



## Selección de Resúmenes de Menopausia

Semana del 15 al 21 de Junio 2016

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### Links Between the Microbiome and Bone.

Hernandez CJ, Guss JD, Luna M, Goldring SR.

The human microbiome has been shown to influence a number of chronic conditions associated with impaired bone mass and bone quality including obesity, diabetes and inflammatory bowel disease. The connection between the microbiome and bone health, however, has not been well studied. The few studies available demonstrate that the microbiome can have a large effect on bone remodeling and bone mass. The gut microbiome is the largest reservoir of microbial organisms in the body and consists of over a thousand different species interacting with one another in a stable dynamic equilibrium. How the microbiome can affect organs distant from the gut is not well understood, but is believed to occur through regulation of nutrition, regulation of the immune system and/or translocation of bacterial products across the gut endothelial barrier. Here we review each of these mechanisms and discuss their potential effect on bone remodeling and bone mass. We review how preclinical studies of bone-microbiome interactions are challenging because the microbiome is sensitive to genetic background, housing environment, and vendor source. Additionally, although the microbiome exhibits a robust response to external stimuli, it rapidly returns to its original steady state after a disturbance, making it difficult to sustain controlled changes in the microbiome over time periods required to detect alterations in bone remodeling, mass or structure. Despite these challenges, an understanding of the mechanisms by which the gut microbiome affects bone has the potential to provide insights into the dissociation between fracture risk and bone mineral density in patients including those with obesity, diabetes or inflammatory bowel disease. In addition, alteration of the gut microbiome has the potential to serve as a biomarker of bone metabolic activity as well as a target for therapies to improve bone structure and quality using pharmaceutical agents or pre- or

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### Association of Vasomotor and Other Menopausal Symptoms with Risk of Cardiovascular Disease: A Systematic Review and Meta-Analysis.

Muka T, Oliver-Williams C, Colpani V, Kunutsor S, Chowdhury S, Chowdhury R, Kavousi M, Franco OH.

**IMPORTANCE:** Vasomotor symptoms (hot flushes and night sweats) and other symptoms, including depression, anxiety and panic attacks, are commonly experienced by menopausal women and have been associated with an unfavourable cardiovascular risk profile. **OBJECTIVE:** To investigate whether presence of menopausal symptoms is associated with the development of cardiovascular disease (CVD). **METHODS:** Five electronic databases (Medline, EMBASE and Web of Science) were search until February 17th, 2015 to identify relevant studies. Observational cohort studies or randomised intervention studies were eligible for inclusion if they followed participants prospectively (at least 1 year of follow-up), and reported relevant estimates on the association of any vasomotor symptoms, or other menopausal symptoms, with risk of CVD, coronary heart disease (CHD), or stroke in perimenopausal, menopausal, or postmenopausal women. Data were extracted by two independent reviewers using a pre-designed data collection form. Separate pooled relative risks (RRs) for age and non-established cardiovascular risk factors (e.g., education, ethnicity) adjusted data and for established cardiovascular risk factors and potential mediators-adjusted data (e.g., smoking, body mass index, and hypertension) were calculated. **RESULTS:** Out of 9,987 initially identified references, ten studies were selected, including 213,976 women with a total of 10,037 cardiovascular disease outcomes. The age and non-established cardiovascular risk factors adjusted RRs) [95% confidence intervals] for development of CHD, Stroke and CVD comparing women with and without any menopausal symptoms were 1.34 [1.13-1.58], 1.30 [0.99-1.70], 1.48 [1.21-1.80] respectively, and the corresponding RRs adjusted for cardiovascular risk factors and potential mediators were 1.18 [1.03-1.35], 1.08 [0.89-1.32], 1.29 [0.98-1.71]. However, these analyses were limited by potential unmeasured confounding and the small number of studies on this topic. **CONCLUSION:** Presence of vasomotor symptoms and other menopausal symptoms are generally associated with an increased risk of cardiovascular disease, which is mainly explained by cardiovascular risk factors. This article is protected by copyright. All rights reserved.

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### **A randomized, double-blind, crossover trial comparing a silicone- versus water-based lubricant for sexual discomfort after breast cancer.**

Hickey M, Marino JL, Braat S, Wong S.

Discomfort during sexual activity is common after breast cancer. Vaginal estrogens are effective but commonly avoided due to systemic absorption. Despite the large commercial market for vaginal lubricants, no randomized studies have compared products. We aimed to compare efficacy and acceptability of two major types of lubricant for discomfort during sexual activity in postmenopausal breast cancer patients. In a single-center, randomized, double-blind, AB/BA crossover design, sexually active postmenopausal breast cancer patients used each lubricant for 4 weeks. The primary patient-reported efficacy outcome was total discomfort related to sexual activity (Fallowfield Sexual Activity Questionnaire Discomfort subscale SAQ-D). Acceptability was measured by patient preference and reported intention to continue using the products. Of 38 women analyzed, over 90 % experienced clinically significant sexually related distress at baseline. Water- and silicone-based lubricants did not differ statistically in efficacy based on total sexual discomfort (difference 0.7, 95 % confidence interval (CI) 0-1.4,  $p = 0.06$ ). In a post hoc analysis, pain/discomfort during penetration improved more during silicone-based lubricant use than during water-based lubricant use (odds ratio 5.4, 95 % CI 1.3-22.1,  $p = 0.02$ ). All aspects of sexual discomfort measured with diaries were reported more commonly with water- than silicone-based lubricant. Almost twice as many women preferred silicone-based to water-based lubricant than the converse ( $n = 20, 65 \%$ , vs.  $n = 11, 35 \%$ ). 88 % continued to experience clinically significant sexually related distress despite use of either lubricant. Total sexual discomfort was lower after use of silicone-based lubricant than water-based, but many women continue to experience sexually related distress.

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### **Elevated levels of circulating thyroid hormone do not cause the medical sequelae of hyperthyroidism.**

Kelly T, Denmark L, Lieberman DZ.

**BACKGROUND:** Clinicians have been reluctant to use high dose thyroid (HDT) to treat affective disorders because high circulating levels of thyroid hormone have traditionally been equated with hyperthyroidism, and understood as the cause of the medical sequelae of hyperthyroidism, such as osteoporosis and cardiac abnormalities. This conclusion is not supported by (HDT) research. **METHODS:** A literature review of research related to the morbidity and mortality of HDT treatment was performed. **RESULTS:** There exists a large body of research involving the use of HDT treatment to prevent the recurrence of differentiated thyroid cancer and to treat affective disorders. A review of this literature finds a lack of support for HDT as a cause of osteoporosis, nor is there support for an increase in morbidity or mortality associated with HDT. This finding contrasts with the well-established morbidity and mortality associated with Graves' disease, thyroiditis, and other endogenous forms of hyperthyroidism. **DISCUSSION:** The lack of evidence that exogenous HDT causes osteoporosis, cardiac abnormalities or increases mortality compared with the significant morbidity and mortality of hyperthyroidism requires an alternative cause for the medical sequelae of hyperthyroidism. One possibility is an autoimmune mechanism. **CONCLUSION:** High circulating levels of thyroid hormone is not the cause of the sequela of hyperthyroidism. The reluctance to using high dose thyroid is unwarranted.

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### **Cardiovascular risk in women with premature ovarian insufficiency compared to premenopausal women at middle age.**

Daan NM, Muka T, Koster MP, Roeters van Lennep JE, Lambalk CB, Laven JS, Fauser CG, Meun C, de Rijke YB.

**CONTEXT:** A young age at menopause has been associated with increased cardiovascular disease (CVD) risk. **OBJECTIVE:** To compare the cardiovascular risk profile between women with premature ovarian insufficiency (POI) and premenopausal controls of comparable age. **DESIGN:** Cross-sectional case control study. **SETTING:** Two University Medical Centers. **PARTICIPANTS:** Women above 45 years of age who were previously diagnosed with POI ( $n=83$ ), and premenopausal population controls of comparable age ( $n=266$ ). **MAIN OUTCOME MEASURES:** blood pressure, body mass index, waist circumference, electrocardiogram (ECG), bilateral carotid intima media

thickness (C-IMT), estradiol, testosterone, androstenedione, dehydroepiandrosterone sulfate (DHEAS), sex hormone binding globulin (SHBG), insulin, glucose, lipids, thyroid stimulating hormone (TSH), freeT4, NTpro-BNP, C-reactive protein (CRP), uric acid, creatinine, homocysteine. Potential associations between POI status and subclinical atherosclerosis were assessed. **RESULTS:** Women with POI exhibited an increased waist circumference ( $\beta=5.7$ ; 95%CI: 1.6, 9.9), CRP ( $\beta=0.75$ ; 95%CI: 0.43, 1.08), free-T4 levels ( $\beta=1.5$ ; 95% CI: 0.6, 2.4), and lower NTpro-BNP ( $\beta= -0.35$ ; 95%CI: -0.62, -0.08), estradiol ( $\beta= -1.98$ ; 95% CI: -2.48, -1.48), testosterone ( $\beta=-0.21$ ; 95%CI: -0.37, -0.06) and androstenedione ( $\beta=-0.54$ ; 95%CI: -0.71, -0.38) concentrations compared to controls, after adjusting for confounders. After adjustment, a trend towards increased hypertension (OR=2.1; 95%CI: 0.99; 4.56) and decreased kidney function was observed in women with POI (creatinine  $\beta=3.5$ ; 95%CI: -0.05, 7.1, eGFR  $\beta=-3.5$ ; 95%CI: -7.5, 0.46). Women with POI exhibited a lower mean C-IMT ( $\beta=-0.17$ ; 95% CI: -0.21, -0.13), and decreased odds of plaque presence compared to controls (OR = 0.08, 95%CI: 0.03; 0.26). **CONCLUSIONS:** Women with POI exhibited an unfavorable cardiovascular risk profile, including higher abdominal fat, elevated chronic inflammatory factors, and a trend towards increased hypertension and impaired kidney function compared to controls. However, we observed no signs of increased subclinical atherosclerosis in women with POI. Additional studies are required to identify specific determinants of long-term CVD risk in women with POI.

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### **Vasomotor symptoms and cardiometabolic risk factors in menopausal women: a MONET Group study.**

Abdulnour J, Stacey D, Dionne IJ, Brochu M, Doucet É, Prud'homme D.

**INTRODUCTION:** Conflicting results have been reported concerning the prevalence of cardiometabolic risk factors in women experiencing vasomotor symptoms (VMS). **OBJECTIVES:** To compare cardiometabolic risk factors between women with and without VMS during the menopause transition and to determine the influence of physical activity on the prevalence of VMS. **METHODS:** Yearly assessment of women transitioning through menopause included self-reported VMS (hot flushes and night sweats), body composition and fat distribution, fasting glucose, insulin and lipids, and physical activity levels. **RESULTS:** Eighty-five of the 102 premenopausal women at baseline were included (age:  $49.9 \pm 2.0$  years; body mass index:  $23.2 \pm 2.2$  kg/m<sup>2</sup>). According to linear mixed model analyses, no statistically significant differences were observed for fat mass, lean body mass, body fat distribution indices and cardiometabolic risk factors, when comparing symptomatic vs. asymptomatic women. Neither physical activity levels nor intensity were associated with the prevalence of VMS. **CONCLUSION:** Our results suggest that women transitioning through menopause who reported VMS did not show greater deteriorations in body composition, body fat distribution and cardiometabolic risk factors. Furthermore, physical activity levels were not associated with lower prevalence of vasomotor symptoms in the present cohort.