



Selección de Resúmenes de Menopausia

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Effects of obesity and diabetes on rate of bone density loss.

Leslie WD, Morin SN, Majumdar SR, Lix LM.

In this large registry-based study, women with diabetes had marginally greater bone mineral density (BMD) loss at the femoral neck but not at other measurement sites, whereas obesity was not associated with greater BMD loss. Our data do not support the hypothesis that rapid BMD loss explains the increased fracture risk associated with type 2 diabetes and obesity observed in prior studies. **INTRODUCTION:** Type 2 diabetes and obesity are associated with higher bone mineral density (BMD) which may be less protective against fracture than previously assumed. Inconsistent data suggest that rapid BMD loss may be a contributing factor. **METHODS:** We examined the rate of BMD loss in women with diabetes and/or obesity in a population-based BMD registry for Manitoba, Canada. We identified 4960 women aged ≥ 40 years undergoing baseline and follow-up BMD assessments (mean interval 4.3 years) without confounding medication use or large weight fluctuation. We calculated annualized rate of BMD change for the lumbar spine, total hip, and femoral neck in relation to diagnosed diabetes and body mass index (BMI) category. **RESULTS:** Baseline age-adjusted BMD was greater in women with diabetes and for increasing BMI category (all $P < 0.001$). In women with diabetes, unadjusted BMD loss was less at the lumbar spine ($P = 0.017$), non-significantly greater at the femoral neck ($P = 0.085$), and similar at the total hip ($P = 0.488$). When adjusted for age and BMI, diabetes was associated with slightly greater femoral neck BMD loss (-0.0018 g/cm²/year, $P = 0.012$) but not at the lumbar spine or total hip. There was a strong linear effect of increasing BMI on attenuated BMI loss at the lumbar spine with negligible effects on hip BMD. **CONCLUSIONS:** Diabetes was associated with slightly greater BMD loss at the femoral neck but not at other measurement sites. BMD loss at the lumbar spine was reduced in overweight and obese women but BMI did not significantly affect hip BMD loss.

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Longevity of daily oral vitamin D3 supplementation: differences in 25OHD and 24,25(OH)2D observed 2 years after cessation of a 1-year randomised controlled trial (ViCtORY RECALL).

Macdonald HM, Gryka A, Tang JCY, Aucott LS, Fraser WD, Wood AD.

To determine how long vitamin D lasts after supplementation ceases, the marker of status was measured 2 and 3 years after a 1-year trial. Compared to placebo, the proportion of vitamin D-deficient women was still lower, if they had taken daily vitamin D3, after 2 years, indicating its longevity. **INTRODUCTION:** The purpose of this study was to determine longevity of vitamin D status following cessation of vitamin D3 supplementation, 2 and 3 years after a 1-year randomised, double-blind placebo controlled trial and to investigate possible predictive factors. **METHODS:** Caucasian non-smoking postmenopausal women randomised to ViCtORY (2009-2010), who had not taken vitamin D supplements since the trial ended, were invited to attend follow-up visits. Total 25-hydroxyvitamin D (25OHD) and 24,25-dihydroxyvitamin D (24,25OH2D) were measured by dual tandem mass spectrometry of serum samples following removal of protein and delipidation; the original randomised controlled trial (RCT) samples were re-analysed simultaneously. Vitamin D-binding protein (VDBP) was measured by monoclonal immunoassay. **RESULTS:** In March 2012 and March 2013, 159 women (mean (SD) age 67.6 (2.1) years) re-attended, equally distributed between the original treatment groups: daily vitamin D3 (400 IU, 1000 IU) and placebo. One month after the RCT ended (March 2010), the proportion of women in placebo, 400 IU and 1000 IU vitamin D3 groups, respectively, with 25OHD < 25 nmol/L was 15, 0 and 0 (chi-square $p < 0.001$, $n = 46, 44, 54$). After 2 years (March 2012), it was 22, 4 and 4% ($p = 0.002$, $n = 50, 48, 57$); after 3 years, it was 23, 13 and 15% ($p = 0.429$, $n = 48, 45, 52$). The respective proportions of women with 24,25OH2D < 2.2 nmol/L were 50, 2 and 2% (1 month, $p < 0.001$, $n = 46, 44, 54$); 42, 33 and 12% (2 years, $p = 0.002$, $n = 50, 48, 57$); and 45, 27 and 29% (3 years, $p = 0.138$, $n = 47, 45, 51$). VDBP was a predictor of circulating 25OHD longevity (beta for VDBP in $\mu\text{g/mL}$ 0.736; 95% CI 0.216-1.255, $p = 0.006$) but not 24,25OH2D. **CONCLUSION:** Four hundred international units or 1000 IU of daily vitamin D3 showed benefits over placebo 2 years after supplementation ceased in keeping 25OHD > 25 nmol/L.

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P62 plasmid can alleviate diet-induced obesity and metabolic dysfunctions.

Halenova T, Savchuk O, Ostapchenko L, Chursov A, Fridlyand N, Komissarov AB, Venanzi F, Kolesnikov SI, Sufianov AA, Sherman MY, Gabai VL, Shneider AM.

A high-calorie diet (HCD) induces two mutually exacerbating effects contributing to diet-induced obesity (DIO): impaired glucose metabolism and increased food consumption. A link between the metabolic and behavioral manifestations is not well understood yet. We hypothesized that chronic inflammation induced by HCD plays a key role in linking together the two components of diet-induced pathology. Based on this hypothesis, we tested if a plasmid (DNA vaccine) encoding p62 (SQSTM1) would alleviate DIO including its metabolic and/or food consumption abnormalities. Previously we reported that injections of the p62 plasmid reduce chronic inflammation during ovariectomy-induced osteoporosis. Here we found that the p62 plasmid reduced levels of pro-inflammatory cytokines IL-1 β , IL-12, and INF γ and increased levels of anti-inflammatory cytokines IL-4, IL-10 and TGF β in HCD-fed animals. Due to this anti-inflammatory response, we further tested whether the plasmid can alleviate HCD-induced obesity and associated metabolic and feeding impairments. Indeed, p62 plasmid significantly reversed effects of HCD on the body mass index (BMI), levels of glucose, insulin and glycosylated hemoglobin (HbA1c). Furthermore, p62 plasmid partially restored levels of the satiety hormone, serotonin, and tryptophan, simultaneously reducing activity of monoamine oxidase (MAO) in the brain affected by the HCD. Finally, the plasmid partially reversed increased food consumption caused by HCD. Therefore, the administering of p62 plasmid alleviates both metabolic and behavioral components of HCD-induced obesity.

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Relationship between sleep quality and cardiovascular disease risk in Chinese post-menopausal women.

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BACKGROUND: Menopause is an inevitable stage affecting every middle-aged woman. China has a large and increasing group of post-menopausal women. Most post-menopausal women suffer from increased risks for cardiovascular diseases (CVD) and sleep problems. Previous studies have demonstrated the associations between sleep disorders and increased CVD risks in general population. The current study is to examine the relationship between sleep quality and CVD risks among Chinese post-menopausal women. **METHODS:** This study was a sub-study nested in a cross-sectional study that investigated the sleep quality of community-dwelling adults in Xian, Shaanxi Province, China. The Chinese version of the Pittsburgh Sleep Quality Index (PSQI) and the Framingham 10-year risk score (FRS) were used to measure sleep quality and CVD risk among 154 Chinese post-menopausal women. Multivariate regression and logistic regression were used to determine the association between sleep quality and CVD risk. **RESULTS:** The participants (age: 63.65 \pm 4.47 years) experienced poor sleep quality (mean score of global PSQI = 8.58) and a 10-year risk of CVD of 12.54%. The CVD risk was significantly associated with sleep duration (β = - 0.18, p = 0.04) and sleep disturbance (β = 0.33, p < 0.001). Women with good sleep quality (PSQI \leq 5) were less likely to be at high risk for CVD (FRS > 10%) (odds ratio = 0.51, p = 0.04). **CONCLUSIONS:** Poor sleep quality might increase the CVD risk in post-menopausal women. Interventions to promote the cardiovascular health of Chinese post-menopausal women may need to include sleep promotion strategies.

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Romosozumab or Alendronate for Fracture Prevention in Women with Osteoporosis.

Saag KG, Petersen J, Brandi ML, Karaplis AC, Lorentzon M, Thomas T, Maddox J, Fan M, Meisner PD, Grauer A.

Background Romosozumab is a monoclonal antibody that binds to and inhibits sclerostin, increases bone formation, and decreases bone resorption. **Methods** We enrolled 4093 postmenopausal women with osteoporosis and a fragility fracture and randomly assigned them in a 1:1 ratio to receive monthly subcutaneous romosozumab (210 mg) or weekly oral alendronate (70 mg) in a blinded fashion for 12 months, followed by open-label alendronate in both groups. The primary end points were the cumulative incidence of new vertebral fracture at 24 months and the cumulative incidence of clinical fracture (nonvertebral and symptomatic vertebral fracture) at the time of the primary analysis (after clinical fractures had been confirmed in \geq 330 patients). Secondary end points included the incidences of nonvertebral and hip fracture at the time of the primary analysis. Serious cardiovascular adverse events, osteonecrosis of the jaw, and atypical femoral fractures were adjudicated. **Results** Over a period of 24 months, a 48% lower risk of new vertebral fractures was observed in the romosozumab-to-alendronate group (6.2% [127 of 2046 patients]) than in the alendronate-to-alendronate group (11.9% [243 of 2047 patients]) (P <0.001). Clinical fractures occurred in 198 of 2046 patients (9.7%) in the romosozumab-to-alendronate group versus 266 of 2047 patients (13.0%) in the alendronate-to-alendronate group, representing a 27% lower risk with romosozumab (P <0.001). The risk of nonvertebral fractures was lower by 19% in the romosozumab-to-alendronate group than in the alendronate-to-alendronate group (178 of 2046 patients [8.7%] vs. 217 of 2047 patients [10.6%]; P =0.04), and the risk of hip fracture was lower by 38% (41 of 2046 patients [2.0%] vs. 66 of 2047 patients [3.2%]; P =0.02). Overall

adverse events and serious adverse events were balanced between the two groups. During year 1, positively adjudicated serious cardiovascular adverse events were observed more often with romosozumab than with alendronate (50 of 2040 patients [2.5%] vs. 38 of 2014 patients [1.9%]). During the open-label alendronate period, adjudicated events of osteonecrosis of the jaw (1 event each in the romosozumab-to-alendronate and alendronate-to-alendronate groups) and atypical femoral fracture (2 events and 4 events, respectively) were observed. Conclusions In postmenopausal women with osteoporosis who were at high risk for fracture, romosozumab treatment for 12 months followed by alendronate resulted in a significantly lower risk of fracture than alendronate alone.

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Associations of 100% fruit juice versus whole fruit with hypertension and diabetes risk in postmenopausal women: Results from the Women's Health Initiative.

Auerbach BJ, Littman AJ, Tinker L, Larson J, Krieger J, Young B, Neuhauser M.

The objective of this study was to determine whether consumption of 100% fruit juice as compared to whole fruit is associated with increased risk of hypertension or diabetes. We analyzed postmenopausal women in the United States enrolled in the Women's Health Initiative between 1993 and 1998. Whole fruit and 100% fruit juice intake were assessed by baseline food frequency questionnaire. Standardized questionnaires assessed outcomes every 6-12 months during a mean 7.8 years of follow-up. Cox regression estimated hazard ratios (HR) and 95% confidence intervals (CI) for incident hypertension (n=36,314 incident cases/80,539 total participants) and diabetes (n=11,488 incident cases/114,219 total participants). In multivariable analyses there was no significant association comparing the highest to lowest quintiles of 100% fruit juice consumption (8oz/day compared to none) and incident hypertension (HR 1.00, 95% CI 0.97-1.03) or diabetes (HR 0.96, 95% CI 0.90-1.03). There was also no significant association between whole fruit consumption (2.4 servings/day compared to 0.3 servings/day) and incident hypertension (HR 1.02, 95% CI 0.98-1.05) or diabetes (HR 1.03, 95% CI 0.96-1.10). Consuming moderate amounts of 100% fruit juice or whole fruit was not significantly associated with risk of hypertension or diabetes among postmenopausal US women.