



## Selección de Resúmenes de Menopausia

Semana del 24 al 30 de julio de 2019

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**Joint Bone Spine. 2019 Jul 25. pii: S1297-319X(19)30111-3. doi: 10.1016/j.jbspin.2019.07.005. [Epub ahead of print]**

### **French Recommendations on Strategies for Preventing and Treating Osteoporosis Induced by Adjuvant Breast Cancer Therapies.**

Bouvard B1, Confavreux CB2, Briot K3, Bonneterre J4, Cormier C3, Cortet B5, Hannoun-Lévi JM6, et al.

Standard adjuvant therapies for breast cancer such as chemotherapy or aromatase inhibitor and LH-RH agonist hormone therapy are associated with significant survival gains but also induce bone loss by aggravating the estrogen deprivation. The bone loss may be substantial, notably during early treatment, and occurs regardless of the baseline bone mineral density values. The objective of developing these recommendations was to achieve a practical consensus among various scientific societies, based on literature review, about osteoporosis prevention and treatment in these patients. The following scientific societies contributed to the work : Société Française de Rhumatologie (SFR), Groupe de Recherche et d'Information sur les Ostéoporoses (GRIO), Groupe Européen d'Etudes des Métastases Osseuses (GEMO), Association Francophone pour les Soins Oncologiques de Support (AFSOS), Société Française de Sénologie et de Pathologie Mammaire (SFSPM), Société Française de Radiothérapie Oncologique (SFRO). Drug prescription and reimbursement modalities in France were taken into account. These recommendations apply to postmenopausal women taking systemic chemotherapy and/or aromatase inhibitor therapy, non-postmenopausal women taking LH-RH agonist therapy, and non-postmenopausal women with persistent amenorrhea 1 year after chemotherapy completion. All women in these three categories should undergo an evaluation of bone health and receive interventions to combat risk factors for bone loss. Patients with a history of severe osteoporotic fracture and/or a T-score value  $< -2.5$  should receive osteoporosis drug therapy. The FRAX® score should be used to guide treatment decisions in patients whose T-score is between  $-1$  and  $-2.5$ . General osteoporosis prevention measures should be applied in patients without criteria for osteoporosis drug therapy, who should undergo bone mineral density measurements 18-24 months later if the baseline T-score is  $< -1$  and 3-5 years later if the baseline T-score is  $> -1$ . The anti-tumor effect of bisphosphonates and denosumab was not considered when establishing these recommendations.

**J Clin Densitom. 2019 Jul 10. pii: S1094-6950(19)30108-8. doi: 10.1016/j.jocd.2019.07.007. [Epub ahead of print]**

### **The Impact of Smoking on Bone Metabolism, Bone Mineral Density and Vertebral Fractures in Postmenopausal Women.**

Trevisan C1, Alessi A2, Girotti G2, Zanforlini BM2, Bertocco A2, Mazzochin M2, Zoccarato F2, et al.

**BACKGROUND:** Smoking is recognized among the risk factors for osteoporosis, but only few studies have comprehensively explored its influence on bone metabolism and strength. We aimed to evaluate smoking effects on calcium-phosphate metabolism, bone mineral density (BMD) and fracture risk in postmenopausal women. **METHODS:** Our sample included 1067 postmenopausal women who arrived to our osteoporosis outpatient clinic. Anamnestic data, smoking habits (categorized as never, former, and current; and by smoking intensity and duration), biochemical parameters, lumbar/femoral BMD, and presence of vertebral fractures were recorded. In a subsample of 357 women, the changes in BMD after a 2-yr follow-up period were also assessed. **RESULTS:** Current smokers had shorter reproductive age, lower body mass index, and higher prevalence of heavy alcohol consumption than former/never smokers. They also had lower PTH values and weaker linear association between serum vitamin D and parathyroid hormone (current  $\beta = -0.11$ [SE = 0.004]; former  $\beta = -0.14$ [SE = 0.01]; never  $\beta = -0.20$ [SE = 0.003];  $p < 0.01$  for all). Baseline BMD did not reflect differences based on smoking habits, duration or intensity. However, after 2 years, only current smokers significantly worsened in femoral BMD. After adjustment for confounders, the chance of having sustained vertebral fractures at the first evaluation increased by 74% (95% confidence interval:1.07-2.83) in current compared with never smokers, especially among heavy smokers. **CONCLUSIONS:** Smoking may negatively affect bone by inhibiting vitamin D-parathyroid hormone axis, reducing estrogen exposure, promoting

risky health behaviors, and accelerating bone loss, especially at the femur. No significant differences were observed in these outcomes among former smokers, suggesting that quitting smoking has beneficial effects on bone health.

**Osteoporos Sarcopenia. 2019 Jun;5(2):29-37. doi: 10.1016/j.afos.2019.05.001. Epub 2019 May 15.**

### **Diabetes and bone.**

Hygum K1, Starup-Linde J1, Langdahl BL1.

Bone disease is a serious complication to diabetes. Patients with type 1 diabetes (T1D) and type 2 diabetes (T2D) suffer from an increased risk of fracture, most notably at the hip, compared with patients without diabetes. Confounders such as patient sex, age, body mass index, blood glucose status, fall risk, and diabetes medications may influence the fracture risk. Different underlying mechanisms contribute to bone disease in patients with diabetes. Bone quality is affected by low bone turnover in T1D and T2D, and furthermore, incorporation of advanced glycation end-products, changes in the incretin hormone response, and microvascular complications contribute to impaired bone quality and increased fracture risk. Diagnosis of bone disease in patients with diabetes is a challenge as current methods for fracture prediction such as bone mineral density T-score and fracture risk assessment tools underestimate fracture risk for patients with T1D and T2D. This review focuses on bone disease and fracture risk in patients with diabetes regarding epidemiology, underlying disease mechanisms, and diagnostic methods, and we also provide considerations regarding the management of diabetes patients with bone disease in terms of an intervention threshold and different treatments.

**Breast. 2019 Jun 17;47:43-55. doi: 10.1016/j.breast.2019.06.002. [Epub ahead of print]**

### **Safety of menopausal hormone therapy in breast cancer survivors older than fifty at diagnosis: A systematic review and meta-analysis.**

Mudhune GH1, Armour M2, McBride KA3.

Due to the higher incidence of hormone responsive tumours in women >50, the safety of hormone replacement therapy (HRT) in older breast cancer survivors may differ from younger age groups. The primary outcome in this review was the risk of tumour recurrence and secondary outcome the relationship with breast cancer-related mortality. Medline, CINAHL, Cochrane, Google Scholar and EMBASE databases were searched through August 2018 for studies reporting exposure to HRT in survivors  $\geq 50$  at primary diagnosis. Random effects models were used to estimate the combined relative risk (RR) of tumour recurrence and breast cancer-related mortality using the Mantel-Haenszel method and the quality of evidence determined for the primary outcome. Overall, nine studies (four cohort, one case-control, four RCTs; n=16,002) were included. Very low quality evidence from observational studies demonstrated no adverse effect on tumour recurrence with HRT use (RR 0.80, 95% CI 0.53 to 1.19; I<sup>2</sup>=66%; n=11,984), while moderate quality evidence from RCTS demonstrated an adverse effect (RR 1.46, 95% CI 1.20 to 1.77; I<sup>2</sup>=17%; n=4108). Similarly, observational studies demonstrated no adverse effect on breast cancer-related mortality (RR 0.32, 95% CI 0.21 to 1.49; I<sup>2</sup>=0%, n=2182), while RCTS demonstrated a non-significant higher risk (RR 1.07, 95% CI 0.77 to 1.49; I<sup>2</sup>=0%; n=3918). Ultimately, despite conflicting findings, evidence of sufficient quality suggests that HRT may increase the risk of tumour recurrence in older survivors. However, adverse effect on mortality is unlikely. Caution with HRT use in survivors is further advised.

**Pharmacoecon Open. 2019 Jul 24. doi: 10.1007/s41669-019-0167-7. [Epub ahead of print]**

### **A Nationwide Study of Prevalence Rates and Characteristics of 199 Chronic Conditions in Denmark.**

Hvidberg MF1, Johnsen SP2, Davidsen M3, Ehlers L4.

**BACKGROUND:** Real-world data of disease prevalence represents an important but underutilised source of evidence for health economic modelling. **AIMS:** The aim of this study was to estimate nationwide prevalence rates and summarise the characteristics of 199 chronic conditions using Danish population-based health registers, to provide an off-the-shelf tool for decision makers and researchers. **METHODS:** The study population comprised all Danish residents aged 16 years or above on 1 January 2013 (n=4,555,439). The study was based on the linkage of national registers covering hospital contacts, contacts with primary care (including general practitioners) and filled-in out-of-hospital prescriptions. **RESULTS:** A total of 65.6% had one or more chronic condition. The ten conditions with the highest degree of prevalence were hypertension (23.3%), respiratory allergy (18.5%), disorders of lipoprotein metabolism (14.3%), depression (10.0%), bronchitis (9.2%), asthma (7.9%), type 2 diabetes (5.3%),

chronic obstructive lung disease (4.7%), osteoarthritis of the knee (3.9%) and finally osteoporosis (3.5%) and ulcers (3.5%) in joint tenth place. Characteristics by gender, age and national geographical differences were also presented. CONCLUSIONS: A nationwide catalogue of the prevalence rates and characteristics of patients with chronic conditions based on a nationwide population is provided. The prevalence rates of the 199 conditions provide important information on the burden of disease for use in healthcare planning, as well as for economic, aetiological and other research.

**Arch Endocrinol Metab. 2019 Jul 18;63(3):190-198. doi: 10.20945/2359-399700000152.**

### **Testosterone therapy for women with low sexual desire: a position statement from the Brazilian Society of Endocrinology and Metabolism.**

Weiss RV, Hohl A, Athayde A, Pardini D, Gomes L, Oliveira M, Meirelles R, Clapauch R, Spritzer PM.

OBJECTIVE: To summarize current evidence regarding testosterone treatment for women with low sexual desire.

MATERIALS AND METHODS: The Female Endocrinology and Andrology Department of the Brazilian Society of Endocrinology and Metabolism invited nine experts to review the physiology of testosterone secretion and the use, misuse, and side effects of exogenous testosterone therapy in women, based on the available literature and guidelines and statements from international societies. RESULTS: Low sexual desire is a common complaint in clinical practice, especially in postmenopausal women, and may negatively interfere with quality of life. Testosterone seems to exert a positive effect on sexual desire in women with sexual dysfunction, despite a small magnitude of effect, a lack of long-term safety data, and insufficient evidence to make a broad recommendation for testosterone therapy. Furthermore, there are currently no testosterone formulations approved for women by the relevant regulatory agencies in the United States, Brazil, and most other countries, and testosterone formulations approved for men are not recommended for use by women. CONCLUSION: Therefore, testosterone therapy might be considered if other strategies fail, but the risks and benefits must be discussed with the patient before prescription.

**JAMA Netw Open. 2019 Jul 3;2(7):e197337. doi: 10.1001/jamanetworkopen.2019.7337.**

### **Association of Normal-Weight Central Obesity with All-Cause and Cause-Specific Mortality Among Postmenopausal Women.**

Sun Y1, Liu B1, Snetselaar LG1, Wallace RB1, Caan BJ2, Rohan TE3, Neuhaus ML4, Shadyab AH5, Chlebowski RT6, Manson JE7, Bao W1,8,9.

Importance: Current public health guidelines for obesity prevention and control focus on promoting a normal body mass index (BMI), rarely addressing central obesity, which is reflected by high waist circumference (WC) and common in the general population. Studies of the association of normal-weight central obesity with long-term health outcomes are sparse. Objective: To examine associations of normal-weight central obesity with all-cause and cause-specific mortality in postmenopausal women in the United States. Design, Setting, and Participants: A nationwide prospective cohort study of 156 624 postmenopausal women enrolled in the Women's Health Initiative at 40 clinical centers in the United States between 1993 and 1998. These women were observed through February 2017. Data analysis was performed from September 15, 2017, to March 13, 2019. Exposures: Different combinations of BMI (calculated as weight in kilograms divided by height in meters squared; normal weight: BMI, 18.5-24.9; overweight: BMI, 25.0-29.9; and obesity: BMI,  $\geq 30$ ) and WC (normal: WC,  $\leq 88$  cm and high: WC,  $> 88$  cm). Main Outcomes and Measures: Mortality from all causes, cardiovascular disease, and cancer. Results: Of the 156 624 women (mean [SD] age, 63.2 [7.2] years), during 2 811 187 person-years of follow-up, 43 838 deaths occurred, including 12 965 deaths from cardiovascular disease (29.6%) and 11 828 deaths from cancer (27.0%). Compared with women with normal weight and no central obesity and adjusted for demographic characteristics, socioeconomic status, lifestyle factors, and hormone use, the hazard ratio for all-cause mortality was 1.31 (95% CI, 1.20-1.42) among women with normal weight and central obesity, 0.91 (95% CI, 0.89-0.94) among women with overweight and no central obesity, 1.16 (95% CI, 1.13-1.20) for women with overweight and central obesity, 0.93 (95% CI, 0.89-0.94) for women with obesity and no central obesity, and 1.30 (95% CI, 1.27-1.34) for women with obesity and central obesity. Compared with normal weight without central obesity, normal-weight central obesity was associated with higher risk of cardiovascular disease mortality (hazard ratio, 1.25; 95% CI, 1.05-1.46) and cancer mortality (hazard ratio, 1.20; 95% CI, 1.01-1.43). Conclusions and Relevance: Normal-weight central obesity in women was associated with excess risk of mortality, similar to that of women with BMI-defined obesity with central obesity. These findings

underscore the need for future public health guidelines to include the prevention and control of central obesity, even in individuals with normal BMI.