

## Selección de Resúmenes de Menopausia

Semana del 4 al 10 de diciembre de 2019

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### **Menopausal symptoms are associated with non-adherence to highly active antiretroviral therapy in human immunodeficiency virus-infected middle-aged women.**

Cutimanco-Pacheco V1, Arriola-Montenegro J1,2, Mezones-Holguin E1,3, Niño-García R3,4, Bonifacio-Morales N1,5, Lucchetti-Rodríguez A1,6, Ticona-Chávez E7, Blümel JE8, Pérez-López FR9,10, Chedraui P11,12.

**Objective:** This study aimed to evaluate the association between the intensity of menopausal symptoms and highly active antiretroviral therapy (HAART) adherence in middle-aged women with human immunodeficiency virus (HIV) infection. **Methods:** In this cross-sectional study, 313 Peruvian women with HIV infection (age 40-59 years) were surveyed and classified as adherent or non-adherent to HAART based on the Antiretroviral Treatment Adherence Evaluation Questionnaire. The intensity of menopausal symptoms was assessed with the Menopause Rating Scale, and categorized as none, mild, moderate, and/or severe. Age, sexual orientation, used HAART scheme, time since HIV diagnosis, menopausal status, risk of depression, and presence of comorbidities were also assessed. Poisson generalized linear models with robust variance were performed in order to estimate crude prevalence ratios (PRs) and adjusted PRs using statistical (a1PR) and epidemiological criteria (a2PR). **Results:** A total of 19.9%, 32.6%, and 15.0% of all women presented mild, moderate, and severe menopausal symptoms, respectively. Overall, 70.6% women were non-adherent to HAART. The probability of non-adherence was higher in women with mild, moderate, and severe symptoms as compared to asymptomatic women in the non-adjusted model (PR: 1.79, 95% confidence interval [CI]: 1.39-2.29; PR: 1.76, 95% CI: 1.38-2.23; and PR: 2.07, 95% CI: 1.64-2.61, respectively) and the adjusted model. **Conclusion:** The severity of menopausal symptoms was associated with HAART non-adherence in HIV-infected middle-aged women.

**Br J Cancer. 2019 Dec 6. doi: 10.1038/s41416-019-0668-2. [Epub ahead of print]**

### **First-time postmenopausal bleeding as a clinical marker of long-term cancer risk: A Danish Nationwide Cohort Study.**

Bengtsen MB1, Veres K2, Nørgaard M2.

**BACKGROUND:** Data on long-term risk of cancer after a postmenopausal bleeding diagnosis are sparse. **METHODS:** We used Danish medical registries to conduct a population-based cohort study of women with a first hospital-diagnosed postmenopausal bleeding during 1995-2013. We computed the absolute risk of cancer and the standardised incidence ratio (SIR) comparing the observed cancer incidence with that expected in the general population. **RESULTS:** Among 43,756 women with postmenopausal bleeding, the absolute 1- and 5-year risk of endometrial cancer were 4.66% and 5.18%, respectively. The SIR of endometrial cancer was elevated during 0-3 months (SIR = 330.36 (95% CI: 315.43-345.81)), 3-12 months (SIR = 11.39 (95% CI: 9.79-13.17)), 1-5 years (SIR = 2.55 (95% CI: 2.19-2.94)) and >5 years of follow-up (SIR = 1.63 (95% CI: 1.40-1.90)). All selected gynaecological and urological, gastrointestinal and haematological cancers had elevated 0-3 months SIRs. Beyond 1 year of follow-up the SIRs of ovarian and bladder cancer remained elevated with a 1-5-year SIR of 2.15 (95% CI: 1.71-2.65) and 1.45 (95% CI: 1.14-1.80), respectively. **CONCLUSIONS:** In the Danish population, women with a first hospital-diagnosed postmenopausal bleeding have an increased 0-3 months risk of gynaecological, urological, gastrointestinal and haematological cancers. The SIR of endometrial, ovarian and bladder cancer remained elevated for several years.

**Hum Reprod. 2019 Dec 5. pii: dez222. doi: 10.1093/humrep/dez222. [Epub ahead of print]**

### **Hormone replacement therapy and the risk of melanoma in post-menopausal women.**

Hicks BM1, Kristensen KB2, Pedersen SA3, Hölmich LR4, Pottegård A2.

**STUDY QUESTION:** Is hormone replacement therapy (HRT) associated with an increased risk of melanoma skin cancer or prognostic outcomes amongst post-menopausal women? **SUMMARY ANSWER:** Whilst we found evidence

of an association with melanoma risk, the lack of dose-response and associations observed with recent use, localised disease and intravaginal oestrogens suggests this is a non-causal association. **WHAT IS KNOWN ALREADY:** Evidence on HRT and melanoma risk remains inconclusive, with studies providing conflicting results. Furthermore, evidence on melanoma survival is sparse, with only one previous study reporting protective associations with HRT use, likely attributable to immortal time bias. **STUDY DESIGN, SIZE, DURATION:** We conducted a nation-wide population-based case-control study and a retrospective cohort study utilising the Danish healthcare registries. Case-control analyses included 8279 women aged 45-85 with a first-ever diagnosis of malignant melanoma between 2000 and 2015, matched by age and calendar time to 165 580 population controls. A cohort of 6575 patients with a diagnosis of primary malignant melanoma between 2000 and 2013 and followed through 2015 was examined to determine if HRT use had an impact on melanoma survival outcomes. **PARTICIPANTS/MATERIALS, SETTING, METHODS:** Based on prescriptions dispensed since 1995, ever-use of HRT was defined as having filled at least one prescription for HRT prior to the index date. In total, 2629 cases (31.8%) and 47 026 controls (28.4%) used HRT. Conditional logistic regression was used to calculate odds ratios (ORs) for melanoma risk according to HRT use, compared with non-use, adjusting for potential confounders. For cohort analyses, Cox proportional hazards models were used to estimate adjusted hazard ratios (HRs) with 95% confidence intervals (CIs) for second melanoma incidence and all-cause mortality associated with HRT. **MAIN RESULTS AND THE ROLE OF CHANCE:** High use of HRT was associated with an OR of 1.21 (95% CI 1.13-1.29) for melanoma risk, with no evidence of a dose-response pattern. Results were most pronounced amongst recent high users (OR, 1.28; 95% CI 1.17-1.41), for localised disease (OR, 1.25; 95% CI 1.15-1.36) and for intravaginal oestrogen therapy (OR, 1.38; 95% CI 1.13-1.68). Compared with non-use, there was no evidence of an association for secondary melanoma for post-diagnostic new-use (fully adjusted HR, 1.56; 95% CI 0.64-3.80) or continuous HRT use (fully adjusted HR, 1.26; 95% CI 0.89-1.78). Similar associations were observed for all-cause mortality. **LIMITATIONS, REASONS FOR CAUTION:** Despite the large sample size and the use of robust population-based registries with almost complete coverage, we lacked information on some important confounders including sun exposure. **WIDER IMPLICATIONS OF THE FINDINGS:** Whilst we cannot rule out an association between HRT use and melanoma risk, the associations observed are also compatible with increased healthcare utilisation and thus increased melanoma detection amongst HRT users. No association between HRT use and melanoma survival outcomes was observed. This should provide some reassurance to patients and clinicians, particularly concerning the use of HRT in patients with a history of melanoma.

**BMC Geriatr. 2019 Dec 3;19(1):341. doi: 10.1186/s12877-019-1359-9.**

## **The efficacy and safety of exercise for prevention of fall-related injuries in older people with different health conditions, and differing intervention protocols: a meta-analysis of randomized controlled trials.**

Zhao R1, Bu W2, Chen X2.

**BACKGROUND:** Whether exercise prevents fall-related injuries in different health conditions and with different training protocols is still unclear. This study aimed to determine the effect of exercise on fall-related injuries by participant characteristics and divergent exercise protocols. The safety and compliance of exercise were also examined. **METHODS:** Electronic database searches were conducted in PubMed, Web of Science, and EMBASE for randomised controlled trials that evaluated the influence of exercise on fall-induced injuries in older people. **RESULTS:** Twenty-five trials met the inclusion criteria. Exercise significantly reduced the risk of fall-related injuries in older adults, risk ratio (RR) 0.879 [95% confidence interval (CI) 0.832-0.928]. Among the injuries, events needing medical care or resulting fractures were also decreased by exercise intervention, with RR 0.681 (0.562-0.825) and 0.561 (0.366-0.860), respectively. When analysis was stratified by participant characteristics and exercise protocols, we found that participants at high risk of falling, or with osteoporosis, were sensitive to exercise intervention. Combined exercise protocols and balance training were the most effective exercise types in reducing fall-related injuries. Exercise-associated beneficial effects were even significant in very old people ( $\geq 80$  years) and across the duration of interventions ( $< 6$  months, 6 to 12 months and  $\geq 12$  months). Exercise only generated a very low injury rate per participant year (0.002, 95% CI 0-0.05) and showed relatively good compliance of exercise (as reported in the included papers) (78.5, 95% CI 72.8-84.2%). **CONCLUSIONS:** Exercise is effective in preventing fall-induced injuries across a variety of baseline participant characteristics and exercise protocols. Exercise was associated with a low injury rate and had a good compliance, suggesting it is a feasible approach to managing fall-related injuries.

**Handb Exp Pharmacol. 2019 Dec 3. doi: 10.1007/164\_2019\_324. [Epub ahead of print]**

## Calcium and Bone.

Reid IR1,2, Bristow SM3.

The maintenance of extracellular calcium levels within a narrow range is necessary for normal function of the nervous system, muscle, and coagulation, to maintain mineralization of the skeleton but to avoid calcification of soft tissues. Accordingly, absorption and excretion of calcium is closely regulated, and adult humans can adapt to a wide range of calcium intakes from 300 to 2,000 mg/day. The evidence that low calcium intakes contribute to osteoporosis development is weak, as is evidence that increasing these intakes significantly changes fracture risk. Consistent with this view, the United States Preventive Services Task Force does not support the use of calcium supplements in healthy community-dwelling adults. While some groups continue to recommend that supplements of calcium and vitamin D are given with drug treatments for osteoporosis, this view is not supported by clinical trials which demonstrate anti-fracture efficacy of estrogens and bisphosphonates in the absence of such supplementation. Thus, calcium supplements have only a minor place in contemporary medical practice.

**Maturitas. 2020 Jan;131:40-47. doi: 10.1016/j.maturitas.2019.10.010. Epub 2019 Nov 4.**

## **Decreased bone mineral density and osteoporotic fractures are associated with the development of echogenic plaques in the carotid arteries over a 10-year follow-up period: The Japanese Population-based Osteoporosis (JPOS) Cohort Study.**

Hamada M1, Kajita E1, Tamaki J2, Kouda K3, Sato Y4, Tachiki T1, Yura A3, Kamiya K2, Nitta A2, Kagamimori S5, Iki M6.

**OBJECTIVES:** To investigate whether low bone mineral density (BMD) and history of fracture at baseline are associated with the development of echogenic carotid plaques over a 10-year follow-up period. **STUDY DESIGN:** A prospective cohort study. **MAIN OUTCOME MEASURES:** Development of echogenic plaques identified by ultrasonography of the carotid arteries. **METHODS:** Among 1048 women aged 40 or more who completed the baseline survey of the Japanese Population-based Osteoporosis (JPOS) cohort study, 500 women who completed the first decade of follow-up and 267 women who completed the second decade of follow-up were included. We identified history and incidence of clinical osteoporotic fracture during the follow-up through medical interviews, and determined vertebral fractures by morphometry of absorptiometric images. **RESULTS:** We identified 67 (13.4%) and 31 (11.6%) women with echogenic plaques at the end of first and second decade of follow-up, respectively. Participants with echogenic plaques were significantly older, exhibited lower spine BMD, and had a higher prevalence of osteoporotic fracture, diabetes, and hypertension. A generalized estimating equation analysis was used to combine the participants from the two follow-up periods into a single cohort, and showed that osteoporotic BMD and osteoporotic fractures were significantly associated with the development of echogenic plaques, after adjusting for atherosclerosis risk factors (odds ratio (OR): 2.15, 95% confidence interval (95% CI): 1.04, 4.44; OR: 1.84, 95% CI: 1.03, 3.28, respectively). **CONCLUSION:** Osteoporotic BMD and osteoporotic fracture history were significantly, and independently, associated with an increased occurrence of echogenic plaques. Ultrasonographic screening of the carotid artery may benefit patients with osteoporosis.