# Selección de Resúmenes de Menopausia

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## Risk of Fracture in Women with Sarcopenia, Low Bone Mass, or Both.

Harris R, Chang Y, Beavers K, Laddu-Patel D, Bea J, Johnson K, LeBoff M, Womack C, Wallace R, Li W, et al.

Objectives: To determine whether women with sarcopenia and low bone mineral density (BMD) are at greater risk of clinical fractures than those with sarcopenia or low BMD alone. Design: Women's Health Initiative (WHI) bservational and Clinical trials. SETTING: Three U.S. clinical centers (Pittsburgh, PA; Birmingham, AL; Phoenix/Tucson, AZ). PARTICIPANTS: Women (mean age 63.3 ± 0.07) with BMD measurements (N = 10,937). Measurements: Sarcopenia was defined as appendicular lean mass values corrected for height and fat mass. Low BMD was defined as a femoral neck T-score less than -1.0 based on the Third National Health and Nutrition Examination Survey reference database for white women. Cox proportional hazards analysis was used to calculate hazard ratios (HRs) and 95% confidence intervals (CIs). We followed women for incident fractures over a median of 15.9 years. Results: Participants were classified into mutually exclusive groups based on BMD and sarcopenia status: normal BMD and no sarcopenia (n = 3,857, 35%), sarcopenia alone (n = 774, 7%), low BMD alone (n = 4,907, 45%), and low BMD and sarcopenia (n = 1,399, 13%). Women with low BMD, with (HR = 1.72, 95% CI = 1.44-2.06) or without sarcopenia (HR = 1.58, 95% CI = 1.37-1.83), had greater risk of fracture than women with normal BMD; the difference remained statistically significant after adjustment for important covariates. Women with low BMD, with (HR = 2.78, 95% CI = 1.78-4.30 and without (HR = 2.42, 95% CI = 1.63-3.59) sarcopenia had higher risk of hip fractures. Women with sarcopenia alone had similar HRs to women with normal BMD.

**J Biol Regul Homeost Agents. 2017 Jul-Sep;31(3):823-827.**

## Serum 25-hydroxy vitamin D concentration in acute coronary syndrome.

Anastasi E, Suppa M, Viggiani V, Tartaglione S, Angeloni A, Granato T.

Vitamin D may have prognostic value in cardiovascular disease (CVD) patients and, in addition to conventional biomarkers, could be a valuable tool for disease management. The aim of this study was to assess the association of vitamin D status in patients with acute coronary syndrome (ACS) and to evaluate its prognostic utility. The levels of 25(OH) vitamin D were correlated with troponin T hs. Forty-eight consecutive outpatients (40 Caucasian and 8 Asian) aged between 40 and 70 years (mean 61.5, range 43-77 years) were enrolled in the study. All patients were admitted to the Emergency Department with chest pain and suspected ACS. The main exclusion criteria were age <18 years, kidney failure, onco-haematological disease, hypo-hyperparathyroidism, hypo/hyperthyroidism, osteoporosis, treatment with bisphosphonate or 25(OH) vitamin D supplementation. Of the 48 subjects included in the study, thoracic pain symptoms were described in 12 patients with unstable angina (UA) and in 6 patients with ST elevation myocardial infarction (STEMI) and in 30 patients with non-ST-elevation myocardial infarction (NSTEMI). Low 25(OH) vitamin D levels correlated with the presence of ACS ($p < 0.02$) and inversely correlated with Troponin T hs (TnT hs) levels ($p < 0.03$). The determination of 25(OH) vitamin D levels in combination with TnT hs could improve the research for possible underlying conditions, and these should be managed meticulously according to current guidelines.

**Endocrinol Metab (Seoul). 2017 Sep;32(3):339-349. doi: 10.3803/EnM.2017.32.3.339.**

## Calcium and Cardiovascular Disease.

Reid IR, Birstow SM, Bolland MJ.

Circulating calcium is a risk factor for vascular disease, a conclusion arising from prospective studies involving hundreds of thousands of participants and extending over periods of up to 30 years. These associations may be partially mediated by other cardiovascular risk factors such as circulating lipid levels, blood pressure, and body mass index, but there appears to be a residual independent effect of serum calcium. Polymorphisms of the calcium-sensing receptor associated with small elevations of serum calcium are also associated with cardiovascular disease, suggesting that calcium plays a causative role. Trials of calcium supplements in patients on dialysis and those with less severe renal failure demonstrate increased mortality and/or acceleration of vascular disease, and meta-analyses of trials in those without overt renal disease suggest a similar adverse effect. Interpretation of the latter trials is complicated by a significant interaction between baseline use of calcium supplements and the effect of randomisation to calcium in the largest trial. Restriction of analysis to those who are calcium-naive demonstrates a consistent adverse effect. Observational studies of dietary calcium do not demonstrate a consistent

adverse effect on cardiovascular health, though very high or very low intakes may be deleterious. Thus, obtaining calcium from the diet rather than supplements is to be encouraged.

**Arch Osteoporos. 2017 Sep 27;12(1):84. doi: 10.1007/s11657-017-0376-6.**

## Trends in osteoporotic hip fracture epidemiology over a 17-year period in a Spanish population: Alcorcón 1999-2015.

Mazzucchelli Esteban R, Pérez-Fernández E, Crespí-Villarías N, García-Vadillo A, Rodriguez-Caravaca G, et al.

Our aim was to analyze trends in osteoporotic hip fracture rates in a suburban health area over a long time period. We detected a steady decrease, especially in women, that could be explained by historical, administrative, lifestyle changes as well as by medical behavior. PURPOSE: The purpose of this study was to analyze trends in osteoporotic hip fracture rates in a suburban health area over a long time period. METHODS: This is an ecological retrospective study of all discharges occurring in the Alcorcón health area and registered in the minimum basic data set (MBDS). The incidence of osteoporotic hip fracture was calculated by age and sex strata over the last 17 years. General lineal models were used to analyze trends. RESULTS: Between 1999 and 2015, 4271 osteoporotic hip fractures occurred in people over 45 (78% women; mean age 83). The annual osteoporotic hip fracture rate was 290/100,000 persons over 45 (women 428; men 134), or 767/100,000 persons over 65 (women 1087, men 364). The incidence of fractures decreased yearly by 3.6% (95% CI 2.8 to 4.5) in the 1999-2015 period ($p < 0.001$) and was more pronounced in women [3.9% (95% CI 3.0 to 4.8)] than in men [2.4% (95% CI 0.9 to 3.8)]. In people over 65 years, fracture incidence decreased yearly by 3.7% (95% CI 2.8 to 4.6; $p < 0.001$). Again, this was more pronounced in women [4% (95% CI 3.05 to 4.9)] than in men [2.4 (95% CI 0.8 to 3.9)] while the female/male ratio decreased from 4.45 in 1999 to 2.4 in 2015. These differences were similar for extracapsular and intracapsular fractures. CONCLUSIONS: These findings suggest a downward trend in the incidence of hip fracture in Alcorcón, both in men and in women. Possible explanations are discussed, including the effectiveness of osteoporosis diagnosis and treatment campaigns over the last 20 years, and the so-called "cohort effect."

**Yale J Biol Med. 2017 Sep 25;90(3):499-507. eCollection 2017 Sep.**

## Premenopausal Reproductive Health Modulates Future Cardiovascular Risk - Comparative Evidence from Monkeys and Women.

Kaplan JR, Manuck SB.

Coronary heart disease (CHD) remains the major cause of mortality among postmenopausal women living in industrialized countries. Several lines of evidence suggest that ovarian hormones (especially estrogen) protect the coronary arteries of premenopausal women. However, it is also known that women commonly experience disruptions in cyclic hormonal function during their reproductive years. In this perspective, we hypothesize that if regular, cyclic ovarian function affords protection against CHD, ovulatory abnormalities in young women may conversely promote the development of atherosclerosis (the pathobiological process underlying CHD) in the years prior to menopause and thus substantially increase the risk of subsequent heart disease. This hypothesis is supported by evidence from premenopausal nonhuman primates showing that relatively common, subclinical ovarian disruptions - as may be induced by psychosocial stress - are associated with the initiation and acceleration of coronary artery atherosclerosis. If extending to women, these findings would suggest that ovarian dysfunction is an early biomarker for CHD risk and, further, that primary prevention of CHD should begin during the premenopausal phase of life.

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## Clinical trials in menopause.

Marko KI, Simon JA.

OBJECTIVE: Clinical trials in menopause have undergone much scrutiny over the years. This has led to significant shifts in the treatment of symptomatic menopause and a substantial impact on women. We aim to delineate the key studies contributing to this controversy and highlight new directions specifically related to menopausal hormone therapy (HT) and vascular disease risk. METHODS: We performed a search of sentinel studies delineating the risks and benefits of HT in otherwise healthy postmenopausal women. Using PubMed we input the following search terms: hormone replacement therapy, cardiovascular disease, coronary artery disease, coronary atherosclerosis, myocardial infarction, angina, coronary heart calcification, carotid intimal thickness, lipids, and/or lipoproteins. We included studies of menopausal women (surgical or natural) using combined estrogen/progestogen therapy or estrogen-only therapy that looked at cardiovascular disease risk factors or outcomes. Studies were evaluated for inclusion by the authors; however, this is not intended to be a systematic or an exhaustive analysis. RESULTS: In women close to the time of menopause, there is a decreased risk of subclinical and clinical coronary heart disease with menopausal HT. Additionally, HT confers a significant benefit to

vasomotor symptoms of menopause, bone health, and colorectal cancer. There is an increased risk of venous thromboembolism with oral formulations that appears mitigated with transdermal estradiol. Mixed data regarding breast cancer risk are available, with some studies suggesting an increased risk of invasive breast cancer with estrogen/progestogen therapy and a null effect with estrogen-only therapy. Other more long-term epidemiologic studies identify a decreased risk. CONCLUSIONS: The available literature suggests that HT is a viable option for the primary prevention of cardiovascular disease in postmenopausal women. Newer trials will likely verify this assessment. If this is enough to change clinical practice, however, remains to be seen given the general fear of HT by many with prescriptive authority, and also the women in our care.

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## Effects of menopause and high-intensity training on insulin sensitivity and muscle metabolism.

Mandrup CM, Egelund J, Nyberg M, Enevoldsen LH, Kjær A, Clemmensen AE, Christensen AN, Suetta C, et al.

OBJECTIVE: To investigate peripheral insulin sensitivity and skeletal muscle glucose metabolism in premenopausal and postmenopausal women, and evaluate whether exercise training benefits are maintained after menopause. METHODS: Sedentary, healthy, normal-weight, late premenopausal (n=21), and early postmenopausal (n=20) women were included in a 3-month high-intensity exercise training intervention. Body composition was assessed by magnetic resonance imaging and dual-energy x-ray absorptiometry, whole body glucose disposal rate (GDR) by hyperinsulinemic euglycemic clamp (40 mU/m/min), and femoral muscle glucose uptake by positron emission tomography/computed tomography, using the glucose analog fluorodeoxyglucose, expressed as estimated metabolic rate (eMR). Insulin signaling was investigated in muscle biopsies. RESULTS: Age difference between groups was 4.5 years, and no difference was observed in body composition. Training increased lean body mass (estimate [95% confidence interval] 0.5 [0.2-0.9] kg, P<0.01) and thigh muscle mass (0.2 [-0.1 to 0.6] kg, P<0.01), and decreased fat percentage (1.0 [0.5-1.5]%, P<0.01) similarly in the two groups. The postmenopausal women had lower eMR in vastus lateralis muscle than the premenopausal women (-14.0 [-26.0 to -2.0] μmol/min/kg, P=0.02), and tended to have lower eMR in femoral muscles (-11.2 [-22.7 to 0.4] μmol/min/kg, P=0.06), and also GDR (-59.3 [-124.8 to 6.3] mg/min, P=0.08), but increased similarly in both groups with training (eMR vastus lateralis muscle: 27.8 [19.6-36.0] μmol/min/kg, P<0.01; eMR femoral muscle: 20.0 [13.1-26.7] μmol/min/kg, P<0.01, respectively; GDR: 43.6 [10.4-76.9] mg/min, P=0.01). Potential mechanisms underlying the training-induced increases in insulin sensitivity included increased expression of hexokinase (19.2 [5.0-24.7] AU, P=0.02) and glycogen synthase (32.4 [15.0-49.8] AU, P<0.01), and also increased insulin activation of Akt2 (20.6 [3.4-29.0], P=0.03) and dephosphorylation of glycogen synthase (-41.8 [-82.9 to -0.7], P=0.05). CONCLUSIONS: Insulin sensitivity was reduced in early postmenopausal women. However, postmenopausal women increased peripheral insulin sensitivity, skeletal muscle insulin-stimulated glucose uptake, and skeletal muscle mass to the same extent as premenopausal women after 3 months of high-intensity exercise training.

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## Associations Between Type and Route of Hormone Use on Urinary Incontinence and Pelvic Organ Prolapse in Premenopausal and Postmenopausal Women.

Cardenas-Trowers OO1, Borgstrom M, Addis I.

OBJECTIVE: The aim of this study was to evaluate the associations between type and route of hormone use and urinary incontinence (UI) and pelvic organ prolapse (POP) in premenopausal and postmenopausal women. METHODS: The authors used the National Health and Nutritional Examination Survey database for data from 2005-2006, 2007-2008, 2009-2010, and 2011-2012. Seven thousand sixty-six of the women included were premenopausal, and 5387 were postmenopausal. Premenopausal women were younger than 51 years and reported menstrual periods in the last 12 months. Postmenopausal women reported being in natural or surgical menopause. Urinary incontinence was defined as experiencing urinary leakage "less than once a month" or more. Pelvic organ prolapse was defined as an affirmative response to "experience bulging in the vaginal area." Hormone route and use were stratified in years. Pearson $\chi$ and Pearson correlations were used, with $P < 0.05$ considered significant. RESULTS: In premenopausal women, birth control pills, estrogen/progestin pills, and estrogen-only patch use are associated with UI ($P < 0.05$). Birth control pills are associated with both UI and POP in premenopausal women ($P < 0.05$ for UI and POP). In postmenopausal women, estrogen-only pills, and estrogen/progestin pill use are associated with UI ($P < 0.05$). Birth control pill use is associated with POP in postmenopausal women ($P = 0.029$). Neither estrogen patch nor estrogen/progestin patch is associated with UI or POP in postmenopausal women. CONCLUSIONS: Type and route of hormone use have varied associations with UI and POP in premenopausal and postmenopausal women. Prospective studies are needed to further evaluate the effect of hormone type and route on UI and POP in premenopausal and postmenopausal women.