



## Selección de Resúmenes de Menopausia

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### Menopause and development of Alzheimer's disease: Roles of neural glucose metabolism and Wnt signaling

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Late onset Alzheimer's disease (AD) is a neurodegenerative disease with gender differences in its onset and progression, being the prevalence predominant in women and at an earlier age than in men. The pathophysiology of the menopausal condition has been associated to this dementia, playing major roles regarding both endocrine and glucose metabolism changes, amongst other mechanisms. In the current review we address the role of estrogen deficiency in the processes involved in the development of AD, including amyloid precursor protein (APP) processing to form senile plaques, Tau phosphorylation forming neurofibrillary tangles, Wnt signaling and AD neuropathology, the role of glucose brain metabolism, Wnt signaling and glucose transport in the brain, and our research contribution to these topics.

**J Obstet Gynaecol. 2022 Nov 4;1-4.doi: 10.1080/01443615.2022.2141618. Online ahead of print.**

### Steroid hormone levels in postmenopausal hysterectomised women with and without ovarian conservation: the continuous endocrine function of the ovaries

Elsa Nunes <sup>1</sup>, Eugenia Gallardo <sup>1 2</sup>, Sara Morgado-Nunes <sup>3</sup>, José Fonseca-Moutinho <sup>1</sup>

This study aims to clarify the effect of postmenopausal bilateral oophorectomy on plasma steroid hormone levels. Women who were submitted in the postmenopausal period to hysterectomy for uterine benign conditions were divided into two groups: 18 women had isolated hysterectomy and 11 had hysterectomy with bilateral salpingo-oophorectomy. In both groups serum hormone levels were quantified by solid phase extraction and gas chromatography and tandem mass spectrometry. Differences in dehydroepiandrosterone (DHEA), testosterone, androstenedione and oestradiol were determined in both groups. The analysis revealed lower steroid levels in the bilateral salpingo-oophorectomy group when compared to the isolated hysterectomy group with statistically significant differences found for DHEA ( $5.8 \pm 3.2$  vs.  $9.4 \pm 4.4$  ng/mL;  $p = 0.019$ ) and oestradiol ( $0.69 \pm 0.4$  vs.  $1.48 \pm 4.3$  ng/mL;  $p = 0.007$ ). The results are consistent with a significant endocrine activity of the postmenopausal ovary. The clinical consequences of these findings need to be clarified and postmenopausal prophylactic bilateral salpingo-oophorectomy re-evaluated. **IMPACT STATEMENT** What is already known on this subject? Although it is consensual that premenopausal prophylactic bilateral oophorectomy should not be performed because it has harmful effects on women's health, the evidence regarding the effects of postmenopausal prophylactic bilateral oophorectomy is scarce and this procedure continues to be a regular practice. Few studies have demonstrated that postmenopausal ovaries still have endocrine activity that may impact older women's health. What do the results of this study add? This is the first study to compare hormone levels of postmenopausal women based on their hysterectomy and oophorectomy status using GC-MS/MS, a highly sensitive bioanalytical assay for the measurement of steroid hormones. Previous studies relied on immunoassays and did not compare DHEA levels, which according to the intracrinology theory is a precursor for androgens and oestrogens. In this study, statistically significant lower levels of DHEA and oestradiol were found after postmenopausal bilateral salpingo-oophorectomy. What are the implications of these findings for clinical practice and/or further research? This is a pilot study that may lead to further investigation in this area to clarify the impact of the prophylactic removal of postmenopausal ovaries on older women's health and lead to changes in surgical procedures.

**J Comp Eff Res. 2022 Nov 4.doi: 10.2217/ceer-2022-0086. Online ahead of print.**

### Quality of life analysis measured with the Cervantes 16 scale in treated menopausal women with genitourinary syndrome

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**Aim:** To assess the quality of life of menopausal women with genitourinary syndrome receiving local drugs (prasterone, estriol or promestriene). **Methods:** Prospective, longitudinal, randomized study in which quality of life was assessed using the 16-item Cervantes scale (EC16) before and after treatment. **Results:** A total of 45 women were assessed (35.6% received prasterone, 33.3% estriol and 31.1% promestriene). After treatment, statistically significant mean score differences were observed in EC16, mainly with prasterone. Improvement in EC16 score only shows a statistically significant relationship with age and drug use. **Conclusion:** The EC16 is an affordable and quick-to-apply tool that allows physicians and patients to know patients' self-perceived quality of life. Local treatment has been shown to improve the quality of life of menopausal patients with genitourinary syndrome.

**Arterioscler Thromb Vasc Biol. 2022 Nov 3;doi: 10.1161/ATVBAHA.122.318408. Online ahead of print.**

## **Higher Habitual Dietary Flavonoid Intake Associates with Less Extensive Abdominal Aortic Calcification in a Cohort of Older Women**

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**Background:** The extent of abdominal aortic calcification (AAC) is a major predictor of vascular disease events. We have previously found regular apple intake, a major source of dietary flavonoids, associates with lower AAC. Whether total dietary flavonoid intake impacts AAC remains unknown. Here, we extend our observations to habitual intakes of total flavonoids, flavonoid subclasses, and specific flavonoid-containing foods, with the odds of extensive AAC. **Methods:** We conducted cross-sectional analyses on 881 females (median [interquartile range] age, 80 [78-82] years; body mass index, 27 [24-30] kg/m<sup>2</sup>) from the PLSAW (Perth Longitudinal Study of Ageing Women). Flavonoid intake was calculated from food-frequency questionnaires. Calcifications of the abdominal aorta were assessed on lateral lumbar spine images and categorized as less extensive or extensive. Logistic regression was used to investigate associations. **Results:** After adjusting for demographic, lifestyle and dietary confounders, participants with higher (Q4), compared with lower (Q1) intakes, of total flavonoids, flavan-3-ols, and flavonols had 36% (odds ratio [95% CI], 0.64 [0.43-0.95]), 39% (0.61 [0.40-0.93]) and 38% (0.62 [0.42-0.92]) lower odds of extensive AAC, respectively. In food-based analyses, higher black tea intake, the main source of total flavonoids (75.9%), associated with significantly lower odds of extensive AAC (2-6 cups/d had 16%-42% lower odds compared with 0 daily intake). In a subset of nonconsumers of black tea, the association of total flavonoid intake with AAC remained (Q4 versus Q1 odds ratio [95% CI], 0.11 [0.02-0.54]). **Conclusions:** In older women, greater habitual dietary flavonoid intake associates with less extensive AAC.

**Ther Adv Endocrinol Metab. 2022 Oct 28;13:20420188221129946;doi: 10.1177/20420188221129946. eCollection 2022.**

## **Menopause, androgens, and cardiovascular ageing: a narrative review**

Eleni Armeni <sup>1</sup>, Irene Lambrinouadaki <sup>2</sup>

Cardiovascular disease is the leading cause of death worldwide; however, women tend to be less affected than men during their reproductive years. The female cardiovascular risk increases significantly around the time of the menopausal transition. The loss of the protective action of ovarian oestrogens and the circulating androgens has been implicated in possibly inducing subclinical and overt changes in the cardiovascular system after the menopausal transition. In vitro studies performed in human or animal cell lines demonstrate an adverse effect of testosterone on endothelial cell function and nitric oxide bioavailability. Cohort studies evaluating associations between testosterone and/or dehydroepiandrosterone and subclinical vascular disease and clinical cardiovascular events show an increased risk for women with more pronounced androgenicity. However, a mediating effect of insulin resistance is possible. Data on cardiovascular implications following low-dose testosterone treatment in middle-aged women or high-dose testosterone supplementation for gender affirmatory purposes remain primarily inconsistent. It is prudent to consider the possible adverse association between testosterone and endothelial function during the decision-making process of the most appropriate treatment for a postmenopausal woman.

**Menopause. 2022 Nov 1;doi: 10.1097/GME.0000000000002081. Online ahead of print.**

## **Changes in cardiovascular disease risk factors during menopausal transition in Japanese women: the Circulatory Risk in Communities Study (CIRCS)**

Saki Teramura <sup>1</sup>, Tomoko Sankai <sup>2</sup>, Kazumasa Yamagishi, Mitsumasa Umesawa <sup>3</sup>, Mina Hayama-Terada, et al.

**Objective:** We aimed to longitudinally clarify the changes in cardiovascular disease risk factors associated with menopause in Japanese women in the 2000s. **Methods:** Of the 4,596 women who underwent health examinations between 2007 and 2012 in three communities of the Circulatory Risk in Communities Study, 263 women who reported going through menopause during that period were included in the study. We randomly selected 1,665 men as control subjects who participated in a health examination at least once between 2001 and 2009 and at least once between 2010 and 2018 by 1:1 pair-matching for age, community, and examination year. The health examination data from 3 to 6 years before (2001-2009) and after menopause age (2010-2018) were compared in terms of body mass index, systolic and diastolic blood pressure levels, serum total cholesterol, high-density lipoprotein cholesterol, non-high-density lipoprotein cholesterol, triglycerides, uric acid, hemoglobin A1c, hemoglobin, aspartate aminotransferase, alanine aminotransferase, and current smoker status. **Results:** Compared with the men, the women showed a greater increase in serum total cholesterol (+16.7 vs -3.1 mg/dL,  $P < 0.001$ ), non-high-density lipoprotein cholesterol (+15.9 vs -6.3 mg/dL,  $P < 0.001$ ), fasting triglycerides (+1.2 vs +1.0 mg/dL,  $P = 0.027$ ), triglycerides regardless of fasting status (+1.2 vs -0.9 mg/dL,  $P < 0.001$ ), uric acid (+0.5 vs +0.2 mg/dL,  $P = 0.008$ ), hemoglobin (+0.9 vs -0.3 g/dL,  $P < 0.001$ ), aspartate aminotransferase (+2.9 vs -2.7 IU/L,  $P < 0.001$ ), and alanine aminotransferase (+2.9 vs -2.6 IU/L,  $P < 0.001$ ). No differences were found in the changes in body mass index, systolic and diastolic blood pressures, and hemoglobin A1c between the women and the matched men. **Conclusions:** Menopause may be a crucial factor related to changes in serum total cholesterol, non-high-density lipoprotein cholesterol, triglycerides, uric acid, hemoglobin, and liver enzymes.

**JAMA. 2022 Nov 1;328(17):1747-1765.doi: 10.1001/jama.2022.18324.**

## **Hormone Therapy for the Primary Prevention of Chronic Conditions in Postmenopausal Persons: Updated Evidence Report and Systematic Review for the US Preventive Services Task Force**

Gerald Gartlehner<sup>1, 2</sup>, Sheila V Patel<sup>1</sup>, Shivani Reddy<sup>1</sup>, Caroline Rains<sup>1</sup>, Manny Schwimmer<sup>3</sup>, et al

**Importance:** It is uncertain whether hormone therapy should be used for the primary prevention of chronic conditions such as heart disease, osteoporosis, or some types of cancers. **Objective:** To update evidence for the US Preventive Services Task Force on the benefits and harms of hormone therapy in reducing risks for chronic conditions. **Data sources:** PubMed/MEDLINE, Cochrane Library, EMBASE, and trial registries from January 1, 2016, through October 12, 2021; surveillance through July 2022. **Study selection:** English-language randomized clinical trials and prospective cohort studies of fair or good quality. **Data extraction and synthesis:** Dual review of abstracts, full-text articles, and study quality; meta-analyses when at least 3 similar studies were available. **Main outcomes and measures:** Morbidity and mortality related to chronic conditions; health-related quality of life. **Results:** Twenty trials ( $N = 39\ 145$ ) and 3 cohort studies ( $N = 1\ 155\ 410$ ) were included. Participants using estrogen only compared with placebo had significantly lower risks for diabetes over 7.1 years (1050 vs 903 cases; 134 fewer [95% CI, 18-237]) and fractures over 7.2 years (1024 vs 1413 cases; 388 fewer [95% CI, 277-489]) per 10 000 persons. Risks per 10 000 persons were statistically significantly increased for gallbladder disease over 7.1 years (1113 vs 737 cases; 377 more [95% CI, 234-540]), stroke over 7.2 years (318 vs 239 cases; 79 more [95% CI, 15-159]), venous thromboembolism over 7.2 years (258 vs 181 cases; 77 more [95% CI, 19-153]), and urinary incontinence over 1 year (2331 vs 1446 cases; 885 more [95% CI, 659-1135]). Participants using estrogen plus progestin compared with placebo experienced significantly lower risks, per 10 000 persons, for colorectal cancer over 5.6 years (59 vs 93 cases; 34 fewer [95% CI, 9-51]), diabetes over 5.6 years (403 vs 482 cases; 78 fewer [95% CI, 15-133]), and fractures over 5 years (864 vs 1094 cases; 230 fewer [95% CI, 66-372]). Risks, per 10 000 persons, were significantly increased for invasive breast cancer (242 vs 191 cases; 51 more [95% CI, 6-106]), gallbladder disease (723 vs 463 cases; 260 more [95% CI, 169-364]), stroke (187 vs 135 cases; 52 more [95% CI, 12-104]), and venous thromboembolism (246 vs 126 cases; 120 more [95% CI, 68-185]) over 5.6 years; probable dementia (179 vs 91 cases; 88 more [95% CI, 15-212]) over 4.0 years; and urinary incontinence (1707 vs 1145 cases; 562 more [95% CI, 412-726]) over 1 year. **Conclusions and relevance:** Use of hormone therapy in postmenopausal persons for the primary prevention of chronic conditions was associated with some benefits but also with an increased risk of harms.

**JAMA. 2022 Nov 1;328(17):1740-1746.doi: 10.1001/jama.2022.18625.**

## **Hormone Therapy for the Primary Prevention of Chronic Conditions in Postmenopausal Persons: US Preventive Services Task Force Recommendation Statement**

US Preventive Services Task Force; Carol M Mangione <sup>1</sup>, Michael J Barry <sup>2</sup>, Wanda K Nicholson, et al.

**Importance:** Menopause is defined as the cessation of a person's menstrual cycle. It is defined retrospectively, 12 months after the final menstrual period. Perimenopause, or the menopausal transition, is the few-year time period preceding a person's final menstrual period and is characterized by increasing menstrual cycle length variability and periods of amenorrhea, and often symptoms such as vasomotor dysfunction. The prevalence and incidence of most chronic diseases (eg, cardiovascular disease, cancer, osteoporosis, and fracture) increase with age, and US persons who reach menopause are expected on average to live more than another 30 years. **Objective:** To update its 2017 recommendation, the US Preventive Services Task Force (USPSTF) commissioned a systematic review to evaluate the benefits and harms of systemic (ie, oral or transdermal) hormone therapy for the prevention of chronic conditions in postmenopausal persons and whether outcomes vary by age or by timing of intervention after menopause. **Population:** **Asymptomatic postmenopausal persons** who are considering hormone therapy for the primary prevention of chronic medical conditions. **Evidence assessment:** The USPSTF concludes with moderate certainty that the use of combined estrogen and progestin for the primary prevention of chronic conditions in postmenopausal persons with an intact uterus has no net benefit. The USPSTF concludes with moderate certainty that the use of estrogen alone for the primary prevention of chronic conditions in postmenopausal persons who have had a hysterectomy has no net benefit. **Recommendation:** The USPSTF recommends against the use of combined estrogen and progestin for the primary prevention of chronic conditions in postmenopausal persons. (D recommendation) The USPSTF recommends against the use of estrogen alone for the primary prevention of chronic conditions in postmenopausal persons who have had a hysterectomy. (D recommendation).