Selección de Resúmenes de Menopausia

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Relationship Between Psychiatric Drug Use and Cognitive Function in Women During the Menopausal Transition: An Analysis Based on the NHANES Database

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Background: Women during the menopausal transition often experience mood disorders, sleep disturbances, and cognitive decline, making the use of psychotropic drugs relatively common. However, the relationship between psychiatric drug use and cognitive function in menopausal women remains unclear. Methods: This was a cross-sectional study that included women aged 45-65 years from the National Health and Nutrition Examination Survey (NHANES) 2021-2023 cycle. Psychiatric drug use was defined based on prescription drug data, including antidepressants, benzodiazepines, and sedative-hypnotics. Cognitive function was assessed using the Digit Symbol Substitution Test (DSST). The Bayesian Kernel Machine Regression model was used to analyse the relationship between psychiatric drug use and cognitive function, with adjustment for potential confounders, including routine demographic characteristics. Results: A total of 956 women during the menopausal transition were included in the analysis. As the number of psychotropic drugs used increased, cognitive function decline became more pronounced. Antidepressants and benzodiazepines played dominant roles in this association (posterior inclusion probability >0.9). The concurrent use of two or more psychotropic drugs was associated with an 11%-24% reduction in DSST cognitive scores. In the context of three-drug combinations, the cognitive impairment associated with antidepressants and benzodiazepines were amplified, resulting in an additional 5.1%-6.3% decrease in cognitive scores. Conclusions: Psychiatric medication use showed a significant cross-sectional association with poorer cognitive performance among women undergoing menopausal transition, and polypharmacy regimens displayed stronger associations than single-drug regimens. Clinically, greater attention should be paid to the potential cognitive impact of psychiatric drug use in menopausal women, and polypharmacy regimens should be optimised.

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Sleep and the Gut-Brain Axis: Bidirectional, Converging Mechanisms Linking Brain Health, Neuroinflammation, and Neurodegeneration

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Sleep and the gastrointestinal (GI) tract interact in a complex and reciprocal relationship, although the molecular and physiological pathways underlying this interaction remain only partially defined. Communication between the central (CNS) and enteric nervous systems (ENS) spans neural, immune, endocrine, and metabolic pathways, including vagal nerve signaling, the hypothalamic-pituitary-adrenal (HPA) axis, gut-resident microbiota, and circulating microbial metabolites, such as bile acids with neuroinflammatory or neurotransmitter activity. In this narrative review, we synthesize evidence from animal models, observational cohorts, and intervention trials to map this bidirectional axis, focusing on several underexamined modulatory mechanisms including the interaction between the gut microbiome and the glymphatic system, the brain's perivascular waste-clearance network, which is implicated in the removal of amyloid-β (Aβ) and tau in Alzheimer's disease; neuroendocrine regulation and sex-related differences in gut microbiome composition and sleep patterns, which may help explain the divergent neurodegenerative disease risks between men and women; and age-related parallel trajectories of microbiome senescence and sleep fragmentation in older adults. We discuss melatonin, cortisol, estrogen, and ghrelin as endocrine mediators linking circadian biology to gut physiology, and we consider how environmental and lifestyle factors further perturb this system. These mechanisms form an integrative framework of the gut-brain-sleep axis and highlight priority directions for mechanistic and translational research, including significant nodes in this pathway where targeted interventions may help cognitive resilience and slow the neurodegenerative disease progression. More research clarifying these mechanisms may help identify the most promising targets, potentially leading to personalized, precision-medicine-based therapeutic strategies.

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Reappraising the safety of menopausal hormone therapy for women-implications for the clinic

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Menopausal hormone therapy (MHT) is currently the most effective treatment for vasomotor and other estrogen deficiency-related symptoms. Despite its proven efficacy, concerns regarding long-term safety, particularly breast cancer, venous thromboembolism, and cardiovascular disease, have influenced clinical practice and patterns of MHT use over the past decades. This review summarizes the evolution of evidence regarding the safety of systemic MHT, from the introduction of conjugated equine estrogens in the 1940s through landmark randomized clinical trials to contemporary evidence and international guideline recommendations. Early concerns regarding endometrial safety with estrogen-only treatment were largely resolved by the addition of progestogens for women with an intact uterus. The Women's Health Initiative trial fundamentally changed perceptions of MHT cardiovascular safety, but subsequent analyses established the "timing hypothesis," demonstrating that the benefit-risk profile depends on age and time since menopause at treatment initiation. More recent evidence has highlighted clinically relevant differences between estrogen formulations, routes of administration, and type of progestogen. Transdermal estradiol is associated with a lower risk of venous thromboembolism than oral estrogen, while micronized progesterone and dydrogesterone may offer a more favorable breast safety profile than some synthetic progestins, although randomized evidence is lacking. Current evidence supports an individualized approach to MHT, with treatment decisions based on symptom burden, age, time since menopause, route of estrogen administration, type of progestogen, and individual risk factors. For healthy women initiating therapy before age 60 years or within 10 years of menopause, the overall benefit-risk profile is favorable. Future research should focus on optimizing formulation-specific safety, generating comparative randomized evidence, and further refining personalized treatment strategies to maximize benefits while minimizing risks.

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Cardiovascular and thromboembolic risks of sex hormone therapy: from contraception to transgender care

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The risk of venous thromboembolism is increased with combined oral contraceptives, rises with the dose of ethinylestradiol, and is higher with desogestrel, gestodene, drospirenone or cyproterone acetate than with levonorgestrel; the determinant is not the generation of the pill but the residual androgen-receptor activity of the progestin, which modulates the hepatic effect of the estrogen. Age over 35 years, obesity, smoking and a family history of thrombosis amplify it. Pills based on a native estrogen have a more limited hepatic impact and rank below most ethinylestradiol combinations in contemporary cohorts, but their clinical safety is not demonstrated and no comparative outcome data exist for estetrol/drospirenone. Androgenicity is not a general marker of venous safety: injectable depot medroxyprogesterone acetate, given alone at supraphysiological doses, carries an increased risk. Myocardial infarction and stroke are also more frequent, but against a very low background - about 21 additional strokes and 10 additional infarctions per 100,000 person-years, four times fewer than the venous excess - and, unlike venous events, independent of progestin type. Menopause hormone therapy increases venous thromboembolic risk, especially in the first year; the route of administration is the main determinant, transdermal estradiol with micronized progesterone appearing safest. In cisgender men, testosterone deficiency carries increased cardiovascular risk, and randomized and real-world data support the safety of transdermal replacement, although more pulmonary embolism and atrial fibrillation have been observed. In trans women, observational data show an increased risk of stroke and venous thromboembolism, particularly with oral estradiol and cyproterone acetate, whereas recent large-scale data show no excess of major cardiovascular events with testosterone in trans men. The practical consequences are specific: no combined pill is acceptable after a venous thromboembolic event, with a thrombogenic mutation or with migraine with aura, native-estrogen pills included; transdermal estradiol should be preferred for menopause and feminising hormone therapy; and haematocrit should guide the dose and route of testosterone.

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Hysterectomy, bilateral oophorectomy, and risk of type 2 diabetes: Evidence from the E3N-generations cohort

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Objectives: Evidence on hysterectomy and the risk of type 2 diabetes is limited, particularly regarding age at surgery. We assessed whether hysterectomy, with or without bilateral oophorectomy, is associated with incident type 2 diabetes, and whether this association is modified by age at surgery. Study design: We followed 82,472 women from the E3N-Generations cohort, free of diabetes at baseline in 1992, until 2008 (median follow-up 16 years). Hysterectomy and oophorectomy were modelled as time-dependent exposures. Hazard ratios were estimated using Cox models with age as the time scale, adjusted for lifestyle, metabolic, and reproductive factors. Main outcome measure: Incidence of type 2 diabetes. Results: During follow-up, 2318 women developed type 2 diabetes. In fully adjusted models, hysterectomy combined with bilateral oophorectomy was associated with a higher risk of type 2 diabetes (hazard ratio 1.23, 95% confidence interval 1.07-1.43) compared with women who underwent neither procedure, whereas hysterectomy alone was not (1.06, 0.91-1.24). Bilateral oophorectomy alone was not associated with the risk of incident type 2 diabetes. The association with hysterectomy and bilateral oophorectomy was strongest among women operated on before age 45 (1.70, 1.35-2.15); it was similarly elevated when the age threshold was changed to 40 (1.54, 1.08-2.20). There was significant heterogeneity by age at surgery for hysterectomy with bilateral oophorectomy ($p = 0.001$) and for hysterectomy alone ($p = 0.010$). Conclusions: Hysterectomy with bilateral oophorectomy was associated with an increased risk of incident type 2 diabetes, independently of conventional metabolic risk factors. This excess risk was particularly pronounced among women who underwent surgery before age 45.

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Efficacy and safety of non-hormonal pharmacotherapies for depressive and anxiety symptoms during the menopausal transition and postmenopause: a systematic review

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Background: Non-hormonal pharmacotherapies are widely used to manage depressive and anxiety symptoms in peri- and postmenopausal women, but comparative evidence across drug classes remains heterogeneous. Objective: To systematically evaluate the efficacy and safety of non-hormonal pharmacological interventions for depressive and anxiety symptoms during the menopausal transition and postmenopause. Methods: A systematic review of six databases and trial registries identified randomized and non-randomized studies evaluating SSRIs, SNRIs, gabapentinoids, and other pharmacotherapies. Due to substantial clinical and methodological heterogeneity, a structured Synthesis Without Meta-analysis (SWiM) approach was applied. Results: A total of Thirty-one studies (n = 8,124 participants) were included. SNRIs showed more frequent positive effects on depressive symptoms compared with other pharmacological classes, while SSRIs demonstrated modest and variable effects. Gabapentinoids consistently improved vasomotor symptoms but showed limited and low-certainty effects on mood outcomes. Evidence for anxiety outcomes was inconsistent across all drug classes. Certainty of evidence ranged from very low to moderate. Conclusions: Non-hormonal pharmacotherapies may provide benefit for mood symptoms during the menopausal transition and postmenopause, particularly SNRIs; however, conclusions are limited by heterogeneity, indirectness, and lack of head-to-head comparative trials.

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Testosterone as part of hormone replacement therapy in menopausal women - what do we know so far? A Narrative Review

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Testosterone, widely known as the male hormone, is also produced naturally in women and plays an important role throughout their lifespan. There has been a growing use of testosterone for a range of symptoms in menopausal women, including low sexual desire, low mood, fatigue, poor memory, and heart and bone health. This review brings together the current evidence and guidelines on testosterone as part of hormone replacement therapy (HRT) in menopausal women, including its impact on reproductive and non-reproductive tissues; when it is indicated to be prescribed and in what forms; safety and gaps in existing evidence. We found that there is high-quality evidence to support the use of testosterone for low sexual desire where conventional HRT has not helped. Transdermal preparations are recommended with no serious side effects at testosterone levels normally found in women. There is insufficient evidence to support its use for brain, heart and bone health. This represents an area of focus for future research.