

Selección de Resúmenes de Menopausia

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Treatment options for glucocorticoid-induced osteoporosis.

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Introduction: Glucocorticoid (GC) induced osteoporosis (GIOP) is the most common form of secondary osteoporosis. It develops in a dose and time dependent manner, due to a rapid and transient increase in bone resorption, followed by the inhibition of bone formation. **Areas covered:** In this review, the authors summarize the pathophysiology of GIOP and give discussion to the clinical management of patients taking GCs, focusing on the currently available drugs that have antiresorptive or anabolic activity on bone. **Expert opinion:** Despite the widespread use of GCs and their well-established detrimental skeletal effects, GIOP remains an under-diagnosed and under-treated condition. Indeed, the clinical management of GIOP is still debated, so that the recent guidelines differ in their indications for pharmacological intervention. Either bone mineral density (BMD) or algorithms such as FRAX do not completely account for the remarkable and rapid increase in fracture risk of most GC-treated patients. Moreover, while oral bisphosphonates remain the most used and cost-effective option, the potential increased benefits of more potent antiresorptive agents (e.g. denosumab and zoledronate) or anabolic compounds (e.g. teriparatide) warrant further investigation. Despite the above limitations, the assessment of fracture risk is recommended for all individuals committed to receiving oral GCs for 3 months or longer.

Osteoporos Int. 2020 Jan 30. doi: 10.1007/s00198-019-05183-4. [Epub ahead of print]

Osteoporosis drugs for prevention of clinical fracture in white postmenopausal women: a network meta-analysis of survival data.

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By Bayesian random effects network meta-analysis stratified by prevalent vertebral fracture (PVF), we conclude that different effective drugs should be used to prevent fragility fractures according to postmenopausal women with or without PVF and that there are two drugs (i.e., parathyroid hormone (1-84) and abaloparatide) less tolerated than placebo. **INTRODUCTION:** No studies have compared various osteoporosis drugs in postmenopausal women (PMW) either with or without prevalent vertebral fracture (PVF). We aimed to compare them in the two different subgroups. **METHODS:** We searched different databases to select relevant studies. We performed Bayesian random effects network meta-analysis to synthesize hazard ratio (HR) and 95% confidence interval (CI) for clinical fracture stratified by PVF and to synthesize risk ratio (RR) for tolerability and vertebral fracture. **RESULTS:** We included 33 trials involving 79,144 PMW. In the PVF $\geq 50\%$ subgroup, teriparatide (HR 0.39, 95% CI 0.28-0.57), romosozumab (HR 0.49, 95% CI 0.29-0.75), risedronate (HR 0.62, 95% CI 0.50-0.79), zoledronate (HR 0.67, 95% CI 0.47-0.96), and alendronate (HR 0.69, 95% CI 0.47-0.97) reduced clinical fracture risk. In the other subgroup, abaloparatide (HR 0.56, 95% CI 0.33-0.92), romosozumab (HR 0.67, 95% CI 0.47-0.95), and denosumab (HR 0.68, 95% CI 0.50-0.85) reduced clinical fracture risk. Five drugs reduced vertebral fracture risk in the PVF $\geq 50\%$ subgroup whereas seven did in the other subgroup. All drugs did not increase withdrawal risk except for parathyroid hormone (1-84) (PTH) (RR 1.9, 95% CI 1.4-2.6) and abaloparatide (RR 1.6, 95% CI 1.2-2.3). **CONCLUSION:** Different effective drugs should be used to prevent fragility fractures according to PMW with or without PVF, and romosozumab is the only one which can reduce clinical and vertebral fractures in both of the two populations. PTH and abaloparatide are less tolerated than placebo whereas the eight other drugs assessed in the study have the same tolerability as placebo.

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The role of vitamin D supplementation for primary prevention of cancer: meta-analysis of randomized controlled trials.

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Background: In the USA cancer is the second leading cause of mortality, as such, primary prevention of cancer is a major public health concern. Vitamin D supplementation has been studied as a primary prevention method for multiple diseases including cardiovascular disease, osteoporosis, diabetes mellitus and cancer. The role of Vitamin D as primary prevention of cancer is still controversial. With fast emergence of large randomized controlled trials (RCTs) in that regards, we

aimed to evaluate the efficacy of Vitamin D supplementation as primary prophylaxis for cancer. Methods: A comprehensive electronic database search was conducted for all RCTs where comparison of Vitamin D supplementation versus placebo for the prevention of any type of disease with at least 3 years of Vitamin D supplementation was used and where cancer incidence or mortality was reported. The primary outcome was cancer-related mortality and cancer incidence. We calculated risk ratios (RRs) and 95% confidence intervals (CIs) using a random-effects model at the longest follow-up. Results: We included 10 RCTs with 79,055 total patients, mean age of 68.07 years, a female percentage of 78.02% and a minimum follow-up of 4 years and more. Vitamin D was associated with significant reduction of cancer-related mortality compared with placebo (RR 0.87; 95% CI: 0.79-0.96; $P = 0.05$; $I^2 = 0\%$). Compared with placebo, Vitamin D was not associated with significant reduction of cancer incidence (RR: 0.96; 95% CI: 0.86-1.07; $P = 0.46$; $I^2 = 31\%$). Conclusion: With inclusion of studies, which did not primarily examine vitamin D for the purpose of preventing cancer or reducing cancer mortality our meta-analysis highlights that the use of vitamin D supplementation for primary prevention of cancer is encouraged as it does possibly decrease cancer-related mortality once cancer is diagnosed; however, it has no role or effect on cancer incidence.

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Association between physical activity, cardiorespiratory fitness, and body composition with menopausal symptoms in early postmenopausal women.

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OBJECTIVE: The aim of this study was to investigate the relationship between daily physical activity (daily activities, exercise, and sitting time), cardiorespiratory fitness (CRF), and body composition (body mass index [BMI], waist to hip ratio [WHR]) with menopausal symptoms and to determine the strongest predictor(s) of menopausal symptoms. **METHODS:** The Menopause Rating Scale questionnaire was used to examine somatic, psychological, urogenital, and total symptoms of menopause. The energy expenditure of daily physical activity, exercise, and sitting time was measured by the International Physical Activity Questionnaire, and CRF was measured by estimating the maximal oxygen intake (VO2max) through the Rockport test. Statistical methods of the Pearson correlation coefficient and hierarchical multiple linear regression were used for data analysis. **RESULTS:** Fifty-six women, aged 50 to 65 years, voluntarily participated in the study. Exercise energy expenditure was inversely correlated with total ($r = -0.403$, $P = 0.002$), somatic ($r = -0.293$, $P = 0.023$), and urogenital ($r = -0.343$, $P = 0.009$) symptoms of menopause. VO2max was inversely correlated with urogenital symptoms of menopause ($r = -0.414$, $P = 0.002$). WHR was positively correlated with somatic symptoms of menopause ($r = 0.286$, $P = 0.032$); sitting was correlated with total ($r = 0.40$, $P = 0.002$), somatic ($r = 0.325$, $P = 0.015$), and psychological ($r = 0.274$, $P = 0.015$) symptoms of menopause. Among the study variables, sitting ($\beta = 0.365$, $P = 0.004$) and VO2max ($\beta = -0.286$, $P = 0.030$) were the most important predictors of total symptoms of menopause; sitting was the predictor of somatic symptoms ($\beta = 0.265$, $P = 0.045$), and VO2max was the predictor of urogenital symptoms of menopause ($\beta = -0.332$, $P = 0.014$). The inclusion of age, BMI, WHR, and duration of menopause as confounding variables in regression analysis did not change the findings related to the predictions of menopausal symptoms. **CONCLUSION:** Reducing sitting time, improving VO2max, decreasing WHR, and exercise can be recommended by priority to alleviate menopausal symptoms. Considering the small number of participants in this investigation, future studies are, however, recommended.

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Marked differences in prediabetes and diabetes associated comorbidities between men and women - epidemiological results from a general population-based cohort aged 6-80 years - the LEAD (Lung, hEart, sociAl, boDy) study.

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Based on biological and behavioural diversity sex and gender may affect co-morbidities associated with prediabetes and diabetes. Besides evaluating the prevalence of prediabetes and diabetes (using fasting plasma glucose and HbA1c levels), the primary aim of the study is to investigate sex and gender differences in the prevalence of co-morbidities in subjects with prediabetes and diabetes and to identify possible risk factors associated with prediabetes and diabetes. **DESIGN:** This observational, population-based cohort study included 11,014 subjects aged 6-80 years. Examinations included blood samples, ankle-brachial index, ECG, dual energy X-ray absorptiometry scan, and an interviewer-administered questionnaire. **RESULTS:** Across all ages, prevalence of prediabetes was 20.2% (male 23.6%; female 17.1%), and 5.4% for diabetes (male 7.3%; female 3.7%). The prevalence of prediabetes ranged from 4.4% (6-10 years) up to 40.4% (70+ years) in men and from 4.8% up to 42.3% in women. Co-morbidity profile was markedly different between male and female, particularly in those with prediabetes: women more often suffered from arrhythmia, non-coronary artery disease,

osteoporosis, increased systemic inflammatory biomarkers, and depression, while men with prediabetes more often showed angina pectoris, myocardial infarction, and media sclerosis. **CONCLUSIONS:** The unexpected 4.6% prevalence of prediabetes in children aged 6-10 underscores the need for population-based studies across all ages and the onset of prevention of diabetes at a young age. Marked differences have been found in co-morbidities as men with prediabetes and diabetes more often suffer from cardiovascular disease, while women more often show arrhythmia, non-coronary artery disease, increased systemic inflammatory biomarkers and depression.

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Metformin use is associated with a lower risk of osteoporosis in adult women independent of type 2 diabetes mellitus and obesity. REDLINC IX study.

Blümel JE1, Arteaga E, Aedo S, Arriola-Montenegro J, López M, Martino M, Miranda C, Miranda O, Mostajo D, Ñañez M, Ojeda E, Pilnik S, Rojas J1, Salinas C, Sosa L, Spritzer PM, Tserotas K, Vallejo MS, Belardo A, Figuera TM, Chedraui P.

Metformin may decrease cell senescence, including bone; hence we aimed at evaluating the association between metformin use and osteoporosis. This was a cross-sectional study carried out in 1259 Latin American adult women aged 40 or more who were not on anti-osteoporotic drugs, were on metformin and had a bone densitometry performed. Of the whole sample, 40.3% reported being on metformin (at least 1 year), 30.2% had type 2 diabetes mellitus and 22.6% had osteoporosis. Median (interquartile range) body mass index (BMI) for the whole cohort was 27.7 (4.6) kg/m² and 30.2% had type 2 diabetes mellitus. Current use of hormone therapy, calcium, and vitamin D corresponded respectively to 10.7%, 47.7%, and 43.1% of all surveyed women. A logistic regression model was used to analyze the association of osteoporosis with various covariates incorporated into the model such as age (OR: 1.07, 95% CI: 1.05-1.09), BMI (OR: 0.92, 95% CI: 0.89-0.96) and metformin use (OR: 0.44, 95% CI: 0.32-0.59). Metformin use, regardless of the presence of type 2 diabetes or obesity, was associated with a lower risk of osteoporosis in adult women. We propose that one explanation for this observation could be the effect of the drug over cellular senescence.

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Female Heart Health: Is GPER the Missing Link?

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The G Protein-Coupled Estrogen Receptor (GPER) is a novel membrane-bound receptor that mediates non-genomic actions of the primary female sex hormone 17 β -estradiol. Studies over the past two decades have elucidated the beneficial actions of this receptor in a number of cardiometabolic diseases. This review will focus specifically on the cardiac actions of GPER, since this receptor is expressed in cardiomyocytes as well as other cells within the heart and most likely contributes to estrogen-induced cardioprotection. Studies outlining the impact of GPER on diastolic function, mitochondrial function, left ventricular stiffness, calcium dynamics, cardiac inflammation, and aortic distensibility are discussed. In addition, recent data using genetic mouse models with global or cardiomyocyte-specific GPER gene deletion are highlighted. Since estrogen loss due to menopause in combination with chronological aging contributes to unique aspects of cardiac dysfunction in women, this receptor may provide novel therapeutic effects. While clinical studies are still required to fully understand the potential for pharmacological targeting of this receptor in postmenopausal women, this review will summarize the evidence gathered thus far on its likely beneficial effects.

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Levonorgestrel-releasing intrauterine system and breast cancer risk: A systematic review and meta-analysis.

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INTRODUCTION: Epidemiological studies have shown that some hormonal contraceptive methods are associated with increased breast cancer risk, especially if used over long periods. Our objective was to conduct a systematic review and meta-analysis of the literature on the risk of breast cancer development in women using the 52-mg levonorgestrel-releasing intrauterine system (LNG-IUS). **MATERIAL AND METHODS:** We performed a thorough review of peer-reviewed publications from January 10, 1999, through July 31, 2019, using combinations of search terms for breast cancer risk and LNG-IUS in the Medline, EMBASE, LILACS (Latin American and Caribbean Health Sciences Literature), and Scielo databases. This review was registered in PROSPERO (CRD42017059076). Studies reporting breast cancer risk estimates among healthy users of LNG-IUS were included according to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analysis) criteria. Two authors performed data extraction, and a third

author resolved disagreements. The quality of evidence was evaluated using the Downs and Black instrument. A funnel plot was generated, and a linear regression test of funnel plot asymmetry was used to assess publication bias. Finally, we performed a random-effects model (owing to high study heterogeneity) meta-analysis of seven suitable studies, stratified by the age distribution of patients (<50 years, ≥50 years, and mixed). **RESULTS:** We identified 96 studies and manually cross-referenced and excluded duplicate articles. Seventy articles were excluded on the basis of the inclusion and exclusion criteria, resulting in the assessment of 26 full-text articles. Eight articles were considered adequate for inclusion in this systematic review, and seven studies were included in the meta-analysis. Three publications were case-control studies and five were cohort studies. According to the Downs and Black instrument, five studies were rated as 'good' and three studies were deemed 'fair'. Our meta-analysis results indicated increased breast cancer risk in LNG-IUS users: for all women, odds ratio (OR)=1.16 (95% confidence interval [CI] 1.06-1.28, I² =78%, P<.01); for women aged <50 years, OR=1.12 (95% CI 1.02-1.22, I² =66%, P=.02); and for women aged ≥50 years, OR=1.52 (95% CI 1.34-1.72, I² =0%, P=.84). **CONCLUSIONS:** Current evidence suggests that LNG-IUS users have an increased breast cancer risk regardless of age and indication. The effect of LNG-IUS on breast cancer risk seems to be larger in older users. However, our systematic review detected methodological issues across the available studies, and confounding factors may be responsible for at least a fraction of the risk effects associated with LNG-IUS use. Nevertheless, users of LNG-IUS should be aware of these trends. We believe that caution is needed, and risks balanced against proven health benefits (e.g. effective treatment of heavy menstrual bleeding and avoidance of surgical interventions), when prescribing LNG-IUS for long periods of use, especially in women with other known breast cancer risk factors such as old age, obesity, and familial predisposition.