

Selección de Resúmenes de Menopausia

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Reproductive Factors and Risk of Mortality in Older Women: A 16-year Follow-up of Guangzhou Biobank Cohort Study

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Background: China's dramatic decline in fertility rates due to family planning policies and socioeconomic changes have significant impacts on women's long-term health. We examined the associations of individual reproductive factors and reproductive risk scores (RRS) with all-cause, cardiovascular disease (CVD), and cancer mortality in Chinese women. Methods: 19,833 women aged 50+ years from the Guangzhou Biobank Cohort Study were included. Reproductive factors include gravidity, parity, number of abortions, age at first pregnancy, duration of breastfeeding, age at menarche, age at menopause, and contraceptive use. Weighted and unweighted RRS was constructed by six reproductive characteristics associated with long-term mortality. Cox models were used to estimate hazard ratios (HRs) and 95% confidence intervals (CIs). Results: During an average follow-up of 16.7 years, 4,310 deaths occurred. Per one-point increase in weighted RRS was associated with higher risks of all-cause (adjusted HR: 1.05, 95% CI: 1.03-1.07) and CVD mortality (1.07, 1.04-1.10), but not with cancer mortality (1.03, 0.99-1.07). Mortality was higher for 0 or ≥ 4 pregnancies than 3 pregnancies (1.32, 1.06-1.64 and 1.12, 1.02-1.22), 0 or ≥ 4 childbirths than 2 childbirths (1.46, 1.20-1.79 and 1.15, 1.05-1.25), ≥ 4 abortions than no abortions (1.10, 1.02-1.19), age at first pregnancy < 22 years than 22-29 years (1.21, 1.13-1.30), and breastfeeding duration < 3 months than the longer (1.23, 1.09-1.38). Age at menopause was negatively associated with all-cause mortality (0.99, 0.98-1.00 per one-year increase). Conclusion: Reproductive factors, including gravidity, parity, abortion, age at first pregnancy, breastfeeding duration, and menopausal age, were significant determinants of mortality risk in older Chinese women.

Eur Heart J Qual Care Clin Outcomes. 2025 Nov 5:qcaf136. doi: 10.1093/ehjqcco/qcaf136. Association of Menopausal Hormone Therapy with Incident Cardiovascular Disease in Women Veterans

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Background: The impact of menopausal hormone therapy (HT), and its timing on cardiovascular disease (CVD) remains controversial in women. Aims: Examine the association of HT with incident CVD in women veterans (WV).

Methods: Veterans Health Administration (VHA) electronic records were used to identify WV aged ≥ 45 years who engaged with VHA from 1/1/2000-12/31/2017. HT was defined as any oral or transdermal estrogen-containing product or combined estrogen-progestin. Incident CVD was defined as new-onset ischemic heart disease (IHD), stroke, heart failure (HF), atrial fibrillation/flutter (AF), aortic stenosis (AS), pulmonary hypertension (PHTN), venous thromboembolism (VTE), peripheral arterial disease (PAD). Propensity score matching was used to match WV with and without HT on demographics, CVD risk factors, mental health conditions, and cardiovascular medication use. Cox proportional hazards models were used to estimate hazard ratios. Stratified analyses were conducted across distinct age categories. Results: A total of 241,943 WV met the inclusion criteria, including 9,295 with HT. After 1:2 propensity score matching the HT cohort had significantly higher rates of CVD compared to non-HT cohort (22.4% versus 11.7%, $p < 0.001$), and all-cause mortality (8.0% versus 5.2%, $p < 0.001$). In the Cox proportional hazards regression model, HT was independently associated with a greater risk of CVD (HR=1.74, 95% CI 1.63-1.85), Death (HR=1.25 95% CI 1.13-1.39), and IHD, stroke, HF, AF, AS, PHTN, PAD and VTE. Conclusions: Our results suggest that menopausal HT is associated with increased risk of a broad range of CVD and death in WV 45 years and older.

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The burden of sleep disturbances and vasomotor symptoms on work productivity, activity impairment and healthcare resource use in perimenopausal and postmenopausal women

Paula Briggs 1, Carina Dinkel-Keuthage, Joehl Nguyen, Nils Schoof, Carsten Moeller, Kristina Rosa Bolling, et al. Objective: To explore relationships between sleep disturbances and vasomotor symptoms (VMS) with work productivity/activity impairment (WPAI) and healthcare visits among peri- and postmenopausal women. Study design: We analyzed data from peri- and postmenopausal women aged 40-65 years who participated in the National Health and Wellness 2019/2021 survey (in the US; N = 27,621) and 2017/2020 survey (in France, Germany, Italy, Spain, and the UK; N = 20,220). We used generalized linear regression to calculate adjusted estimated marginal means (EMMs) to assess differences between four subgroups based on self-reported sleep disturbances and VMS. Main outcome measures: Scores on the WPAI questionnaire (higher scores indicating worse outcomes); number of healthcare visits in the previous 6 months. Results: Among postmenopausal women, those with symptoms had worse WPAI outcomes than those with neither type of symptom. The highest scores (worst outcomes) were seen for women with both symptoms: the EMMs for this group in the US survey, vs. those with neither symptom, were 11.9 % vs. 9.3 % for presenteeism, 12.8 % vs. 10.2 % for work productivity impairment, and 20.3 % vs. 16.2 % for activity impairment. Corresponding estimates for Europe were 17.4 % vs. 12.9 % for presenteeism, 18.8 % vs. 14.4 % for work productivity impairment, and 28.1 % vs. 20.9 % for activity impairment. Worse WPAI outcomes were not clearly observed in perimenopausal women with symptoms vs. those with no symptoms. However, both peri- and postmenopausal women with symptoms had more previous healthcare visits than those with neither symptom, especially those with sleep disturbances irrespective of co-occurring VMS. Conclusions: Sleep disturbances and VMS were associated with worse WPAI scores and more healthcare visits in postmenopausal women, indicating a need for effective management of these symptoms among this population.

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Beneficial glycometabolic effects of transdermal 17-β estradiol in a population of hypertensive postmenopausal women

Rosario Rossi 1, Fabio A Sgura 2, Francesca Coppi 2, Salvatore Arrotti 2, Daniel E Monopoli 2, Giuseppe Boriani 2 Background: It is known that 17-beta estradiol, administered in the postmenopausal period, is able to positively influence blood glucose concentration, as well as the incidence of DM over time. Postmenopausal hypertensive women are a group of patients at high risk of developing diabetes mellitus. The aim of this prospective matched cohort study was to evaluate whether estrogen influences the glycometabolic profile also in postmenopausal hypertensive women. Methods: The present study selected hypertensive postmenopausal women, treated with 17-beta estradiol administered transdermally at a dose of 50 µg per 24 hours. Hypertensive patients who were never treated with hormones served as control group. Results: We compared HbA1c among 1418 postmenopausal hypertensive women: 709 treated with 17-beta estradiol, and 709 age-matched never treated with hormones. Length of the follow-up resulted in a median time of 4.5 years (25th-75th percentiles=3.0-5.5 years). At baseline, the concentration of HbA1c was 5.6% in both groups. HbA1c (mean±SEM) was significantly lower at 6-months in patients treated with 17-beta estradiol (5.0±0.05%) compared with no-hormones group (5.5±0.04%); absolute decline from baseline was -0.6±0.06% with 17-beta-estradiol, compared with -0.1±0.04% (P<0.0001). New-onset DM was significantly reduced in the group of 17-beta estradiol (adjusted relative risk=2.04; 95%CI: 1.03-3.05; P=0.01). Conclusions: 17-beta estradiol significantly improved HbA1c and reduced the long-term incidence of new-onset diabetes mellitus in the postmenopausal hypertensive population.

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The burden of sleep disturbances on quality of life and mental well-being in nearly 50,000 perimenopausal and postmenopausal women with and without concurrent vasomotor symptoms from the United States and Europe

Claudio N Soares, Paula Briggs, Carina Dinkel-Keuthage, Nils Schoof, Carsten Moeller, Joehl Nguyen, et al. Objectives: To quantify the burden of sleep disturbances on health-related quality of life (HRQoL) and mental well-being in perimenopausal and postmenopausal women with/without co-occurring vasomotor symptoms (VMS). Methods: Perimenopausal and postmenopausal women aged 40 to 65 years who participated in the National Health and Wellness 2019/2021 (US; N=27,621) and 2017/2020 cross-sectional surveys (France, Germany, Italy, Spain, UK;

N=20,220) were included. Patient-reported outcomes were HRQoL (Short-Form Health Survey physical and mental component summary scores, EuroQol Visual Analogue Scale, EQ-5D-5L), depression (Patient Health Questionnaire-9), and anxiety (Generalized Anxiety Disorder-7 assessment). Associations between self-reported sleep disturbances and/or VMS and study outcomes were evaluated using generalized multivariable linear regression. Results: Among perimenopausal women, sleep disturbances were reported by 61.7% (US) and 60.6% (Europe) with VMS, and 38.0% (US) and 40.8% (Europe) without VMS. Among postmenopausal women, sleep disturbances were reported by 66.7% (US) and 63.4% (Europe) with VMS, and 44.5% (US) and 40.9% (Europe) without VMS. Compared with women with neither symptom, perimenopausal and postmenopausal women with sleep disturbances had worse HRQoL ($P<0.001$) and higher (worse) depression and anxiety scores ($P<0.05$ perimenopausal, $P<0.001$ postmenopausal) irrespective of VMS. In addition, among postmenopausal women, those with sleep disturbances alone had worse HRQoL and higher (worse) depression and anxiety scores than those with VMS alone ($P<0.001$). Conclusions: Sleep disturbance was common among perimenopausal and postmenopausal women irrespective of VMS, and independently associated with negative effects on HRQoL, depression, and anxiety. Effective treatments for sleep disturbances and VMS in menopausal women are needed to mitigate the associated burden and improve well-being.

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Association between metabolic syndrome and risk of cardiovascular disease among postmenopausal women: A cohort study

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Aim: Cardiovascular disease is the leading cause of death among women worldwide. Metabolic syndrome is more prevalent after menopause. The decline in estrogen during this transition promotes adverse metabolic and vascular changes, substantially elevating cardiovascular risk. However, evidence on the impact of metabolic syndrome on cardiovascular risk in postmenopausal women remains limited. **Materials and methods:** This study utilized data from the Kailuan cohort, which initially enrolled 32959 women. After matching participants by age in a 1:2 ratio, a total of 5210 postmenopausal women were included, with a median follow-up of 15.53 years. Multivariable Cox proportional hazards models were employed to evaluate the associations between metabolic syndrome and incident cardiovascular disease, including cerebrovascular disease and myocardial infarction, while adjusting for confounding variables. Stratified and sensitivity analyses were conducted to validate the robustness of the findings. **Results:** During follow-up there were 398 incident CVD events (MetS-: 197; MetS+: 201). After full adjustment, MetS was associated with a two-fold higher CVD risk (HR 2.01, 95% CI 1.64-2.46). Comparable associations were observed for the subtypes: cerebrovascular disease (HR, 1.83; 95% CI, 1.47-2.27) and myocardial infarction (HR, 3.28; 95% CI, 1.97-5.46). The association was strongest in women with early menopause ((45 years) (HR 3.86, 95% CI 1.29-11.53). Among MetS components, elevated fasting blood glucose appeared the largest contributor: excluding the glucose component reduced the overall MetS-CVD HR from 2.01 to 1.82 (95% CI 1.48-2.24). Results were robust in sensitivity analyses. **Conclusions:** Postmenopausal women with metabolic syndrome have significantly higher risks of cardiovascular disease. In subgroup analyses, these findings were more pronounced among those with early menopause or elevated fasting blood glucose. In Conclusion, the findings underscore the importance of early detection of metabolic syndrome and targeted prevention strategies to reduce cardiovascular morbidity and mortality in this high risk population.

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Mechanistic pathways of estrogen mitigating postmenopausal gut dysbiosis

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Estrogen is classically considered an essential hormone signal and exerts profound effects on several physiological and pathological states, including gut health. Estrogen deficiency after menopause in most women leads to increased androgenicity and changes in body composition. It is recommended to manipulate the composition of gut bacteria, which alters gut integrity and hence leads to gut microbiota (GM) dysbiosis. Normally, the gut maintains its epithelial microvilli integrity with the help of intestinal barriers, such as tight junction (TJ) proteins (claudin, occludin, and epithelial cadherin), short-chain fatty acids (SCFAs) (acetic acid, propionic acid, isobutyric acid, formic acid, and butyric acid), and mucin. Estrogen influences the bacteria present in the gut. It appears to safeguard the integrity of the gut by inhibiting the breakdown of SCFAs, TJ proteins, and mucin. This protective mechanism serves to prevent the onset of dysbiosis. The estrobolome specialises in the processing of estrogen, playing a pivotal role in regulating estrogen metabolism within the gut. This imbalance is intricately linked to alterations in the estrobolome and endobolome, thereby influencing estrogen metabolism and availability. The estrogen deficiency and associated expressions of TJ proteins, SCFAs, and

mucin advance the progression of postmenopausal-induced gynaecological disorders. However, the alterations in the composition and diversity of GM observed during menopause emphasize the pivotal role of estrogen in shaping the gut environment. Estrogen intricately regulates the estrobolome, TJ proteins, mucin, and SCFAs. Via this review, we have tried our best to enlighten on the detailed mechanisms showing the crosslink between estrogen and gut health.

Nota. El estroboloma es el conjunto de microorganismos intestinales capaces de metabolizar los estrógenos.

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Association between central adiposity and cognitive domain function in recently postmenopausal women: an analysis from the KEEPS-Cog substudy of the Kronos Early Estrogen Preventive Study

Taryn T James, N Maritza Dowling, Carola Ferrer Simó, Hector Salazar, Carol A Van Hulle, Gilda Ennis, et al. Objective: To determine associations between central adiposity, cognitive function, and randomized menopausal hormone therapy (MHT) in a reanalysis of the Kronos Early Estrogen Prevention Study-Cognitive and Affective (KEEPS-Cog) sub-study participants. Methods: KEEPS randomized 727 women (ages 42-58) who were <36 months postnatural menopause to oral conjugated equine estrogens (o-CEE), transdermal 17- β -estradiol (t-E2), or placebo for 48 months. Participants with diabetes, body mass index >35 kg/m², coronary artery calcium score >50 Agatston Units, and other cardiometabolic disease risk indicators were excluded from enrollment. In the ancillary KEEPS-Cog study, cognitive tests were completed at baseline, 18-, 36-, and 48-month post-randomization. In these analyses, cognitive variables were summarized as four cognitive domain-specific factor scores: verbal learning and memory, auditory attention and working memory, visual attention and executive function, and speeded language and mental flexibility. Waist-hip-ratio (WHR), an indicator of central adiposity, was measured at screening (baseline) and modeled as a covariate in linear latent growth models assessing associations of MHT with cognitive functions at baseline and over time. Results: Higher baseline WHR was associated with poorer performance on all domain-specific cognitive outcomes at baseline and with changes in visual attention and executive function across time. Models including interaction effects were not significant for either o-CEE x WHR or t-E2 x WHR. Conclusion: Central adiposity is a risk factor for domain-specific cognitive decline, and thus, cognitive health effects should be investigated in early postmenopausal women, even in women with low cardiovascular risk statuses.

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Metabolic impact of endogenously produced estrogens by adipose tissue in females and males across the lifespan

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The aged population, expected to double by 2050, makes up a large proportion of people living with metabolic disease. Obesity rates in the elderly are rapidly increasing, with estimates that nearly 40% of men and women over the age of 60 are classified as obese. White adipose tissue (WAT) is a highly metabolically active organ that undergoes significant changes during both obesity and aging, and metabolic dysfunction in WAT is a major cause for elevated diabetes risk. A marked difference in fat distribution is often reported between men and women. Many studies suggest that premenopausal women are protected from the accumulation of visceral adiposity due to gonadal estrogen, which exerts cardiometabolic benefits. Men with obesity harbor a disproportionately higher volume of intra-abdominal fat than premenopausal age-matched women with obesity, an effect that is negated by menopause as women begin to gain intra-abdominal fat. Post-menopausal women are at increased risk of developing diabetes, which can be mitigated by estrogen replacement therapy, suggesting an important role for sex steroids in diabetes risk. In addition to being highly responsive to gonadal estrogens, WAT has the capacity to convert androgens into estrogens, which may similarly impact WAT distribution and metabolism. Estrogens, comprised primarily of estrone (E1) and estradiol (E2) within WAT, are biosynthesized from circulating androgens androstenedione (A4) and testosterone (T) by aromatase (CYP19A1), which is highly expressed in human and mouse adipose tissue. In post-menopausal women, WAT becomes the predominant source of estrogen production, with age-associated increases in WAT aromatase expression that are mirrored by obesity. In contrast to ovarian estrogen production, in which E2 is the predominant estrogen type, E1 tends to be the predominant estrogen post-menopause. To date, little is known about WAT-derived estrogens and their impact on metabolic health, but emerging evidence suggests that increased E1 levels may contribute to metabolic dysfunction in aging. This review will introduce known sex differences in adipose metabolism associated with aging, obesity, and diabetes, and discuss the impact of WAT-derived sex hormones on local and systemic metabolism.