# Selección de Resúmenes de Menopausia

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## Should DHEA be Administered to Women?

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Context: Androgen prohormones like dehydroepiandrosterone (DHEA) increase in early puberty, peak in the second and third decade and thereafter decline, independent of menopausal status. Investigators have examined their potential beneficial effects in normal women and those with DHEA deficient states. Evidence acquisition: A review of the literature from 1985-2021 on the potential benefits and risks of androgen prohormones in women. Evidence synthesis: Studies have examined the potential benefit of DHEA therapy for anti-aging, sexual dysfunction, infertility, metabolic bone health, cognition and wellbeing in hormone deficient states such as primary adrenal insufficiency, hypopituitarism and anorexia as well as administration to normal women across the lifespan. Conclusions: Data support small benefits in quality of life and mood but not for anxiety or sexual function in women with primary or secondary adrenal insufficiency or anorexia. No consistent beneficial effects of DHEA administration have been observed for menopausal symptoms, sexual function, cognition, or overall wellbeing in normal women. Local administration of DHEA shows benefit in vulvovaginal atrophy. Use of DHEA to improve induction of ovulation response in women with diminished ovarian reserve is not recommended. Risks of high physiologic or pharmacologic use of DHEA include androgenic and estrogenic side effects which are of concern for long term administration.

## High Low-Density Lipoprotein Cholesterol Levels are Associated with Osteoporosis Among Adults 20-59 Years of Age

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Background: Serum lipids are highly inheritable and play a major role in bone health. However, the relationship between low-density lipoprotein cholesterol (LDL-C) and bone mineral density (BMD) remains uncertain. The goal of this study was to see if there was a link between LDL-C levels and BMD in persons aged 20 to 59. Methods: Using data from the National Health and Nutrition Examination Survey (NHANES) 2011-2018, multivariate logistic regression models were utilized to investigate the association between LDL-C and lumbar BMD. Fitted smoothing curves and generalized additive models were also used. Results: The analysis included a total of 4909 adults. After controlling for various variables, we discovered that LDL-C was negatively linked with lumbar BMD. The favorable connection of LDL-C with lumbar BMD was maintained in subgroup analyses stratified by gender and race in both males and females, Whites and Mexican Americans, but not in Blacks and other races. The relationship between LDL-C and lumbar BMD in other races was an inverted U-shaped curve with the inflection point: 2.327 (mmol/L). Conclusion: In people aged 20 to 59, our research discovered a negative relationship among LDL-C and lumbar BMD. Among races other than Whites, Blacks, Mexican Americans, this relationship followed an inverted U-shaped curve (inflection point: 2.327mmol/L). LDL-C measurement might be used as a responsive biomarker for detecting osteoporosis early and guiding therapy.

## Calcium deficiency worldwide: prevalence of inadequate intakes and associated health outcomes

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Dietary calcium deficiency is considered to be widespread globally, with published estimates suggesting that approximately half of the world's population has inadequate access to dietary calcium. Calcium is essential for bone health, but inadequate intakes have also been linked to other health outcomes, including pregnancy complications, cancers, and cardiovascular disease. Populations in low- and middle-income countries (LMICs) are at greatest risk of low calcium intakes, although many individuals in high-income countries (HICs) also do not meet recommendations. Paradoxically, many LMICs with lower calcium intakes show lower rates of osteoporotic fracture as compared with

HICs, though data are sparse. Calcium intake recommendations vary across agencies and may need to be customized based on other dietary factors, health-related behaviors, or the risk of calcium-related health outcomes. The lack of standard methods to assess the calcium status of an individual or population has challenged efforts to estimate the prevalence of calcium deficiency and the global burden of related adverse health consequences. This paper aims to consolidate available evidence related to the global prevalence of inadequate calcium intakes and associated health outcomes, with the goal of providing a foundation for developing policies and population-level interventions to safely improve calcium intake and status where necessary.

## Association between metabolic syndrome and 13 types of cancer in Catalonia: A matched case-control study

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Background: Metabolic syndrome (MS) is the simultaneous occurrence of a cluster of predefined cardiovascular risk factors. Although individual MS components are associated with increased risk of cancer, it is still unclear whether the association between MS and cancer differs from the association between individual MS components and cancer. The aim of this matched case-control study was to estimate the association of 13 types of cancer with (1) MS and (2) the diagnosis of 0, 1 or 2 individual MS components. Methods: Cases included 183,248 patients ≥40 years from the SIDIAP database with incident cancer diagnosed between January 2008-December 2017. Each case was matched to four controls by inclusion date, sex and age. Adjusted conditional logistic regression models were used to evaluate the association between MS and cancer risk, comparing the effect of global MS versus having one or two individual components of MS. Results: MS was associated with an increased risk of the following cancers: colorectal (OR: 1.28, 95%CI: 1.23-1.32), liver (OR: 1.93, 95%CI: 1.74-2.14), pancreas (OR: 1.79, 95%CI: 1.63-1.98), post-menopausal breast (OR: 1.10, 95%CI: 1.06-1.15), pre-menopausal endometrial (OR: 2.14, 95%CI: 1.74-2.65), post-menopausal endometrial (OR: 2.46, 95%CI: 2.20-2.74), bladder (OR: 1.41, 95%CI: 1.34-1.48), kidney (OR: 1.84, 95%CI: 1.69-2.00), non-Hodgkin lymphoma (OR: 1.23, 95%CI: 1.10-1.38), leukaemia (OR: 1.42, 95%CI: 1.31-1.54), lung (OR: 1.11, 95%CI: 1.05-1.16) and thyroid (OR: 1.71, 95%CI: 1.50-1.95). Except for prostate, pre-menopause breast cancer and Hodgkin and non-Hodgkin lymphoma, MS is associated with a higher risk of cancer than 1 or 2 individual MS components. Estimates were significantly higher in men than in women for colorectal and lung cancer, and in smokers than in non-smokers for lung cancer. Conclusion: MS is associated with a higher risk of developing 11 types of common cancer, with a positive correlation between number of MS components and risk of cancer.

## Men with COVID-19 die. Women survive

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The severity and mortality rate of COVID-19 differ between the sexes. Several biopsychosocial determinants may account for the better outcomes in women. The notion that sex steroid hormones account for the gender disparity is reasonable but not proven; the same is true of the role of menopause as a risk factor. A retrospective analysis of patients (=1764) hospitalized in Italy showed a higher mortality (HR 1.58, 95%CI 1.30-1.91, adjusted for age and multi-comorbidities) in males only after the age of 65 (the rate is twice as high in the 65-79-year age group and 1.5-fold higher in those aged over 80). The higher mortality of men is mostly evident among those aged over 65 years, long after the average age of menopause.

## Preliminary cost variance modeling to compare autologous intraovarian platelet-rich plasma vs. standard hormone replacement therapy for menopause management

Eric Scott Sills, Seang Lin Tan

Background: Menopause symptoms and hormone replacement therapy (HRT) are among the most common reasons patients seek gynecological advice. Although at least half of all women in developed countries will use HRT during their lifetime, the treatment is not without risk and guidance on HRT is mixed. Greater awareness of HRT risks from extended use has piqued interest in safer options. Menopause reversal with autologous ovarian platelet-rich plasma

(OPRP) has brought this restorative approach forward for consideration, but appropriateness and cost-effectiveness require examination. Methods: HRT and OPRP data from USA were projected to compare cumulative 1yr patient costs using stochastic Monte Carlo modeling. Results: Mean ± SD cost-to-patient for HRT including initial consult plus pharmacy refills was estimated at about $576 ± 246/yr. While OPRP included no pharmacy component, an estimated 4 visits over 1yr for OPRP maintenance entailed ultrasound, phlebotomy/sample processing, surgery equipment, and incubation/laboratory expense, yielding mean ± SD cost for OPRP at $8,710 ± 4,911/yr (P &lt; 0.0001 vs. HRT, by T-test). Upper-bound estimates for annual HRT and OPRP costs were $1,341 and $22,232, respectively. Conclusions: While HRT and OPRP may have similar efficacy and safety for menopause therapy, they diverge sharply in cost-effectiveness. Most patients would likely find OPRP too complex, invasive, and expensive to be competitive vs. HRT. Although OPRP is an interesting and cautiously useful technique for selected menopause patients reluctant to use HRT, repurposing this infertility treatment for wider use appears inefficient compared to standard HRT options that are currently marketed.

## FSH blockade improves cognition in mice with Alzheimer's disease

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Alzheimer's disease has a higher incidence in older women, with a spike in cognitive decline that tracks with visceral adiposity, dysregulated energy homeostasis and bone loss during the menopausal transition1,2. Inhibiting the action of follicle-stimulating hormone (FSH) reduces body fat, enhances thermogenesis, increases bone mass and lowers serum cholesterol in mice3-7. Here we show that FSH acts directly on hippocampal and cortical neurons to accelerate amyloid-β and Tau deposition and impair cognition in mice displaying features of Alzheimer's disease. Blocking FSH action in these mice abrogates the Alzheimer's disease-like phenotype by inhibiting the neuronal C/EBPβ-δ-secretase pathway. These data not only suggest a causal role for rising serum FSH levels in the exaggerated Alzheimer's disease pathophysiology during menopause, but also reveal an opportunity for treating Alzheimer's disease, obesity, osteoporosis and dyslipidaemia with a single FSH-blocking agent.

## Metabolic effects of menopause: a cross-sectional characterization of body composition and exercise metabolism

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Objectives: To evaluate body composition, fat distribution, and metabolism at rest and during exercise in premenopausal, perimenopausal, and postmenopausal women. Methods: This cross-sectional study in 72 women ages 35 to 60 years evaluated body composition via a four-compartment model, fat distribution using dual-energy x-ray absorptiometry-derived android to gynoid ratio, metabolic measures via indirect calorimetry, and lifestyle factors using surveys. One-way analyses of variance and one-way analyses of covariance covaried for age and hormone levels (estrogen and progesterone) were used to compare groups. Results: Body fat percent was significantly lower in premenopausal than perimenopausal women (mean difference ± standard error: -10.29 ± 2.73%, P=0.026) despite similarities in fat mass and fat-free mass between groups (P≥0.217). Android to gynoid ratio was significantly lower in premenopausal than perimenopausal women (MD ± SE: -0.16 ± 0.05 a.u., P = 0.031). Resting energy expenditure was similar between groups (P = 0.999). Fat oxidation during moderate intensity cycle ergometer exercise was significantly greater in premenopausal than postmenopausal women (MD±SE: 0.09 ± 0.03 g/min, P = 0.045). The change in respiratory exchange ratio between rest and moderate intensity exercise was significantly lower in premenopausal women than peri- (MD±SE: -0.05 ± 0.03 a.u., P = 0.035) and postmenopausal women (MD±SE: -0.06 ± 0.03 a.u., P = 0.040). Premenopausal women reported significantly fewer menopause symptoms than peri- (MD±SE: -6.58 ± 1.52 symptoms, P = 0.002) and postmenopausal participants (MD±SE: -4.63 ± 1.52 symptoms, P = 0.044), while similarities between groups were observed for lifestyle factors including diet and physical activity (P > 0.999). Conclusions: Perimenopause may be the most opportune window for lifestyle intervention, as this group experienced the onset of unfavorable body composition and metabolic characteristics.