investigate the specific mechanisms by which sexual dysfunction could lead to mood disorders (or vice versa). Future studies should specifically address sexual dysfunctions and attitudes of partners, BMI, family support, sleep, and multiparity.

Climacteric. 2023 Apr 13;1-7. doi: 10.1080/13697137.2023.2194526. Online ahead of print. Safety and acceptability of intravaginal rings releasing estradiol and progesterone

M L Hull 1, B Stuckey 2, K Hartman 3, N Zack 3 4, A Thurman 3, D R Friend 3

Objective: This study aimed to evaluate the safety and acceptability of two fixed-dose 28-day vaginal ring formulations of 17β-estradiol (E2) and progesterone (P4) to treat vasomotor symptoms (VMS) and the genitourinary syndrome of menopause. Design: DARE HRT1-001 was the first-in-woman study of 28-day exposure to two 28-day intravaginal rings (IVRs) designed to release $80 \mu g/day E2 + 4 mg/day P4$ (IVR1) or $160 \mu g/day E2 + 8 mg/day P4$ (IVR2) compared with oral E2 1 mg/day + oral P4 100 mg/day. To assess safety, participants completed a daily diary to record treatment emergent adverse events (TEAEs). To determine acceptability, at the end of treatment IVR users completed a questionnaire assessing tolerability and usability. Results: Enrolled women (n = 34) were randomized to use IVR1 (n =10), IVR2 (n = 12) or oral (n = 12). Thirty-one participants (IVR1 = 10, IVR2 = 10, oral = 11) completed the study. The TEAE profile of those in the IVR groups were similar to the referent oral regimen. TEAEs related to the study product were more common with IVR2 use. Endometrial biopsies were not performed unless endometrial thickness was >4 mm or for clinically significant postmenopausal bleeding. One IVR1 participant had an endometrial stripe increase from 4 mm at screening to 8 mm at the end of treatment. The biopsy indicated no evidence of plasma cells or endometritis and no evidence of atypia, hyperplasia or malignancy. Two other endometrial biopsies were performed for postmenopausal bleeding with similar findings. There were no clinically meaningful laboratory or vital sign abnormalities or trends identified in observed values or changes from baseline. Pelvic speculum examination identified no clinically significant abnormalities in any participant at any visit. Tolerability and usability data demonstrated that both IVRs were generally highly acceptable. Conclusions: Both IVR1 and IVR2 were safe and well tolerated in healthy postmenopausal women. TEAE profiles were comparable to the referent oral regimen.

Nutrients. 2023 Apr 6;15(7):1794. doi: 10.3390/nu15071794.

The Hidden Dangers of Plant-Based Diets Affecting Bone Health: A Cross-Sectional Study with U.S. National Health and Nutrition Examination Survey (NHANES) Data from 2005-2018

Yi Zheng 1, Jiacheng Wang 2, Yawen Wang 3, Kelin Xu 3 4, Xingdong Chen 1 4 5

The plant-based dietary pattern has been recommended for its potential health and environmental benefits, but its association with bone loss needs to be further explored. This study aimed to investigate the association between three plant-based diet indexes and bone loss in 16,085 adults, using data from the National Health and Nutrition Examination Survey. Three plant-based diet indexes (PDI, hPDI, and uPDI) were calculated from two NHANES 24-h dietary recall interviews, to characterize a plant-based diet. A multinomial logistic regression model was used to estimate the odds ratios (OR) and 95% confidence intervals (95% CI). Higher hPDI and PDI were associated with increased risk of bone loss (ORQ5 vs. Q1 = 1.50; 95% CI: 1.24-1.81 for hPDI; ORQ5 vs. Q1 = 1.22; 95% CI: 1.03-1.45 for PDI), while higher uPDI was associated with increased risk of osteoporosis (ORQ5 vs. Q1 = 1.48; 95% CI: 1.04-2.11). A harmful association between plant-based diet indexes (hPDI and PDI) and osteopenia was observed at the lumbar spine rather than the femoral neck. We conducted several sensitivity analyses to ensure the robustness of results, including subgroup analysis, exclusion of people taking anti-osteoporotic and estrogenic drugs, further adjustment for menopausal status, corticosteroid usage, and dietary supplements, and calculation of E-value. Our study demonstrates the deleterious effects of a plant-based diet on bone health and emphasizes the importance of a balanced diet.

Int J Mol Sci. 2023 Mar 31;24(7):6566. doi: 10.3390/ijms24076566.

Cognitive Decline in Early and Premature Menopause

Marta Sochocka 1, Julia Karska 2, Magdalena Pszczołowska 2, Michał Ochnik 1, Michał Fułek 3, et al. Early and premature menopause, or premature ovarian insufficiency (POI), affects 1% of women under the age of 40 years. This paper reviews the main aspects of early and premature menopause and their impact on cognitive decline. Based on the literature, cognitive complaints are more common near menopause: a phase marked by a decrease in hormone levels, especially estrogen. A premature reduction in estrogen puts women at a higher risk for cardiovascular disease, parkinsonism, depression, osteoporosis, hypertension, weight gain, midlife diabetes, as well as cognitive disorders and dementia, such as Alzheimer's disease (AD). Experimental and epidemiological studies suggest that female sex hormones have long-lasting neuroprotective and anti-aging properties. Estrogens seem to prevent cognitive disorders arising from a cholinergic deficit in women and female animals in middle age premature menopause that affects the central nervous system (CNS) directly and indirectly, both transiently and in the long term, leads to cognitive impairment or even dementia, mainly due to the decrease in estrogen levels and comorbidity with cardiovascular risk factors, autoimmune diseases, and aging. Menopausal hormone therapy from menopause to the age of 60 years may provide a "window of opportunity" to reduce the risk of mild cognitive impairment (MCI) and AD in later life. Women with earlier menopause should be taken care of by various specialists such as gynecologists, endocrinologists, neurologists, and psychiatrists in order to maintain their mental health at the highest possible level.

Gynecol Oncol. 2023 Apr 6;173:8-14. doi: 10.1016/j.ygyno.2023.03.021. Online ahead of print. Ovarian preservation compared to oophorectomy in premenopausal women with early-stage, low-grade endometrial Cancer: A cost-effectiveness analysis

Miriam L Hernandez-Zepeda 1, Elizabeth G Munro 2, Aaron B Caughey 2, Amanda S Bruegl 2 Objectives: Standard treatment for endometrial cancer is a hysterectomy, bilateral salpingo-oophorectomy, and lymph node assessment. In premenopausal women, removal of the ovaries may not be necessary and could increase the risk of all-cause mortality. We sought to estimate the outcomes, costs, and cost-effectiveness of oophorectomy versus ovarian preservation in premenopausal women with early-stage, low-grade endometrial cancer. Methods: A decision-analytic model was designed using TreeAge software comparing oophorectomy to ovarian preservation in premenopausal women with early-stage, low-grade endometrial cancer. We used a theoretical cohort of 10,600 women to represent our population of interest in the United States in 2021. Outcomes included cancer recurrences, ovarian cancer diagnoses, deaths, rates of vaginal atrophy, costs, and quality-adjusted life years (QALYs). The cost-effectiveness threshold was set at \$100,000/QALY. Model inputs were derived from the literature. Sensitivity analyses were conducted to evaluate the robustness of the results. Results: Oophorectomy resulted in more deaths and higher rates of vaginal atrophy, while ovarian preservation resulted in 100 cases of ovarian cancer. Ovarian preservation resulted in lower costs and higher QALYs making it cost effective when compared to oophorectomy. Sensitivity analyses demonstrated the probability of cancer recurrence after ovarian preservation and probability of developing ovarian cancer were the most impactful variables in our model. Conclusion: Ovarian preservation is cost-effective in premenopausal women with early-stage, low-grade endometrial cancer when compared to oophorectomy. Ovarian preservation may prevent surgical menopause, which may improve quality of life and overall mortality without compromising oncologic outcomes, and should be strongly considered in premenopausal women with early stage disease.