Selección de Resúmenes de Menopausia

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María Soledad Vallejo. Clínica Quilín. Universidad de Chile

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Role of ovarian hormones in the modulation of sleep in females across the adult lifespan.

Brown AMC1, Gervais NJ1.

Ovarian hormones, including 17β-estradiol, are implicated in numerous physiological processes, including sleep. Beginning at puberty, girls report more sleep complaints than boys, which is maintained throughout the reproductive life stage. Sleep problems are exacerbated during the menopausal transition, evidenced by greater risk for sleep disorders. There is emerging evidence that menopause-associated hormone loss contributes to this elevated risk, but age is also an important factor. The extent to which menopause-associated sleep disturbance persists into postmenopause above and beyond the effects of age remains unknown. Untreated sleep disturbances have important implications for cognitive health, as they are emerging as risk factors for dementia. Given that sleep loss impairs memory, an important knowledge gap concerns the role played by menopause-associated hormone loss in exacerbating sleep disturbance and ultimately, cognitive function in aging women. In this review, we take a translational approach to illustrate the contribution of ovarian hormones in maintaining the sleep-wake cycle in younger and middle-aged females, with evidence implicating 17β-estradiol in supporting the memory-promoting effects of sleep. Sleep physiology is briefly reviewed before turning to behavioural and neural evidence from young females linking 17β-estradiol to sleep-wake cycle maintenance. Implications of menopause-associated 17β-estradiol loss is also reviewed before discussing how ovarian hormones may support the memory-promoting effects of sleep, and why menopause may exacerbate pathological aging via effects on sleep. While still in its infancy, this research area offers a new sex-based perspective on aging research, with a focus on a modifiable risk factor for pathological aging.

Curr Osteoporos Rep. 2020 Jul 31. doi: 10.1007/s11914-020-00612-4. [Epub ahead of print]

Benefits of Bisphosphonate Therapy: Beyond the Skeleton.

Billington EO1,2, Reid IR3.

PURPOSE OF REVIEW: Recent evidence from clinical trials and observational studies raises the possibility that bisphosphonate use might confer a lower risk of cardiovascular disease and cancer, resulting in a mortality benefit. This review summarizes clinical and preclinical studies examining the non-skeletal effects of bisphosphonates. RECENT FINDINGS: Data from clinical trials are conflicting regarding whether or not bisphosphonates have beneficial effects on mortality, cardiovascular events, or cancer incidence. No clinical trials have assessed these outcomes as primary endpoints, and most trials were shorter than 4 years. Observational data suggest that bisphosphonate users may have lower mortality, delayed progression of vascular calcification and atherosclerotic burden, and reduced incidence of breast and colorectal cancer compared to non-users. Preclinical studies confirm that bisphosphonates can be taken up by macrophages and monocytes, and nitrogen-containing bisphosphonates have the ability to disrupt the mevalonate pathway within these cells. In this manner, bisphosphonates exert anti-atherogenic and anti-cancer effects. Bisphosphonates also appear to exert protective effects on vascular smooth muscle cells and endothelial cells and may have direct cytotoxic effects on cancer cells. The balance of evidence does not support bisphosphonate treatment for the primary purpose of improving non-skeletal outcomes, although appropriately designed controlled trials that further explore this possibility are both justified and required. Patients with skeletal indications for bisphosphonate therapy can be reassured that these agents are not associated with increased mortality, cardiovascular disease, or cancer incidence.

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Trabecular Bone Score and Fracture.

Greendale GA1, Huang M2, Cauley JA3, Harlow S4, Finkelstein JS5, Karlamangla AS6.

BACKGROUND: Evidence that trabecular bone score (TBS), an index of bone microstructure, is a risk factor for future fracture comes mainly from studies of late postmenopausal women. OBJECTIVE: To discern whether

premenopausal TBS or early postmenopausal TBS predict fracture. DESIGN: A 22-year, prospective analysis from the Study of Women's Health Across Nation. SETTING: Community-based cohort. PARTICIPANTS: 272 Black, 174 Japanese, and 364 White women Main Outcome Measures Incident fractures: 292 in premenopausal sample and 141 in early postmenopausal sample. RESULTS: Separate Cox proportional hazard regressions modeled time to incident fracture as a function of TBS measured during premenopause or early postmenopause. Models were initially adjusted for age, race/ethnicity, SWAN clinical site, body mass index, use of calcium, vitamin D, bone beneficial or bone adverse medication. Next, we added lumbar spine (LS) or femoral neck (FN) bone mineral density (BMD) and, finally, history of prior fracture, to the models. For each standard deviation decrement in premenopausal TBS, fracture hazard was elevated by 17% (relative hazard [RH] 1.17 [95% CI, 1.02-1.35]); after adjusting for LS or FN BMD, the relation between premenopausal TBS and fracture was no longer statistically significant. There was a similar-magnitude, marginally statistically significant, association between early postmenopausal TBS and fracture, unadjusted for BMD (RH 1.15 [0.95- 1.39]). CONCLUSIONS: Variation in premenopausal TBS is related to fracture risk, but this association is not independent of BMD.

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Quality of systematic reviews on osteoporotic treatments.

Tsoi AKN1, Ho LTF2, Wu IXY3, Wong CHL4, Ho RST1, Lim JYY1, Mao C5, Lee EKP1, Chung VCH6.

PURPOSE: Systematic reviews (SRs) provide the best evidence on the effectiveness of treatment strategies for osteoporosis. Carefully conducted SRs provide high-quality evidence for supporting decision-making, but the trustworthiness of conclusions can be hampered by limitation in rigour. We aimed to appraise the methodological quality of a representative sample of SRs on osteoporosis treatments in a cross-sectional study. METHODS: Cochrane Database of Systematic Reviews, EMBASE, MEDLINE, and PsycINFO were searched for SRs on osteoporotic treatments. AMSTAR (A MeaSurement Tool to Assess systematic Reviews) 2 was used to evaluate methodological quality of SRs. Associations between bibliographical characteristics and methodological quality ratings were explored using multivariate regression analyses. RESULTS: A total of 101 SRs were appraised. Overall, one (1.0%) was rated "high quality", three (3.0%) were rated "moderate quality", eleven (10.9%) were rated "low quality", and eighty-six (85.1%) were rated "critically low quality". Ninety-nine (98.0%) did not explain study design selection, eighty-five (84.2%) did not provide a list of excluded studies (84.2%), and eighty-five (84.2%) did not report funding sources of included studies. SRs published in 2018 or after were associated with higher overall quality [adjusted odds ratio (AOR): 5.48; 95% confidence interval (CI): 1.12-26.89], while SRs focused on pharmacological interventions were associated with lower overall quality [AOR: 0.24; 95% CI: 0.06-0.96]. CONCLUSION: The methodological quality of the included SRs is far from satisfactory. Future reviewers must strengthen rigour by improving literature search comprehensiveness, registering and publishing a priori protocols, and optimising study selection and data extraction. Better transparency in reporting conflicts of interest among reviewers, as well as sources of funding among included primary studies, are also needed.

Rev Med Chil. 2020 Feb;148(2):145-150. doi: 10.4067/s0034-98872020000200145.

Coronary artery disease in pre and postmenopausal women. The influence of type 2 diabetes mellitus.

Gajardo-Navarrete J1, Ibieta G1, Concha M1, Garcés P1, Robles I2, Vera-Calzaretta A3, et al.

BACKGROUND: Postmenopausal women have higher severity of coronary heart disease (CHD) than premenopausal women and type 2 diabetes mellitus (T2DM) is an independent risk factor. AIM: To assess the severity of CHD in pre and postmenopausal patients undergoing coronary angiography and the impact of T2DM in both groups. MATERIAL AND METHODS: A coronary angiography was performed to 707 women due to suspected CHD during 2013 and 2014. Of these, 579 were older than 55 years and were considered as postmenopausal. Factors such as hypertension, obesity, smoking, creatinine and T2DM were registered. The severity of CHD in coronary angiography was evaluated according to the number of vessels with more than 50% stenosis. RESULTS: Compared to their postmenopausal counterparts, premenopausal women had less frequency of T2DM (31% and 42% $p < 0.033$), hypertension (52 and 78%, $p < 0.001$) and alteration of renal function (11 vs. 39%, $p < 0.001$). Absence of coronary lesions was found in 44 and 32% of premenopausal and postmenopausal women, respectively ($p < 0.01$). Premenopausal women with T2DM had a higher frequency of multi-vessel disease than those without the disease (25 and 4.5%, $p < 0.001$). The frequency of multi-vessel disease was higher in postmenopausal than premenopausal women (24 and 11%, $p < 0.01$).

Hypertension, T2DM and renal involvement were associated with a higher frequency multiple vessel disease. CONCLUSIONS: The severity of CHD is higher in postmenopausal women and T2DM is associated with the disease.

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Breast Cancer Population Attributable Risk Proportions Associated with Body Mass Index and Breast Density by Race/Ethnicity and Menopausal Status.

Bissell MCS1, Kerlikowske K2, Sprague BL3, Tice JA4, Gard CC5, Tossas KY6, Rauscher GH7, et al.

BACKGROUND: Overweight/obesity and dense breasts are strong breast cancer risk factors whose prevalences vary by race/ethnicity. The breast cancer population attributable risk proportions (PARPs) explained by these factors across racial/ethnic groups are unknown. METHODS: We analyzed data collected from 3,786,802 mammography examinations (1,071,653 women) in the Breast Cancer Surveillance Consortium, associated with 21,253 invasive breast cancers during a median of 5.2 years follow-up. Hazard ratios (HRs) for body mass index (BMI) and breast density, adjusted for age and registry were estimated using separate Cox regression models by race/ethnicity (white, black, Hispanic/Latina, Asian) and menopausal status. HRs were combined with observed risk-factor proportions to calculate PARPs for shifting overweight/obese to normal BMI and shifting heterogeneously/extremely dense to scattered fibroglandular densities. RESULTS: The prevalences and HRs for overweight/obesity and heterogeneously/extremely dense breasts varied across races/ethnicities and menopausal status. BMI PARPs were larger for post- vs. premenopausal women (12.0-28.3% vs. 1.0-9.9%) and nearly double among postmenopausal black women (28.3%) than other races/ethnicities (12.0-15.4%). Breast density PARPs were larger for pre- vs. postmenopausal women (23.9-35.0% vs. 13.0-16.7%) and lower among premenopausal black women (23.9%) than other races/ethnicities (30.4-35.0%). Postmenopausal density PARPs were similar across races/ethnicities (13.0-16.7%). CONCLUSIONS: Overweight/obesity and dense breasts account for large proportions of breast cancers in white, black, Hispanic, and Asian women despite large differences in risk-factor distributions. IMPACT: Risk prediction models should consider how race/ethnicity interacts with BMI and breast density. Efforts to reduce BMI could have a large impact on breast cancer risk reduction, particularly among postmenopausal black women.

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Assessment of Cardiovascular Safety of Anti-Osteoporosis Drugs.

Fuggle NR1, Cooper C2,3, Harvey NC1, Al-Daghri N4, Brandi ML5, Bruyere O6, Cano A7, Dennison EM1, el al.

The incidence of osteoporosis and cardiovascular disease increases with age, and there are potentially shared mechanistic associations between the two conditions. It is therefore highly relevant to understand the cardiovascular implications of osteoporosis medications. These are presented in this narrative review. Calcium supplementation could theoretically cause atheroma formation via calcium deposition, and in one study was found to be associated with myocardial infarction, but this has not been replicated. Vitamin D supplementation has been extensively investigated for cardiac benefit, but no consistent effect has been found. Despite findings in the early 21st century that menopausal hormone therapy was associated with coronary artery disease and venous thromboembolism (VTE), this therapy is now thought to be potentially safe (from a cardiac perspective) if started within the first 10 years of the menopause. Selective estrogen receptor modulators (SERMs) are associated with increased risk of VTE and may be related to fatal strokes (a subset of total strokes). Bisphosphonates could theoretically provide protection against atheroma. However, data from randomised trials and observational studies have neither robustly supported this nor consistently demonstrated the potential association with atrial fibrillation. Denosumab does not appear to be associated with cardiovascular disease and, although parathyroid hormone analogues are associated with palpitations and dizziness, no association with a defined cardiovascular pathology has been demonstrated. Finally, romosozumab has been shown to have a possible cardiovascular signal, and therefore post-market surveillance of this therapy will be vital.

J Obstet Gynaecol Can. 2020 Apr 27. doi: 10.1016/j.jogc.2020.03.022. [Epub ahead of print]

Hormone Therapy Use After Premature Surgical Menopause Based on Prescription Records: A Population-Based Study.

Jang JH1, Arora N2, Kwon JS3, Hanley GE3.

OBJECTIVE: Premature surgical menopause (PSM) without subsequent hormone replacement therapy (HRT) can lead to morbidity and mortality. Our objective was to describe the use of HRT following PSM and identify variables

associated with HRT use based on prescription records from a population-based cohort. METHODS: A population-based retrospective cohort of women in British Columbia, Canada who underwent PSM between the ages of 19 and 49 years. Women were identified using surgical data from the Discharge Abstract Database and linked to HRT prescription histories from the BC PharmaNet database for the period of 2004 to 2014. HRT prescription rates were calculated, and factors associated with postoperative HRT use were identified. RESULTS: A total of 12 837 women were included, with a median age of 43 years. They had undergone BSO with concurrent hysterectomy (49.9%). bilateral salpingo-oophorectomy (BSO) alone (42.1%), or bilateral oophorectomy (BO) (8%). The most common indications for surgery were endometriosis (17.9%), benign adnexal neoplasm (17.2%), and abnormal bleeding (14.0%). Only 55.3% of women ever used HRT, and 47.9% of these women used HRT for less than 1 year. HRT use was higher among women who underwent concurrent hysterectomy (60.7% vs. 50%, P < 0.001). This association remained significant after multivariate adjustment (aOR 1.64; 95% CI 1.50-1.79). Women with a known BRCA mutation were also more likely to use HRT postoperatively (aOR 3.73; 95% CI 2.14-6.81). CONCLUSION: In this large population-based study, HRT use after PSM was 50%. Our study highlights the need for education of both health care providers and patients, and for ongoing follow-up in this young population.

JAMA. 2020 Jul 28;324(4):369-380. doi: 10.1001/jama.2020.9482.

Association of Menopausal Hormone Therapy With Breast Cancer Incidence and Mortality During Long-term Follow-up of the Women's Health Initiative Randomized Clinical Trials.

Chlebowski RT1, Anderson GL2, Aragaki AK2, Manson JE3, Stefanick ML4, Pan K1, Barrington W5, et al.

Importance: The influence of menopausal hormone therapy on breast cancer remains unsettled with discordant findings from observational studies and randomized clinical trials. Objective: To assess the association of prior randomized use of estrogen plus progestin or prior randomized use of estrogen alone with breast cancer incidence and mortality in the Women's Health Initiative clinical trials. Design, Setting, and Participants: Long-term follow-up of 2 placebo-controlled randomized clinical trials that involved 27 347 postmenopausal women aged 50 through 79 years with no prior breast cancer and negative baseline screening mammogram. Women were enrolled at 40 US centers from 1993 to 1998 with follow-up through December 31, 2017. Interventions: In the trial involving 16 608 women with a uterus, 8506 were randomized to receive 0.625 mg/d of conjugated equine estrogen (CEE) plus 2.5 mg/d of medroxyprogesterone acetate (MPA) and 8102, placebo. In the trial involving 10 739 women with prior hysterectomy, 5310 were randomized to receive 0.625 mg/d of CEE alone and 5429, placebo. The CEE-plus-MPA trial was stopped in 2002 after 5.6 years' median intervention duration, and the CEE-only trial was stopped in 2004 after 7.2 years' median intervention duration. Main Outcomes and Measures: The primary outcome was breast cancer incidence (protocol prespecified primary monitoring outcome for harm) and secondary outcomes were deaths from breast cancer and deaths after breast cancer. Results: Among 27 347 postmenopausal women who were randomized in both trials (baseline mean [SD] age, 63.4 years [7.2 years]), after more than 20 years of median cumulative follow-up, mortality information was available for more than 98%. CEE alone compared with placebo among 10 739 women with a prior hysterectomy was associated with statistically significantly lower breast cancer incidence with 238 cases (annualized rate, 0.30%) vs 296 cases (annualized rate, 0.37%; hazard ratio [HR], 0.78; 95% CI, 0.65-0.93; P = .005) and was associated with statistically significantly lower breast cancer mortality with 30 deaths (annualized mortality rate, 0.031%) vs 46 deaths (annualized mortality rate, 0.046%; HR, 0.60; 95% CI, 0.37-0.97; P = .04). In contrast, CEE plus MPA compared with placebo among 16 608 women with a uterus was associated with statistically significantly higher breast cancer incidence with 584 cases (annualized rate, 0.45%) vs 447 cases (annualized rate, 0.36%; HR, 1.28; 95% CI, 1.13-1.45; P < .001) and no significant difference in breast cancer mortality with 71 deaths (annualized mortality rate, 0.045%) vs 53 deaths (annualized mortality rate, 0.035%; HR, 1.35; 95% CI, 0.94-1.95; P= .11). Conclusions and Relevance: In this long-term follow-up study of 2 randomized trials, prior randomized use of CEE alone, compared with placebo, among women who had a previous hysterectomy, was significantly associated with lower breast cancer incidence and lower breast cancer mortality, whereas prior randomized use of CEE plus MPA, compared with placebo, among women who had an intact uterus, was significantly associated with a higher breast cancer incidence but no significant difference in breast cancer mortality.

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Vitamin D high doses supplementation could represent a promising alternative to prevent or treat COVID-19 infection.

Mansur JL1, Tajer C2, Mariani J2, Inserra F3, Ferder L3, Manucha W4.

Although we lack enough evidence to justify supplementing with vitaminD in the prevention and treatment of COVID-19 infection, it is increasingly feasible that this hypothesis is valid. Two general underlying mechanisms should be considered. One would be the anti-infectious and immunomodulatory action that it exerts by improving intercellular barriers by stimulating innate immunity, as well as by modulating adaptive immunity. Also, vitaminD reduces the production of inflammatory cytokines, such as IL-2 and interferon-gamma (INF-γ). More recently, multiple pleiotropic effects have been demonstrated on the actions of vitaminD at the anti-inflammatory and immunomodulatory level with positive results in studies with influenza, coronavirus, and other respiratory infections. An inverse relationship between serum vitaminD levels and the prevalence of the respiratory infectious disease has been described. Of interest, another mechanistic approach responds to considering the inhibition of the renin-angiotensin-aldosterone system (RAAS), which is exacerbated in COVID-19 infection because the virus binds to the enzyme ACE2, making more angiotensinII available to cause damage. VitaminD inhibits mediators of RAAS - present in all cells of the body - and by inhibiting ACE activity and increasing ACE2, it lowers angiotensinII levels. We present studies with proposals for recommended doses of vitaminD, and although a single guideline is not specified, the possible benefits are promising. Finally, the purpose of this review is to share this idea with health professionals to ignite the debate and call for critical reflection, so that it can contribute to the undertaking of more and better clinical designs to validate the benefits of using high doses of vitaminD for the benefit of public health and especially in times of crisis for COVID-19.

Clin Exp Hypertens. 2020 Jul 27:1-6. doi: 10.1080/10641963.2020.1790584. [Epub ahead of print]

The link of depression, untreated hypertension, and diabetes with mortality in postmenopausal women: A cohort study.

Guan S1,2, Fang X1,2, Gu X3, Zhang Z4, Tang Z2, Wu X1,2, Liu H1,2, Wang C1,2.

Objective To explore the association of depression, as well as untreated hypertension or diabetes with all-cause death in community-based postmenopausal women in Beijing. Methods A cohort of 863 community-based postmenopausal women with no history of cardiovascular heart disease (CHD), stroke, cancer, or dementia was investigated on 20 July-28 September 2009 at baseline. Depression was diagnosed using the 30-item Center for Epidemiologic Studies Depression (CES-D) scale with CES-D ≥ 11. Meanwhile, data on health behavior, physical comorbidity, and social support at baseline were collected. These individuals were followed up from 20 July to 30 August 2014. All-cause mortality and cause of death were surveyed. Results After a median follow-up of 4.97 years, 120 subjects died of all-cause. Twenty-four died of stroke, 19 died of myocardial infarction, 21 died of cancer. The others died of aging, infection, and accident. Depression and untreated HP were significantly associated with all-cause mortality in Cox models after full adjustment for all of the potential confounders (Depression HR: 2.16, 95%CI: 1.35-3.46; Untreated hypertension HR: 1.84, 95%CI: 1.12-3.02). However, negative correlation of untreated diabetes on all-cause mortality was observed in this population (HR: 1.36, 95%CI: 0.75-2.49). When depression was co-existing with hypertension/diabetes, the HR for mortality elevated significantly (Depression co-existing with hypertension HR = 3.87, 95% CI: 2.07-7.23; Depression co-existing with diabetes HR = 5.02, 95% CI: 1.5-16.79). Conclusions It is suggested we should take sufficient care of postmenopausal females with depression and control blood pressure and glucose more effectively. Abbreviations HP: Hypertension; DM: Diabetes; TC: Cholesterol; TG: Triglyceride; BMI: Body-Mass Index; CES-D: Center for Epidemiologic Studies Depression; CDC: Centers for Disease Control and Prevention; HR: Hazard Ratio; CI: Confidence Interval; ADL: Activities of daily living scale.