Selección de Resúmenes de Menopausia

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Exercise frequency and bone mineral density development in exercising postmenopausal osteopenic women. Is there a critical dose of exercise for affecting bone? Results of the Erlangen Fitness and Osteoporosis Prevention Study.

Kemmler W, von Stengel S, Kohl M.

Due to older people's low sports participation rates, exercise frequency may be the most critical component for designing exercise protocols that address bone. The aims of the present article were to determine the independent effect of exercise frequency (ExFreq) and its corresponding changes on bone mineral density (BMD) and to identify the minimum effective dose that just relevantly affects bone. Based on the 16-year follow-up of the intense, consistently supervised Erlangen Fitness and Osteoporosis Prevention-Study, ExFreq was retrospectively determined in the exercise-group of 55 initially early-postmenopausal females with osteopenia. Linear mixed-effect regression analysis was conducted to determine the independent effect of ExFreq on BMD changes at lumbar spine and total hip. Minimum effective dose of ExFreq based on BMD changes less than the 90% quantile of the sedentary control-group (n=43). Cut-offs were determined after 4, 8, 12 and 16years using bootstrap with 5000 replications. After 16years, average ExFreq ranged between 1.02 and 2.96sessions/week (2.28±0.40sessions/week). ExFreq has an independent effect on LS-BMD (p<.001) and hip-BMD (p=.005) changes. Bootstrap analysis detected a minimum effective dose at about 2sessions/week/16years (cut-off LS-BMD: 2.11, 95% CI: 2.06-2.12; total hip-BMD: 2.22, 95% CI: 2.00-2.78sessions/week/16years). In summary, the minimum effective dose of exercise frequency that relevantly addresses BMD is quite high, at least compared with the low sport participation rate of older adults. This result might not be generalizable across all exercise types, protocols and cohorts, but it does indicate at least that even when applying high impact/high intensity programs, exercise frequency and its maintenance play a key role in bone adaptation.

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Direct comparison of FRAXR and a simplified fracture risk assessment tool in routine clinical practice: a registry-based cohort study.

Leslie WD, Majumdar SR, Lix LM, Josse RG, Johansson H, Oden A, McCloskey EV, Kanis JA.

INTRODUCTION: There is debate over the value of seemingly more complex fracture prediction tools over simpler fracture prediction tools. FRAXR and the simplified CAROC tool are both widely used in Canada for estimating 10-year probability of major osteoporotic fractures. We compared the performance of these tools for predicting fracture outcomes. METHODS: Using a bone densitometry registry for Manitoba, Canada, we identified 34,060 individuals age ≥50 years not receiving anti-osteoporosis therapy. Fracture Risk Assessment (FRAX) and CAROC were used to classify 10-year fracture risk as low (<10 %), moderate (10-20 %) and high (>20 %). Net reclassification improvement (NRI) was used to quantify the performance of FRAX versus CAROC. RESULTS: During mean 9.8 years of follow-up, 3905 individuals sustained fractures. There were 10 (of 35 total) situations where observed fracture risk fell outside of the predicted range, and all 10 discordances favoured FRAX. NRI among incident fracture cases was not significantly changed, but there was a significant improvement in risk categorization for those who remained fracture-free (+1.7 %, $P < 0.001$) resulting in overall improvement (NRI overall +0.028, $P < 0.001$). Within nine pre-specified subgroups, there was no case of significant worsening in NRI when using FRAX instead of CAROC. In absolute terms, only 36 individuals would need to be assessed using FRAX instead of CAROC to yield an improvement in prediction (8 among individuals with prior fracture and 4 among those with prolonged glucocorticoid use). CONCLUSIONS: FRAX provides improvement in fracture risk prediction compared with the simplified CAROC tool in individuals referred for osteoporosis screening, supporting the use of FRAX as the international reference tool for fracture risk assessment.

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The Intestinal Microbiome and Estrogen Receptor-Positive Female Breast Cancer.

Kwa M, Plottel CS, Blaser MJ, Adams S.

The huge communities of residential microbes, including bacteria, viruses, Archaea, and Eukaryotes, that colonize humans are increasingly recognized as playing important roles in health and disease. A complex populous ecosystem, the human

gastrointestinal (GI) tract harbors up to 1011 bacterial cells per gram of luminal content, whose collective genome, the gut metagenome, contains a vastly greater number of individual genes than the human genome. In health, the function of the microbiome might be considered to be in dynamic equilibrium with the host, exerting both local and distant effects. However, 'disequilibrium' may contribute to the emergence of disease, including malignancy. In this review, we discuss how the intestinal bacterial microbiome and in particular how an 'estrobolome,' the aggregate of enteric bacterial genes capable of metabolizing estrogens, might affect women's risk of developing postmenopausal estrogen receptor-positive breast cancer. Estrobolome composition is impacted by factors that modulate its functional activity. Exploring variations in the composition and activities of the estrobolome in healthy individuals and in women with estrogen-driven breast cancer may lead to development of microbiome-based biomarkers and future targeted interventions to attenuate cancer risk.

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Pharmacological Inhibition of Cathepsin K: a Promising Novel Approach for Postmenopausal Osteoporosis Therapy.

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Osteoporosis is a metabolic bone disease that is characterized by heightened state of bone resorption accompanied by diminished bone formation, leading to a reduction of bone mineral density (BMD) and deterioration of bone quality, thus increasing the risk of developing fractures. Molecular insight into bone biology identified cathepsin K (CatK) as a novel therapeutic target. CatK is a lysosomal cysteine protease secreted by activated osteoclasts during bone resorption, whose primary substrate is type I collagen, the major component of organic bone matrix. Available anti-resorptive drugs affect osteoclast survival and influences both resorption and formation of bone. CatK inhibitors are distinct from the existing anti-resorptives as they only target the resorption process itself without impairing osteoclast differentiation and do not interfere with bone formation. An inhibitor of CatK, odanacatib, robustly increased both trabecular and cortical BMD in postmenopausal osteoporosis patients. The phase III fracture prevention trial with odanacatib ended early due to good efficacy and a favorable benefit/risk profile, thus, enhancing the opportunity for CatK as a pharmacological target for osteoporosis. So far, all the inhibitors that reached to the stage of clinical trial targeted active site of CatK to abrogate the entire proteolytic activity of the enzyme in addition to the desired blockage of excessive elastin and collagen degradation, and could thus pose safety concerns with long term use. Identification of selective exosite inhibitors that inhibit CatK's elastase and/or collagenase activity but do not affect the hydrolysis of other physiologically relevant substrates of CatK would be an improved strategy to inhibit this enzyme.

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Serum leptin, adiponectin and ghrelin concentrations in post-menopausal women: Is there an association with bone mineral density?

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OBJECTIVE: Adipokines and ghrelin exert well-documented effects on energy expenditure and glucose metabolism. Experimental data also support a role in bone metabolism, although data from clinical studies are conflicting. The purpose of this cross-sectional study was to investigate the association of serum concentrations of leptin, adiponectin and ghrelin with bone mineral density (BMD) in post-menopausal women. METHODS: BMD in lumbar spine and femoral neck, and circulating leptin, adiponectin and ghrelin concentrations were measured in 110 healthy post-menopausal women. Patients with secondary causes of osteoporosis were excluded. RESULTS: Osteoporosis was diagnosed in 30 (27%) women and osteopenia in 54 (49%). Serum leptin concentrations were positively correlated with both lumbar spine ($r=0.343$, $p<0.01$) and femoral neck BMD ($r=0.370$, $p<0.01$). Adiponectin concentrations were negatively associated with BMD at both sites ($r=-0.321$, $p<0.01$ and $r=-0.448$, $p<0.01$ respectively). No significant correlation between ghrelin concentrations and BMD was found. Osteoporotic women had lower body weight, body mass index (BMI) and leptin concentrations, but higher adiponectin concentrations compared with non-osteoporotic women. In multivariate stepwise regression analysis, the association of adiponectin concentrations with BMD remained significant only for femoral neck, after adjustment for body weight or BMI. CONCLUSIONS: An inverse association between adiponectin and femoral neck BMD was found in post-menopausal women, independently of body weight. The positive association between leptin and BMD was dependent on body weight, whereas no effect of ghrelin on BMD was evident.

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Effects of low dose estrogen therapy on the vaginal microbiomes of women with atrophic vaginitis.

Shen J, Song N, Williams CJ, Brown CJ, Yan Z, Xu C, Forney LJ.
Atrophic vaginitis (AV) is common in postmenopausal women, but its causes are not well understood. The symptoms, which include vaginal itching, burning, dryness, irritation, and dyspareunia, can usually be alleviated by low doses of estrogen given orally or locally. Regrettably, the composition of vaginal bacterial communities in women with AV have not been fully characterized and little is known as to how these communities change over time in response to hormonal therapy. In the present intervention study we determined the response of vaginal bacterial communities in postmenopausal women with AV to low-dose estrogen therapy. The changes in community composition in response to hormonal therapy were rapid and typified by significant increases in the relative abundance of Lactobacillus spp. that were mirrored by a decreased relative abundance of Gardnerella. These changes were paralleled by a significant four-fold increase in serum estradiol levels and decreased vaginal pH, as well as nearly a two-fold increase in the Vaginal Maturation Index (VMI). The results suggest that after menopause a vaginal microbiota dominated by species of Lactobacillus may have a beneficial role in the maintenance of health and these findings that could lead to new strategies to protect postmenopausal women from AV.

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Lipid biomarkers and long-term risk of cancer in the Women's Health Study.

Chandler PD, Song Y, Lin J, Zhang S, Sesso HD, Mora S, Giovannucci EL, Rexrode KE, Moorthy MV, Li C, et al.
BACKGROUND: Lipid biomarkers, such as HDL-cholesterol concentrations, have been shown to have positive, inverse, and null associations with total, breast, and colorectal cancer risks. Studies of novel lipid biomarkers, such as apolipoprotein A-I (apo A-I) and apolipoprotein B-100 (apo B-100), and cancer risk have been sparse, to our knowledge. OBJECTIVES: We evaluated the prospective association of total, breast, colorectal, and lung cancers and cancer mortality with circulating lipid biomarkers in 15,602 female health professionals in the Women's Health Study (aged ≥45 y, free of cardiovascular disease and cancer, and without hormone replacement therapy or lipid-lowering medications at baseline). DESIGN: Cox regression models estimated HRs of cancer endpoints (19 y median follow-up) across quartiles 1 (reference) to 4 of each lipid biomarker after adjustment for cancer risk factors. RESULTS: Confirmed cases included 2163 incident cancer cases (864 breast, 198 colorectal, and 190 lung cancers) and 647 cancer deaths. Total cancer risk was significantly lower in the highest quartile of apo A-I (adjusted HR: 0.79; 95% CI: 0.70, 0.90; P-trend = 0.0008) and HDL cholesterol (HR: 0.85; 95% CI: 0.75, 0.97; P-trend = 0.01). For site-specific cancers, significant associations included colorectal cancer risk with HDL cholesterol (HR: 0.63; 95% CI; 0.41, 0.98; P-trend = 0.03), triglycerides (HR: 1.86; 95% CI: 1.17, 2.97; P-trend = 0.02), and apo B-100 (HR: 1.60; 95% CI: 1.03, 2.49; P-trend = 0.006) and lung cancer risk with HDL cholesterol (HR: 0.59; 95% CI: 0.38, 0.93;P-trend = 0.01). LDL cholesterol was not significantly associated with risk of total cancer or any site-specific cancers. In time-dependent models that were adjusted for the use of a lipid-lowering medication after baseline, these associations remained. CONCLUSIONS: Lipids were associated with total, lung, and colorectal cancer risks in women. Lifestyle interventions for heart-disease prevention, which reduce apo B-100 or raise HDL cholesterol, may be associated with reduced cancer risk.

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The Association Between Long-Term Bisphosphonate Use and the Risk of Fracture among Women Aged 50 or Older with Osteoporosis.

Wang CC, Lu HT, Dusetzina SB, Wu CH.
BACKGROUND: Osteoporosis is a prevalent disease, and bisphosphonates can effectively reduce the risk of osteoporotic fractures. However, the association between the length of the medication treatment and the risk of fractures remains unclear. The purpose of this study was to evaluate the association between long-term bisphosphonate use (treatment duration ≥5 years) and the risk of fractures among women with osteoporosis aged 50 or older. MATERIALS AND METHODS: We conducted a retrospective cohort study by using the 2001-2011 National Health Insurance Research Database in Taiwan. We included women who were 50 years or older, who had a diagnosis of osteoporosis, and who were newly initiating oral bisphosphonates between January 1, 2002 and December 31, 2003. The index date was the date of the first dispensing of oral bisphosphonate during the enrollment period. Women were considered to be using bisphosphonates until they had a gap in supply of more than 3 months. We classified bisphosphonate use as long term (≥5 years) and regular (<5 years) based on its length of use. The dependent variable was the time to the first observed clinical fracture. Cox-proportional hazard regression models were used to evaluate the association between long-term bisphosphonate use and the risk of fractures. RESULTS: The study included 1342 women with a mean age of 71 years. Of them, 83 (6.2%) were long-term bisphosphonate users. A total of 185 (13.8%) had a fracture. After adjustments, long-term bisphosphonate use was not associated with a lower risk of fractures than was regular bisphosphonate use (adjusted hazard ratio: 1.49, 95% CI: 0.91-2.45). CONCLUSION: This study found no evidence of a lower risk of fractures to be associated with long-term

bisphosphonate use among women aged 50 or older with osteoporosis in Taiwan. Orthopedists as well as other healthcare providers should be aware of the limited benefits of long-term bisphosphonate use.