

## Selección de Resúmenes de Menopausia

Semana del 28 de octubre al 3 de noviembre, 2020  
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**Climacteric. 2020;23(sup1):S24-S27.doi: 10.1080/13697137.2020.1804544.**

### **Sexual function after vaginal erbium laser: the results of a large, multicentric, prospective study**

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The aim of this multicentric, prospective study was to evaluate the effects of vaginal erbium laser (VEL-SMOOTH®) on sexual function in postmenopausal women suffering from the genitourinary syndrome of menopause (GSM). This study was performed on an outpatient basis without anesthesia or drug use before or after the intervention, using an erbium laser (XS Fotona Smooth®, Fotona, Ljubljana, Slovenia) in 1081 postmenopausal women (age  $54.3 \pm 3.9$  years) treated with up to three laser applications every 30 days. Patients were assessed using the Female Sexual Function Index (FSFI) and the Female Sexual Distress Scale-Revised (FSDS-R). No adverse events were recorded during the study. The FSDS-R scores ( $n = 554$ ), from basal values of  $25.5 \pm 3.5$ , were  $11.5 \pm 3.0$ ,  $10.5 \pm 3.5$  and  $11.5 \pm 3.5$  at the 4-, 12- and 24-week follow-ups, respectively ( $p < 0.01$  vs. corresponding basal values). Individual FSFI domain scores ( $n = 569$ ) significantly ( $p < 0.001$ ) increased after VEL-SMOOTH® treatment and remained significantly higher up to the 24th week after the end of treatment. The total scores, from basal values of  $15.5 \pm 1.5$ , were  $27.5 \pm 2.5$ ,  $27.6 \pm 2.7$  and  $27.0 \pm 3.5$  at the 4-, 12- and 24-week follow-ups, respectively ( $p < 0.01$  vs. corresponding basal values). Albeit not randomized, this large, prospective study shows that VEL-SMOOTH® treatment may improve sexual function in postmenopausal women suffering from GSM.

**Diabetes Metab Syndr Obes. 2020 Oct 13;13:3667-3690.doi: 10.2147/DMSO.S275560. eCollection 2020. (FREE)**

### **Relationship Between Metabolic Syndrome and Bone Health - An Evaluation of Epidemiological Studies and Mechanisms Involved**

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Metabolic syndrome (MetS) and osteoporosis are two medical problems plaguing the ageing populations worldwide. Though seemingly distinctive to each other, metabolic derangements are shown to influence bone health. This review summarises the relationship between MetS and bone health derived from epidemiological studies and explains the mechanistic basis of this relationship. The discourse focuses on the link between MetS and bone mineral density, quantitative sonometric indices, geometry and fracture risk in humans. The interesting sex-specific trend in the relationship, probably due to factors related to body composition and hormonal status, is discussed. Mechanistically, each component of MetS affects the bone distinctly, forming a complex interacting network influencing the skeleton. Lastly, the effects of MetS management, such as pharmacotherapies, exercise and bariatric surgery, on bone, are presented. This review aims to highlight the significant relationship between MetS and bone, and proper management of MetS with the skeletal system in mind could prevent cardiovascular and bone complications.

**BMJ. 2020 Oct 28;371:m3873.doi: 10.1136/bmj.m3873.**

### **Use of hormone replacement therapy and risk of breast cancer: nested case-control studies using the QResearch and CPRD databases**

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Objective: To assess the risks of breast cancer associated with different types and durations of hormone replacement therapy (HRT). Design: Two nested case-control studies. Setting: UK general practices contributing to QResearch or Clinical Practice Research Datalink (CPRD), linked to hospital, mortality, social deprivation, and cancer registry (QResearch only) data. Participants: 98 611 women aged 50-79 with a primary diagnosis of breast cancer between 1998 and 2018, matched by age, general practice, and index date to 457 498 female controls. Main outcome measures: Breast cancer diagnosis from general practice, mortality, hospital, or cancer registry records. Odds ratios for HRT types, adjusted for personal characteristics, smoking status, alcohol consumption, comorbidities, family history, and other prescribed drugs. Separate results from QResearch or CPRD were combined. Results: Overall, 33 703 (34%) women with a diagnosis of breast cancer and 134 391 (31%) controls had used HRT prior to one year before the index date.

Compared with never use, in recent users (<5 years) with long term use ( $\geq 5$  years), oestrogen only therapy and combined oestrogen and progestogen therapy were both associated with increased risks of breast cancer (adjusted odds ratio 1.15 (95% confidence interval 1.09 to 1.21) and 1.79 (1.73 to 1.85), respectively). For combined progestogens, the increased risk was highest for norethisterone (1.88, 1.79 to 1.99) and lowest for dydrogesterone (1.24, 1.03 to 1.48). Past long term use of oestrogen only therapy and past short term (<5 years) use of oestrogen-progestogen were not associated with increased risk. The risk associated with past long term oestrogen-progestogen use, however, remained increased (1.16, 1.11 to 1.21). In recent oestrogen only users, between three (in younger women) and eight (in older women) extra cases per 10 000 women years would be expected, and in oestrogen-progestogen users between nine and 36 extra cases per 10 000 women years. For past oestrogen-progestogen users, the results would suggest between two and eight extra cases per 10 000 women years. Conclusion: This study has produced new generalisable estimates of the increased risks of breast cancer associated with use of different hormone replacement preparations in the UK. The levels of risks varied between types of HRT, with higher risks for combined treatments and for longer duration of use.

**Climacteric. 2020 Oct 28;1-11.doi: 10.1080/13697137.2020.1828854. Online ahead of print.**

### **Dietary intake and menopausal symptoms in postmenopausal women: a systematic review**

P R E S Noll <sup>1 2</sup> , C A S Campos <sup>3</sup> , C Leone <sup>3</sup> , J Zangirolami-Raimundo <sup>1</sup> , M Noll <sup>2</sup> , E C Baracat <sup>1</sup> , et al. Despite literature pointing to a relation between dietary intake and menopausal symptoms, most studies have evaluated either only supplements or only specific nutrients or foods. Therefore, this study aimed to provide a systematic review of the literature regarding the association between dietary intake and menopausal symptoms in postmenopausal women. A systematic search was conducted across PubMed/Medline, Web of Science, Scopus, and Embase to identify studies published between 2009 and 2019. We identified 3828 studies; after screening, 73 studies were reviewed and 19 of these investigated nutrient and food intake and eating patterns associated with the intensity of menopausal symptoms. Studies evaluating diet quality or dietary patterns showed an association between lower intensity of psychological symptoms, sleep disorders, and vasomotor, urogenital, and somatic symptoms and higher consumption of vegetables, whole grains, and unprocessed foods. Also, the intensity of these symptoms is associated with high-processed foods, saturated fats, and sugars. Regarding nutrient and/or specific food, the studies indicated an association between caffeine intake and type of fat intake and the intensity of menopausal symptoms. Dietary intake was found to be associated with the severity of menopausal symptoms; however, evidence for the association between dietary intake and menopausal symptoms is inconsistent and inconclusive, and is provided by a small number of studies.

**Eur J Endocrinol. 2020 Oct 1;EJE-20-0702.R2.doi: 10.1530/EJE-20-0702. Online ahead of print.**

### **Cancer occurrence in Turner syndrome and the effect of sex hormone substitution therapy**

Mette Hansen Viuff <sup>1</sup> , Kirstine Stochholm <sup>2</sup> , Angela Lin <sup>3</sup> , Agnethe Berglund <sup>4</sup> , Svend Juul <sup>5</sup> , et al. Objective: Although the overall risk of cancer is not increased in Turner syndrome, the pattern of cancer occurrence differs from the general population. We aim to describe the cancer morbidity pattern in Turner syndrome and evaluate the effect of long-term hormone replacement therapy (HRT). Design: Nationwide epidemiological study. Methods: 1,156 females with Turner syndrome diagnosed during 1960-2014, were linked with data from the Danish National Patient Registry. Statistics Denmark randomly identified 115,578 female controls. Stratified Cox regression was used to analyze cancer morbidity, mortality and effect of HRT. Results: Overall risk of cancer was not elevated (Hazard ratio 1.04 (95%CI 0.80-1.36)). The risk of skin cancer and benign skin neoplasms was two-fold increased, while the risk of breast cancer was decreased (Hazard ratio 0.4 (0.2-0.9)). Turner syndrome (45,X) had a two- to five-fold increased risk of benign central nervous system tumors, colon and rectal cancers, benign skin neoplasms and skin cancer. Turner syndrome women with a 45,X/46,XX karyotype had increased risk of tongue cancer. HRT had no impact on the risk of any cancer investigated in this study. Conclusions: The lack of one X chromosome might play a role in skin neoplasms, central nervous system tumors, colon and rectal cancers. The risk of breast cancer is lower than in the general population. Long-term HRT during the premenopausal age range seem not to exert a cancerous effect in Turner syndrome. Increased vigilance concerning specific types of cancer in Turner syndrome harboring a 45,X karyotype is needed.

**Menopause. 2020 Nov;27(11):1265-1273.doi: 10.1097/GME.0000000000001667.**

## **The severity of vasomotor symptoms and number of menopausal symptoms in postmenopausal women and select clinical health outcomes in the Women's Health Initiative Calcium and Vitamin D randomized clinical trial**

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**Objective:** This study evaluated whether vasomotor symptom (VMS) severity and number of moderate/severe menopausal symptoms (nMS) were associated with health outcomes, and whether calcium and vitamin D (CaD) modified the risks. **Methods:** The Women's Health Initiative CaD study was a double blind, randomized, placebo-controlled trial, which tested 400 IU of 25-hydroxyvitamin-D and 1,000 mg of calcium per day in women aged 50 to 79 years. This study included 20,050 women (median follow-up of 7 y). The outcomes included hip fracture, colorectal cancer, invasive breast cancer, all-cause mortality, coronary heart disease, stroke, cardiovascular death, and total cardiovascular disease (CVD). **MS included:** hot flashes, night sweats, dizziness, heart racing, tremors, feeling restless, feeling tired, difficulty concentrating, forgetfulness, mood swings, vaginal dryness, breast tenderness, migraine, and waking up several times at night. Associations between VMS severity and nMS with outcomes were tested. **Results:** No association between VMS severity and any outcome were found. In contrast, nMS was associated with higher stroke (hazard ratio [HR] 1.40 95% confidence interval [CI] 1.04-1.89 for  $\geq 2$  MS vs none; HR 1.20 95% CI 0.89-1.63 for 1 MS vs none,  $P$  trend = 0.03) and total CVD (HR 1.35, 95% CI, 1.18-1.54 for  $\geq 2$  MS vs none; HR 0.99, 95% CI, 0.87-1.14 for 1 MS vs none  $P$  trend < 0.001). CaD did not modify any association. **Conclusion:** Severity of VMS was not associated with any outcome. Having  $\geq 2$  moderate or severe MS was associated with an increased risk for CVD. The number of moderate/severe MS may be a marker for higher CVD risk.

**Menopause. 2020 Oct 26.doi: 10.1097/GME.0000000000001688. Online ahead of print.**

## **Age, menstruation history, and the brain**

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**Objectives:** To investigate the cross-sectional association between measures of menstruation history (including menopausal status, age of menopause, age of menarche, and duration of reproductive stage) and brain volume. **Methods:** Women (aged 45 to 79 years) from the UK Biobank were included ( $n = 5,072$ ) after excluding those who had (1) hysterectomy or bilateral oophorectomy, (2) ever used menopausal hormone therapy, (3) ever had a stroke, or (4) were perimenopausal. Multiple linear hierarchical regression models were computed to quantify the cross-sectional association between measures of menstruation history and brain volume. Sensitivity analysis based on propensity matching for age (and other demographic/health covariates) were applied to estimate differences in brain volumes between matched premenopausal and postmenopausal women. **Results:** Postmenopausal women had 1.06% (95% confidence interval [CI]; 1.05-1.06) and 2.17% (95% CI, 2.12-2.22) larger total brain volume (TBV) and hippocampal volumes (HV), respectively, than premenopausal women. Sensitivity analysis with age matched samples produced consistent results (TBV: 0.82%, 95% CI, 0.25-1.38; HV: 1.33%, 95% CI, 0.01-2.63). For every year increase in age above 45 years, postmenopausal women experienced 0.23% greater reduction in TBV than premenopausal women (95% CI, -0.60 to -0.14), which was not observed for HV. Moreover, every 1 year delayed onset of menopause after 45 was associated with 0.32% (95% CI, -0.35 to -0.28) and 0.31% (95% CI, -0.40 to -0.22) smaller TBV and HV, respectively. Every additional year in age of menarche was associated with 0.10% (95% CI, 0.04-0.16) larger TBV, which was not detected for HV. Similarly, every 1 year increase in duration of reproductive stage was associated with 0.09% smaller TBV (95% CI, -0.15 to -0.03), which was not detected for HV. **Conclusions:** Menopause may contribute to brain volume beyond typical aging effects. Furthermore, early age of menarche, delayed age of menopause and increasing duration of reproductive stage were negatively associated with brain volume. Further research is required to determine whether the negative association between age of menopause and HV is potentially an indicator of future vulnerability for dementia.

**Menopause. 2020 Oct 26.doi: 10.1097/GME.0000000000001676. Online ahead of print.**

## **Efficacy of progestin-only treatment for the management of menopausal symptoms: a systematic review**

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**Importance:** Menopause is associated with bothersome symptoms for many women, including mood changes, hot flashes, sleep problems, and fatigue. Progesterone is commonly prescribed in combination with estrogen therapy. Although monotherapy with progestins has been used as treatment of menopausal symptoms in women with contraindications to estrogens, the optimal route, and dosage of progestin monotherapy has not been established.

**Objective:** To assess whether progestin as a standalone treatment is effective for treating vasomotor and mood symptoms associated with menopause. **Evidence review:** We conducted a systematic review using PubMed and Embase databases from January 1980 to January 2020. We included randomized controlled trials (RCTs) that investigated different forms of progestin for the treatment of vasomotor or mood symptoms associated with menopause. **Findings:** A systematic search of 892 studies identified seven RCTs involving a total of 601 patients. The available literature was heterogeneous in terms of formulation and dose of progesterone; administration ranged from 5 to 60 mg of transdermal progesterone, 10 to 20 mg oral medroxyprogesterone acetate, and 300 mg of oral micronized progesterone. Duration of treatment also differed between studies, ranging from 21 days to 12 months (median: 12 wks). Three of seven RCTs reported that progestin therapy led to an improvement of vasomotor symptoms (VMS) in postmenopausal women. The largest study administering oral progestin using 300 mg oral medroxyprogesterone reported a 58.9% improvement in VMS (vs 23.5% in placebo group,  $n = 133$ ), whereas the largest study using transdermal progesterone reported no improvement ( $n = 230$ ). No study reported an improvement of mood symptoms. Side effects, such as headaches and vaginal bleeding, were significant in five of seven RCTs and led to discontinuation of treatment in 6% to 21% of patients. **Conclusions and relevance:** A beneficial effect was reported in some trials with the transdermal route at longer duration and with oral treatment at higher doses for VMS for progesterone-only therapy. This report may help to inform future studies of progestin-only therapy for the treatment of menopausal symptoms.

**Osteoporosis Sarcopenia. 2020 Sep;6(3):146-150. doi: 10.1016/j.afos.2020.07.002. Epub 2020 Aug 8.**

### **Comparison of morbidity and mortality of hip and vertebral fragility fractures: Which one has the highest burden?**

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**Objectives:** Hip fragility fractures were regarded as one of the most severe, but recent papers report on the underestimated burden of vertebral compression fractures. This study aims to compare morbidity and mortality of hip and vertebral fragility fractures in patients treated in the same setting. **Methods:** Patients aged  $\geq 50$  years with hip fracture, and those with vertebral fracture presenting to our hospital between January 2014 and January 2017 were included. Patients were evaluated 1 year after their index fracture. SF-36 scores, mortality, and institutionalization are then recorded. Patients were divided into 2 groups: hip fractures and vertebral fractures. **Results:** There were 106 and 90 patients respectively evaluated in hip and vertebral fracture groups at 1 year. Patients in both groups were comparable for age, sex, comorbidities and neuropsychiatric condition ( $P > 0.05$ ). At 1 year follow-up, SF-36 showed better averages in all 8 scales in hip fracture group compared to vertebral fracture group. Mortality in the hip fracture group reached 32.1% compared to 10% for the vertebral fracture group ( $P < 0.01$ ). Fifteen patients were institutionalized in the hip fracture group compared to 18 patients in the vertebral fracture group ( $P > 0.05$ ). **Conclusions:** When comparing patients treated in the same setting, hip fracture is associated with significantly increased mortality than vertebral fracture; however, the latter is associated with more morbidity.

**J Neuroinflammation. 2020 Oct 23;17(1):317.doi: 10.1186/s12974-020-01998-9.**

### **The peri-menopause in a woman's life: a systemic inflammatory phase that enables later neurodegenerative disease**

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The peri-menopause or menopausal transition-the time period that surrounds the final years of a woman's reproductive life-is associated with profound reproductive and hormonal changes in a woman's body and exponentially increases a woman's risk of cerebral ischemia and Alzheimer's disease. Although our understanding of the exact timeline or definition of peri-menopause is limited, it is clear that there are two stages to the peri-menopause. These are the early menopausal transition, where menstrual cycles are mostly regular, with relatively few interruptions, and the late transition, where amenorrhea becomes more prolonged and lasts for at least 60 days, up to the final menstrual period. Emerging evidence is showing that peri-menopause is pro-inflammatory and disrupts estrogen-regulated neurological systems. Estrogen is a master regulator that functions through a network of estrogen receptors subtypes alpha (ER- $\alpha$ ) and beta (ER- $\beta$ ). Estrogen receptor-beta has been shown to regulate a key component of the innate immune response known as the inflammasome, and it also is involved in regulation of neuronal mitochondrial function. This review will present an overview of the menopausal transition as an inflammatory event, with associated systemic and central nervous system inflammation, plus regulation of the innate immune response by ER- $\beta$ -mediated mechanisms.