# Selección de Resúmenes de Menopausia

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## Isoflavone Consumption and Risk of Breast Cancer: An Updated Systematic Review with Meta-Analysis of Observational Studies

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Rationale: Epidemiological studies that focus on the relationship between dietary isoflavone intake and the risk of breast cancer still lead to inconsistent conclusions. Herein, we conducted a meta-analysis of the latest studies to explore this issue. Method: We performed a systematic search using Web of Science, PubMed, and Embase from inception to August 2021. The robust error meta-regression (REMR) model and generalized least squares trend (GLST) model were used to establish dose-response relationships between isoflavones and breast cancer risk. Results: Seven cohort studies and 17 case-control studies were included in the meta-analysis, and the summary OR for breast cancer was 0.71 (95% CI 0.72-0.81) when comparing the highest to the lowest isoflavone intake. A subgroup analysis further showed that neither menopausal status nor ER status has a significant influence on the association between isoflavone intake and breast cancer risk, while the isoflavone intake doses and study design does. When the isoflavones exposure was less than 10 mg/day, no effects on breast cancer risk were detected. The inverse association was significant in the case-control studies but not in the cohort studies. In the dose-response meta-analysis of the cohort studies, we observed an inverse association between isoflavone intake and breast cancer: a 10 mg/day increase in isoflavone intake was related to reductions of 6.8% (OR = 0.932, 95% CI 0.90-0.96) and 3.2% (OR = 0.968, 95% CI 0.94-0.99) in breast cancer risk when using REMR and GLST, respectively. In the dose-response meta-analysis of the case-control studies, the inverse association for every 10 mg/day isoflavone intake was associated with breast cancer risk reductions by 11.7%. Conclusion: present evidence demonstrated that taking in dietary isoflavone is helpful in reducing the breast cancer risk.

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## Bone health in breast cancer

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Early breast cancer is among the most common cancers worldwide. Recent advances continue to improve outcomes and increase long-term survivorship. However, therapeutic modalities are deleterious for patients' bone health. While antiresorptive therapy may partially negate this, consequent reduction in rates of fragility fractures remains unproven. Selective prescription of bisphosphonates or denosumab may be an amicable middle ground. Recent evidence also suggests a possible role of osteoclast inhibitors as adjuvant therapy, but the evidence is modest at best. In this narrative clinical review, we explore the impact of various adjuvant modalities on bone mineral density and fragility fracture rates of early breast cancer survivors. We also review optimal patient selection for antiresorptive agents, their impact on rates of fragility fractures, and the possible role of these agents as adjuvant therapy.

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## The Role of Vitamin D in Reducing the Risk of Metabolic Disturbances that Cause Cardiovascular Diseases

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Among the most common problems facing public health today is a lack of vitamin D, which plays a role in the physiological processes of chronic illness conditions. Vitamin D deficiency in metabolic disorders has primary effects on osteoporosis, obesity, hypertension, diabetes, and cardiovascular disease (CVD). Vitamin D acts as a "co-hormone" in the various tissues of the body, and it has been found that vitamin D receptors (VDR) are present on all cell types, suggesting that vitamin D has a wide range of effects on most cells. Recently, there has been a surge in interest in assessing its roles. Vitamin D insufficiency increases the risk of diabetes because it lowers insulin sensitivity, and also raises the risk of obesity and CVD because of its effect on the body's lipid profile, particularly in terms of the prevalence

of dangerously high levels of low-density lipoproteins (LDL). Furthermore, vitamin D insufficiency is often related to CVD and connected risk factors, highlighting the need to know vitamin D's functions in relation to metabolic syndrome and related processes. Through looking at previous studies, this paper explains why vitamin D is important, how deficiency is related to risk factors for metabolic syndrome through different mechanisms, and how deficiency affects CVD.

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## Impacts of pregnancy and menopause on COVID-19 severity: A systematic review and meta-analysis of 4.6 million women

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Background: COVID-19 pandemic is still a public health emergency of international concern. However, whether pregnancy and menopause impact the severity of COVID-19 remain unclear. Aim: This study is performed to investigate the truth. Design: Study appraisal and Synthesis follows PRISMA guideline. Meta-analysis is performed in random-effects model. Methods: PubMed, Embase, Cochrane database, Central, CINAHL, ClinicalTrials.gov, WHO COVID-19 database, and WHO-ICTRP are searched until March 28 2023. Results: In total, 57 studies (4,640,275 COVID-19 women) were analyzed. Pregnant women were at a lower risk of severe COVID-19, intensive care unit (ICU) admission and disease mortality compared to those nonpregnant women with comparable comorbidities. In contrast, pregnant women with more prepregnancy comorbidities were at a higher risk of severe COVID-19, ICU admission and invasive mechanical ventilation (IMV). In addition, pregnant women with pregnancy complications had a significantly increased risk of severe COVID-19 and ICU admission. Menopause increased COVID-19 severity, IMV requirement and disease mortality. Hormone replacement therapy (HRT) inhibited COVID-19 severity in postmenopausal women. Premenopausal and postmenopausal women had a lower chance of severe illness than age-matched men. The impact of pregnancy on COVID-19 severity was significant in Americans and Caucasians, while the effect of menopause on COVID-19 severity was only significant in Chinese. Conclusions: Pregnancy and menopause are protective and risk factors for severe COVID-19, respectively. The protective role of pregnancy on COVID-19 is minimal and could be counteracted or masked by prepregnancy or pregnancy comorbidities. The administration of estrogen and progesterone may prevent severe COVID-19.

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## Understanding of and clinical approach to cardiometabolic transition at the menopause

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Cardiovascular disease (CVD) represents the leading cause of death and accounts for almost 50% of all deaths in women worldwide. The menopausal transition is associated with central body fat accumulation, a decrease in energy expenditure, weight gain, insulin resistance and a pro-atherogenic lipid profile. Moreover, menopause is independently associated with an adverse effect on functional and structural indices of subclinical atherosclerosis. Women with premature ovarian insufficiency have heightened CVD risk compared to women of natural age at menopause. Furthermore, women with severe menopausal symptoms may have a more adverse cardiometabolic profile than those without symptoms. We reviewed the latest evidence on the cardiovascular management of perimenopausal or postmenopausal women. Clinicians should aim for cardiovascular risk stratification, followed by dietary and lifestyle advice as required based on individual needs. The medical management of cardiometabolic risk factors at midlife should always be individualized, focusing on hypertension, diabetes and dyslipidemia. Menopausal hormone therapy, when prescribed for the management of bothersome menopausal symptoms or for the prevention of osteoporosis, has also a beneficial effect on cardiometabolic risk factors. This narrative review aims to summarize the cardiometabolic alternations occurring during the menopausal transition and to outline the appropriate prevention strategies to prevent future cardiovascular adverse outcomes.

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## Prediabetes and Fracture Risk Among Midlife Women in the Study of Women's Health Across the Nation

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Importance: Whether prediabetes is associated with fracture is uncertain. Objective: To evaluate whether prediabetes before the menopause transition (MT) is associated with incident fracture during and after the MT. Design, setting, and participants: This cohort study used data collected between January 6, 1996, and February 28, 2018, in the Study of Women's Health Across the Nation cohort study, an ongoing, US-based, multicenter, longitudinal study of the MT in diverse ambulatory women. The study included 1690 midlife women in premenopause or early perimenopause at study inception (who have since transitioned to postmenopause) who did not have type 2 diabetes before the MT and who did not take bone-beneficial medications before the MT. Start of the MT was defined as the first visit in late perimenopause (or first postmenopausal visit if participants transitioned directly from premenopause or early perimenopause to postmenopause). Mean (SD) follow-up was 12 (6) years. Statistical analysis was conducted from January to May 2022. Exposure: Proportion of visits before the MT that women had prediabetes (fasting glucose, 100-125 mg/dL [to convert to millimoles per liter, multiply by 0.0555]), with values ranging from 0 (prediabetes at no visits) to 1 (prediabetes at all visits). Main outcomes and measures: Time to first fracture after the start of the MT, with censoring at first diagnosis of type 2 diabetes, initiation of bone-beneficial medication, or last follow-up. Cox proportional hazards regression was used to examine the association (before and after adjustment for bone mineral density) of prediabetes before the MT with fracture during the MT and after menopause. Results: This analysis included 1690 women (mean [SD] age, 49.7 [3.1] years; 437 Black women [25.9%], 197 Chinese women [11.7%], 215 Japanese women [12.7%], and 841 White women [49.8%]; mean [SD] body mass index [BMI] at the start of the MT, 27.6 [6.6]). A total of 225 women (13.3%) had prediabetes at 1 or more study visits before the MT, and 1465 women (86.7%) did not have prediabetes before the MT. Of the 225 women with prediabetes, 25 (11.1%) sustained a fracture, while 111 of the 1465 women without prediabetes (7.6%) sustained a fracture. After adjustment for age, BMI, and cigarette use at the start of the MT; fracture before the MT; use of bone-detrimental medications; race and ethnicity; and study site, prediabetes before the MT was associated with more subsequent fractures (hazard ratio for fracture with prediabetes at all vs no pre-MT visits, 2.20 [95% CI, 1.11-4.37]; P = .02). This association was essentially unchanged after controlling for BMD at the start of the MT. Conclusions and relevance: This cohort study of midlife women suggests that prediabetes was associated with risk of fracture. Future research should determine whether treating prediabetes reduces fracture risk.

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## Antimüllerian Hormone as a Tool to Predict the Age at Menopause

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This study aimed to assess an eligible cut-off value of anti-Müllerian hormone (AMH) to detect ovarian senescence in a group of premenopausal Greek women to evaluate the possible link between AMH-values and the severity of climacteric symptoms during a follow-up of 24 months. This study included 180 women (group A, 96 women of late reproductive stage/early perimenopause; group B, 84 women in late perimenopause). We measured AMH blood levels and assessed climacteric symptoms using the Greene scale. Log-AMH is inversely associated with postmenopausal status. The AMH cut-off of 0.012 ng/mL predicts the postmenopausal status with a sensitivity of 24.2% and specificity of 30.5%. The postmenopausal stage associated with age (OR = 1.320, 95%CI: 1.084-1.320) and AMH (values ≥ vs. <0.012 ng/mL, OR = 0.225, 95%CI: 0.098-0.529, p-value < 0.001). Moreover, the severity of vasomotor symptoms (VMS) was only associated inversely with AMH (b-coefficient = -0.272, p-value = 0.027). In conclusion, AMH levels measured in the late premenopausal period are inversely associated with the time to ovarian senescence. In contrast, AMH levels measured in the perimenopausal period are inversely associated only with the severity of VMS. Therefore, a cut-off of 0.012 ng/mL predicts menopause with low sensitivity and specificity, making it challenging to use in a clinical setting.