Selección de Resúmenes de Menopausia

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Sex-specific hormonal trajectories reveal an early neuroendocrine vulnerability window preceding menopausal depressive symptoms

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Depressive symptoms show marked sex differences in prevalence and symptom profiles, with sex hormones thought to play a key role. However, systematic evaluations of age-related hormone variation across the adult lifespan remain limited. We analyzed data from 8421 adults (4204 males and 4217 females) drawn from the National Health and Nutrition Examination Survey (NHANES) collected between 2013 and 2016. Estradiol and testosterone levels, along with depressive symptoms assessed using the Patient Health Questionnaire-9 (PHQ-9), were included in the analysis. Participants were stratified by decade-based age groups, and group means were plotted to characterize age-related hormone levels and depressive symptom severity. Differences between groups were examined using independent t-tests and one-way ANOVA with Bonferroni correction. Decade-based age stratification was used because it reflects major endocrine transition stages across adulthood. Compared to the non-depressed group, both male and female participants aged 28-57 showed altered hormone trajectories. Notably, in females, estradiol levels began to abnormally elevate in the 28-37 age range and were associated with depressive symptom severity in the 38-57 age range among the depressed group. Within the PHQ-9 item-level analysis, depressed females exhibited significantly higher fatigue and lower insomnia scores compared to depressed males ($p < .05$). In the non-depressed groups, males scored significantly lower on all depressive symptoms except for psychomotor changes and self-harm or suicidal ideation compared to females (all $p < .05$). Estradiol showed a clear midlife inflection with pronounced instability emerging between ages 28 and 47. Our findings reveal sex- and age-specific trajectories of hormones and depressive symptoms across adulthood, with early estradiol variation emerging in female and externalizing features predominating in males at distinct life stages. These previously underrecognized patterns suggest an early neuroendocrine sensitive window, underscoring the need for mechanism-focused longitudinal studies and highlighting opportunities for earlier, sex-tailored clinical strategies.

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Use of vaginal estrogens in urogynecology: current evidence, controversies and clinical applications

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Purpose of review: Genitourinary syndrome of menopause (GSM) is a prevalent yet underrecognized condition in postmenopausal women, characterized by progressive vulvovaginal and lower urinary tract symptoms from estrogen deficiency. Vaginal estrogen therapy is the first-line pharmacologic treatment for GSM. However, as new evidence emerges, understanding of its efficacy, safety, and use in special populations continues to evolve. This review summarizes current evidence on vaginal estrogen formulations, clinical effectiveness, safety, and therapeutic applications. Recent findings: Recent randomized controlled trials confirm that low-dose vaginal estrogen significantly improves GSM symptoms - including vaginal dryness, dyspareunia, and irritation - while restoring epithelial integrity and normalizing pH. Evidence also supports its role in reducing recurrent urinary tract infections by restoring lactobacilli-dominant flora, reinforced by a 2025 multisociety clinical guideline recommending topical, but not systemic, estrogen for this indication. Comparative studies show similar efficacy across creams, tablets, inserts, and rings, differing primarily in convenience and absorption rather than effectiveness. Large cohort studies indicate no increased risk of cardiovascular disease, venous thromboembolism, or malignancy. Use in breast cancer survivors remains controversial, but emerging data suggest minimal systemic absorption and no clear increase in recurrence risk, supporting shared decision-making. In addition, long-term outcomes show that adjunctive vaginal estrogen does not improve anatomic surgical success after native tissue apical prolapse repair. Nonhormonal therapies and agents like ospemifene or prasterone offer alternative options, though they demonstrate lower or more variable efficacy than vaginal estrogen. Summary: Vaginal estrogen therapy is the most effective, evidence-based treatment for GSM and helps prevent recurrent urinary tract infections in postmenopausal women. Its favorable safety profile and multiple formulations enable individualized care. Recent evidence clarifies that

while overall safety is reassuring, caution is necessary for breast cancer survivors using aromatase inhibitors. Additionally, longer-term perioperative trial data temper expectations regarding surgical-recurrence benefits, while confirming its value for local tissue optimization. Ongoing research should focus on long-term safety in high-risk groups and the effectiveness of emerging non-estrogen alternatives.

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Gynecologist and Menopausal Patient Perspectives on Vaginal Hormone Therapy for the Management of the Genitourinary Syndrome of Menopause in Canada: A Real-World Survey

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Purpose: The genitourinary syndrome of menopause (GSM) is common during menopause and can have a profound negative impact on quality of life. Vaginal hormone therapy (HT) is a guideline-recommended second-line treatment for GSM but its real-world utilization in Canada is poorly described in the literature. The objectives of this real-world study were to examine current patterns of practice and potential gaps in the management of GSM in Canada and to evaluate factors affecting patient satisfaction with vaginal hormone therapy for GSM. Patients and methods: Real-world study that surveyed 13 Canadian gynecologists and 119 patients diagnosed with GSM who were eligible for vaginal HT but had not been prescribed this treatment (naïve cohort) or were currently being treated with vaginal HT (on-treatment cohort). Data were analyzed using descriptive statistics. Results: The main therapies prescribed by gynecologists for GSM were vaginal moisturizers or lubricants (49%), vaginal estrone/conjugated estrogen creams (35%), vaginal estradiol inserts (26%) or tablets (20%), and vaginal dehydroepiandrosterone (DHEA) ovules (12%). Among vaginal HT-naïve patients, the most important factors impacting treatment selection were ease of use, onset of action, and low risk of systemic hormone absorption. Most patients in the on-treatment cohort (77%) were satisfied with their current vaginal HT yet 77% would consider switching treatment most commonly due to convenience factors. After consultation with their gynecologist, 43% of patients on vaginal HT switched treatment, mainly to estradiol inserts (43%) or DHEA ovules (36%). Even patients who had no change to their GSM treatment had experienced issues with their current vaginal HT, suggesting an opportunity to discuss alternative treatment options with their gynecologist. Conclusion: Gaps and opportunities to improve the current management of GSM in Canada were identified. Discussions about GSM and available treatment options could be strengthened to support shared decision-making.

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Premenopausal Depression and Risk of Cardiovascular Disease After Menopause: A Large Real-world Cohort Study

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Objective: While depression has been linked to adverse cardiometabolic profiles in postmenopausal women, its temporal relationship with cardiovascular disease (CVD) when occurring before menopause remains unclear. This study examined whether depression diagnosed prior to menopause was associated with incident CVD after menopause. Methods: We conducted a retrospective cohort study using the TriNetX Global Collaborative Network. Postmenopausal women were assigned to two cohorts: cohort 1 included women with depression diagnosed before menopause and without preexisting CVD, premature menopause, or conventional CVD risk factors (smoking, diabetes mellitus, hypertension, dyslipidemia, overweight/obesity, or family history of ischemic heart disease); cohort 2 included comparable women without premenopausal depression. Propensity score matching balanced baseline characteristics, including age at menopause, current age, and ethnicity. Risk differences and risk ratios (RRs) with 95% confidence intervals(CIs) were calculated to compare incident CVD (myocardial infarction, coronary heart disease, stroke, heart failure, or cardiovascular death). Time-to-event outcomes were assessed using Kaplan-Meier curves and log-rank testing, and hazard ratios (HRs) were estimated using Cox proportional hazards regression. Results: Initial queries identified 90,638 women in cohort 1 and 1,237,202 in cohort 2. After matching, 88,884 women remained in each cohort, with a mean (SD) age of 57.6(11.4) years. Follow-up varies according to database entry time, with maximum follow-up of 20 years. Women with premenopausal depression had a higher incidence of postmenopausal CVD than those without depression (4.0% vs. 3.3%; RR,1.23; 95% CI, 1.17-1.29; p<.001), corresponding to an absolute risk difference of 0.7% (95% CI, 0.6%-0.9%). Because the proportional hazards assumption was not satisfied, the Cox hazard ratio was interpreted as a secondary average time-to-event summary rather than as the primary effect estimate. The estimated hazard ratio for incident CVD was 1.21 (95% CI, 1.15-1.27; log-rank p<.001), representing an average association across the follow-up period rather than a constant

hazard over time. Conclusion: Women with premenopausal depression had a higher cumulative incidence of postmenopausal cardiovascular disease than matched women without depression, suggesting that premenopausal depression may represent a marker of increased cardiovascular vulnerability in midlife women.

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ACOG Clinical Practice Guideline: Management of Menopause-Related Vasomotor, Sleep, and Mood Symptoms

American College of Obstetricians & Gynecologists' Committee on Clinical Practice Guidelines–Gynecology.

Purpose: To provide evidence-based recommendations for the management of vasomotor, sleep, and mood symptoms related to spontaneous menopause and induced menopause (at or beyond age 40 years). Target population: Perimenopausal and postmenopausal individuals assigned female sex at birth (ie, women, transgender men, and gender-diverse individuals) with vasomotor, sleep, and mood symptoms related to spontaneous or induced menopause. Methods: This guideline was developed using an a priori protocol in conjunction with a writing team consisting of a subspecialist in reproductive endocrinology and infertility, a Menopause Society Certified Practitioner and subspecialist in reproductive endocrinology and infertility, and a specialist in obstetrics and gynecology. Studies that moved forward to the full-text screening stage were assessed by two authors from the writing team based on standardized inclusion and exclusion criteria. Included studies underwent quality assessment, and a modified GRADE (Grading of Recommendations Assessment, Development and Evaluation) evidence-to-decision framework was applied to interpret and translate the evidence into recommendation statements. Recommendations: This Clinical Practice Guideline includes recommendations on pharmacologic and nonpharmacologic interventions for the management of menopause-related vasomotor, sleep, and mood symptoms. Recommendations are classified by strength and evidence quality. Ungraded Good Practice Points are included to provide clinical guidance when a formal recommendation could not be made because of inadequate or nonexistent evidence.

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Regular physical activity is associated with lower odds of bodily pain in midlife women

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Objective: To evaluate the association between regular physical activity and bodily pain domain of the SF-36 in midlife women, considering pharmacological and physical factors. Methods: This cross-sectional study included 3,523 women aged 40 to 60 years. Participants reported whether they had generalized body pain, physical activity, menopause status, menopause hormone therapy (MHT) use, psychotropic medication use, and comorbidities. Multivariable logistic regression was used to identify independent predictors of bodily pain. Results: Women reporting regular physical activity (n=1806; 56.3%) had 34% lower odds of bodily pain (OR 0.66; 95% CI: 0.58-0.76), independent of BMI, menopause status, psychotropic drug use, and comorbidities. MHT use showed an even stronger association (OR 0.50; 95% CI: 0.41-0.61). Conversely, obesity (OR 1.61; 95% CI: 1.36-1.92), postmenopause status (OR 1.45; 95% CI: 1.26-1.68), psychotropic drug use (OR 1.45; 95% CI: 1.24-1.70), and comorbidities (OR 1.52; 95% CI: 1.31-1.77) were associated with increased pain risk. Conclusions: Regular physical activity is independently associated with lower odds of bodily pain in midlife women. Exercise programs, in combination with MHT, may contribute to optimizing pain management in this population and warrant further prospective investigation.

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Menopausal hormone therapy combined with antiresorptive therapy for skeletal outcomes in postmenopausal women: a systematic review and network meta-analysis of randomized controlled trials

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Importance: Postmenopausal bone loss is a major contributor to osteoporosis, fracture-related morbidity, loss of independence, and mortality. Although systemic menopausal hormone therapy (MHT), antiresorptive therapy, and combination regimens improve bone mineral density (BMD), their comparative skeletal benefits and safety profiles remain incompletely defined. Objective: The study aims to compare the therapeutic and preventive skeletal effects of systemic MHT, antiresorptive therapy, and combined MHT plus antiresorptive therapy on site-specific BMD, fracture outcomes, and selected safety outcomes in postmenopausal women. Evidence review: PubMed, Embase, Scopus, and the Cochrane Library were searched from database inception until April 14, 2026, for randomized controlled trials evaluating systemic MHT, bisphosphonate therapy, calcitonin therapy, or MHT combined with antiresorptive therapy in postmenopausal women. Eligible comparators included placebo, no active bone-specific therapy, or another eligible randomized treatment arm. Study selection and data extraction were performed using predefined eligibility criteria and standardized extraction forms. Treatment effects were synthesized using frequentist random-effects network meta-analysis. Findings: Sixteen randomized controlled trials, including 2,861 postmenopausal women, were included. Compared with control, all active treatment nodes were associated with greater increases in lumbar spine BMD. The largest estimates were observed for MHT plus calcitonin therapy (mean difference [MD], 12.24%; 95% CI, 7.46-17.01) and MHT plus bisphosphonate therapy (MD, 9.71%; 95% CI, 6.99-12.42), although calcitonin-based estimates were informed by limited evidence. Across hip-region outcomes, MHT plus bisphosphonate therapy showed the most favorable BMD profile, including at the femoral neck (MD, 4.87%; 95% CI, 2.66-7.07) and femoral trochanter (MD, 6.65%; 95% CI, 5.12-8.17). MHT alone and MHT plus bisphosphonate therapy were associated with higher risks of mastalgia and vaginal spotting or bleeding. MHT plus bisphosphonate therapy was associated with a lower risk of any fracture compared with control (risk ratio, 0.51; 95% CI, 0.28-0.93), but fracture events were sparse and were often not prespecified efficacy outcomes. Conclusions and relevance: In postmenopausal women, systemic MHT, bisphosphonate therapy, and their combination improved BMD compared with control. Combination MHT plus bisphosphonate therapy showed the most favorable hip-region BMD profile; however, current evidence is insufficient to establish superior fracture prevention or long-term safety.

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Premature menopause and risk of type 2 diabetes among postmenopausal women: findings from the Women's Health Initiative

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Objective: The association between premature menopause (age below 40 y) and subsequent risk of type 2 diabetes (T2D) is not fully understood. Sex hormone fluctuation due to ovarian function, hormone therapy (HT), and menopause-related changes in body composition may likely modify or mediate this relationship, which is the focus of this study. Methods: We included 136,759 postmenopausal women aged 50-70 years from the Women's Health Initiative. Menopausal age and type (natural vs. surgery-associated) were determined using self-reported reproductive history, surgeries, menopausal symptoms, and postmenopausal HT use. T2D incidence was determined through self-reported initiation of diabetes treatment. Multivariable Cox models assessed the association between premature menopause and T2D, adjusting for demographic, lifestyle, reproductive, and health-related factors. Interaction terms were used to evaluate effect modification by HT use. Mediation analysis quantified the contribution of body mass index (BMI) to this association. Results: Premature menopause (n=13,230; 9.7%) was associated with a higher risk of T2D compared with menopause at ages 50-54 (hazard ratio [HR]: 1.10; 95% confidence interval [CI]: 1.05-1.16). Among women with natural menopause, HT use modified the relationship between premature menopause and T2D (Pinteraction=0.047). Elevated risks were observed among women who never used HT (HR: 1.24; 95% CI: 1.08-1.42) or used estrogen plus progestogen (HR: 1.35; 95% CI: 1.09-1.68), but not among estrogen-only users. BMI mediated (indirect effect: 27.9%; 95% CI: 19.0%-45.8%) of the association. Conclusions: Premature menopause was modestly associated with an increased T2D risk; this association varied by HT use and was partially mediated by BMI.