Selección de Resúmenes de Menopausia

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Effects of Teriparatide Compared with Risedronate on the Risk of Fractures in Subgroups of Postmenopausal Women with Severe Osteoporosis: The VERO Trial.

Geusens P, Marin F, Kendler DL, Russo LA, Zerbini CAF, Minisola S, Body JJ, Lespessailles E, et al.

The 2-year, randomized, double-blind, active-controlled fracture endpoint VERO study included postmenopausal women with established osteoporosis, who had at least 2 moderate or 1 severe baseline vertebral fractures (VFx), and BMD T-score ≤-1.5. Patients were treated with either s.c. daily teriparatide 20 µg or oral weekly risedronate 35 mg. As previously reported, the risk of new VFx and clinical fractures (a composite of clinical VFx and non vertebral fragility fractures [NVFFx]) was statistically significantly reduced with teriparatide compared with risedronate. Here we present the prospectively planned subgroup analyses of fracture data across subgroups which were predefined by the following baseline characteristics: age, number and severity of prevalent VFx, prevalent non vertebral fractures (NVFx), glucocorticoid use, prior osteoporosis drugs, recent bisphosphonate use, clinical VFx in the year before study entry, and baseline BMD. Heterogeneity of the treatment effect on the primary endpoint (new VFx), and the 4 key secondary endpoints (including clinical fractures and NVFFx) were investigated by logistic and Cox proportional hazards regression models. 1,360 women were randomized and treated (680 per group). Mean age was 72.1 years, mean (SD) number of prevalent VFx was 2.7 (2.1), 55.4% had a BMD T score <-2.5, 36.5% had a recent clinical VFx, 28.3% had a prior major NVFx, 43.2% were osteoporosis drug naïve, 39.3% were recent bisphosphonate users, and 9.3% were taking glucocorticoids at a prednisone-equivalent dose of >5 mg/day. For most fracture endpoints, the risk reduction of teriparatide versus risedronate did not significantly differ in any of the subgroups analyzed (treatment-by-subgroup interaction p>0.1), with most subgroups mirroring results from the total study population. In conclusion, in postmenopausal women with severe osteoporosis, the anti-fracture efficacy of teriparatide compared with risedronate was consistent in a wide range of patient settings including treatment-naïve and previously treated patients.

Horm Metab Res. 2018 Jan;50(1):17-22. doi: 10.1055/s-0043-123265. Epub 2018 Jan 12.

Association Between Body Weight Change Before and After Delivery and Development of Nonmetabolic Syndrome: A Prospective Study.

Ya Z, Yue Z, Dan L, Neng-Bo L, Yi L, Ying M, Qin W.

The aim of the work was to investigate the association between body weight change before and after delivery and development of nonmetabolic syndrome in Chinese females aged ≥40 years. We selected 789 participants without metabolic syndrome randomly from a baseline survey performed in Luzhou, China in 2011. We took the group with decreasing or no increasing body mass index difference during a pregnancy as "R-Body Mass Index 1" (n=286) and divided the group with increasing body mass index difference during a pregnancy into "R-Body Mass Index 2" (n=254) and "R-Body Mass Index 3" (n=249) based upon P50. All study participants were followed up every year, and a questionnaire, physical examination, and biochemical detection were administered after 3 years. Of 789 participants, 82 nonmetabolic syndrome women developed metabolic syndrome during 3-year follow-up. The morbidity of metabolic syndrome in the R-BMI1, R-BMI2, and R-BMI3 groups was 5.2%, 11.8%, and 14.9%, respectively. Compared to the R-BMI1 group, the relative risk for R-BMI2 was 1.92 (95% confidence interval: 1.03-3.58, p=0.040) and for R-BMI3 was 2.20 (95% confidence interval: 1.20-4.03, p=0.011). After adjusting for age, BMI, WHR, baseline blood glucose, HbA1c, TG, HDL-C, SBP, DBP, age of menarche and menopause, and delivery times, the relative risks were similar to the unadjusted relative risks. In conclusion, body weight change after delivery was associated with metabolic syndrome: the higher the weight gain, the higher the risk of metabolic syndrome.

Womens Midlife Health. 2017;3. pii: 2. doi: 10.1186/s40695-017-0021-y. Epub 2017 Jul 27.

It is not just menopause: symptom clustering in the Study of Women's Health Across the Nation.

Harlow SD, Karvonen-Gutierrez C, Elliott MR, Bondarenko I, Avis NE, Bromberger JT, Brooks MM, et al.

Patterns of symptom clustering in midlife women may suggest common underlying mechanisms or may identify women at risk of adverse health outcomes or, conversely, likely to experience healthy aging. This paper assesses symptom clustering in the Study of Women's Health Across the Nation (SWAN) longitudinally by stage of reproductive aging and estimates the probability of women experiencing specific symptom clusters. We also evaluate factors that influence the likelihood of specific symptom clusters and assess whether symptom clustering is associated with women's self-reported health status. Methods: This analysis includes 3289 participants in the multiethnic SWAN cohort who provided information on 58 symptoms reflecting a broad range of physical, psychological and menopausal symptoms at baseline and 7 follow-up visits over 16 years. We conducted latent transition analyses to assess symptom clustering and to model symptomatology across the menopausal transition (pre, early peri-, late peri- and post-menopausal). Joint multinomial logistic regression models were used to identify demographic characteristics associated with premenopausal latent class membership. A partial proportional odds regression model was used to assess the association between latent class membership and self-reported health status. Results: We identified six latent classes that ranged from highly symptomatic (LC1) across most measured symptoms, to moderately symptomatic across most measured symptoms (LC2), to moderately symptomatic for a subset of symptoms (vasomotor symptoms, pain, fatigue, sleep disturbances and physical health symptoms) (LC3 and LC5) with one class (LC3) including interference in life activities because of physical health symptoms, to numerous milder symptoms, dominated by fatigue and psychological symptoms (LC4), to relatively asymptomatic (LC6). In pre-menopause, 10% of women were classified in LC1, 16% in LC2, 14% in LC3 and LC4, 26% in LC5, and 20% in LC6. Intensity of vasomotor and urogenital symptoms as well as sexual desire) differed minimally by latent class. Classification into the two most symptomatic classes was strongly associated with financial strain, White race/ethnicity, obesity and smoking status. Over time, women were most likely to remain within the same latent class as they transitioned through menopause stages (range 39-76%), although some women worsened or improved. The probability of moving between classes did not differ substantially by menopausal stage. Women in the highly symptomatic classes more frequently rated their health as fair to poor compared to women in the least symptomatic class. Conclusion: Clear patterns of symptom clustering were present early in midlife, tended to be stable over time, and were strongly associated with self-perceived health. Notably, vasomotor symptoms tended to cluster with sleep disturbances and fatigue, were present in each of the moderate to highly symptomatic classes, but were not a defining characteristic of the symptom clusters. Clustering of midlife women by symptoms may suggest common underlying mechanisms amenable to interventions. Given that one-quarter of midlife women were highly or moderately symptomatic across all domains in the pre-menopause, addressing symptom burden in early midlife is likely critical to ameliorating risk in the most vulnerable populations.

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Efficacy of Transdermal Estradiol and Micronized Progesterone in the Prevention of Depressive Symptoms in the Menopause Transition: A Randomized Clinical Trial.

Gordon JL, Rubinow DR, Eisenlohr-Moul TA, Xia K, Schmidt PJ, Girdler SS.

The menopause transition and early postmenopausal period are associated with a 2- to 4-fold increased risk for clinically significant depressive symptoms. Although a few studies suggest that hormone therapy can effectively manage existing depression during this time, to our knowledge, there have been no studies testing whether hormone therapy can prevent the onset of perimenopausal and early postmenopausal depressive symptoms. Objective: To examine the efficacy of transdermal estradiol plus intermittent micronized progesterone (TE+IMP) in preventing depressive symptom onset among initially euthymic perimenopausal and early postmenopausal women. A secondary aim was to identify baseline characteristics predicting TE+IMP's beneficial mood effects. Design, Setting, and Participants: Double-blind, placebo-controlled randomized trial at the University of North Carolina at Chapel Hill from October 2010 to February 2016. Participants included euthymic perimenopausal and early postmenopausal women from the community, aged 45 to 60 years. Interventions: Transdermal estradiol (0.1 mg/d) or transdermal placebo for 12 months. Oral micronized progesterone (200 mg/d for 12 days) was also given every 3 months to women receiving active TE, and identical placebo pills were given to women receiving placebo. Main Outcome Measures: Scores on the Center for Epidemiological Studies-Depression Scale (CES-D), assessed at baseline and months 1, 2, 4, 6, 8, 10, and 12 after randomization, and the incidence of clinically significant depressive symptoms,

defined as a CES-D score of at least 16. Results: Of 172 participants, 130 were white (76%), and 70 were African American (19%), with a mean household income of $50 000 to $79 999. The mean age was 51 years, and 43 developed clinically significant depressive symptoms. Women assigned to placebo were more likely than those assigned to TE+IMP to score at least 16 on the CES-D at least once during the intervention phase (32.3% vs 17.3%; odds ratio [OR], 2.5; 95% CI, 1.1-5.7; P = .03) and had a higher mean CES-D score across the intervention period (P = .03). Baseline reproductive stage moderated the effect of treatment (β, -1.97; SEM, 0.80; P for the interaction = .03) such that mood benefits of TE+IMP vs placebo were evident among women in the early menopause transition (β, -4.2; SEM, 1.2; P < .001) but not the late menopause transition (β, -0.9; SEM, 0.3; P = .23) or among postmenopausal women (β, -0.3; SEM, 1.1; P = .92). Stressful life events in the 6 months preceding enrollment also moderated the effect of treatment on mean CES-D score such that the mood benefits of TE+IMP increased with a greater number of events (β, 1.22; SEM, 0.40; P = .003). Baseline estradiol levels, baseline vasomotor symptoms, history of depression, and history of abuse did not moderate treatment effects. Conclusions: Twelve months of TE+IMP were more effective than placebo in preventing the development of clinically significant depressive symptoms among initially euthymic perimenopausal and early postmenopausal women.

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The effect of protein diets in postmenopausal women with osteoporosis: Systematic review of randomized controlled trials.

Koutsofta I, Mamais I, Chrysostomou S.

The main objective of this systematic review was to examine the effectiveness of protein supplementation through diet or dietary supplements on osteoporosis in postmenopausal women as evidenced by randomized controlled trials (RCTs). Five RCTs were included using dietary protein (N = 2), protein supplements (N = 2), and proteins through diet and supplements (N = 1). A total of 677 postmenopausal woman were included, all diagnosed with osteoporosis (T score < -2.5) and aged between 50 and 80 years. Results have found that combined protein administration through diet, mainly from animal sources and supplemental proteins (whey proteins, 86 g/d PRO including 6 g WPI), for a short period of time (up to 12 months) may positively affect osteoporosis in postmenopausal women. In addition, a positive effect can also be achieved by the single administration of a 250 mg/d supplement in which 10 g was WPI for a six-month period. In this review, it is shown that both combined administration of proteins through diet and supplements and single administration through protein supplements may reduce the risk of fracture in postmenopausal osteoporotic women. In contrast, dietary proteins alone, in doses similar to and/or higher than the RDA values, may not have any positive effect on treating osteoporosis.

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Treatment-Related Changes in Bone Turnover and Fracture Risk Reduction in Clinical Trials of Anti-Resorptive Drugs: A Meta-Regression.

Bauer DC, Black DM, et al; Foundation for the National Institutes of Health (FNIH) Bone Quality Project.

Few pooled analyses of antiresorptive (AR) treatment trials relate short-term changes in bone turnover markers (BTMs) to subsequent fracture reduction. Such information would be useful to assess new ARs or novel dosing regimens. In the Foundation for the National Institutes of Health (FNIH) Bone Quality project, we analyzed individual-level data from 28,000 participants enrolled in 11 bisphosphonate (BP) and three selective estrogen receptor modulator (SERM) placebo-controlled fracture endpoint trials. Using BTM results for two bone formation markers (bone-specific alkaline phosphatase [bone ALP] and pro-collagen I N-propeptide [PINP]) and two bone resorption markers (N-terminal and C-terminal telopeptide of type I collagen) and incident fracture outcome data, we performed a meta-regression relating the mean net effect of treatment on change in bone turnover (active minus placebo % difference after 3 to 12 months) to the log of study-wide fracture risk reduction, and used linear regression to plot the best fitting line. Separate analyses were performed for incident morphometric vertebral, nonvertebral, and hip fractures over 1 to 4 years of follow-up. Change in bone ALP and PINP were available for over 16,000 and 10,000 participants, respectively. For vertebral fracture, the results showed a strong relationship between treatment-related bone ALP or PINP changes and vertebral fracture risk reduction ($r2 = 0.82$ [$p < 0.001$] and $r2 = 0.75$ [$p = 0.011$], respectively) Relationships were weaker and no longer statistically significant for nonvertebral ($r2 = 0.33$ [$p = 0.053$] and $r2 = 0.53$ [$p = 0.065$], respectively) and hip fracture ($r2 = 0.17$ [$p = 0.24$] and $r2 = 0.43$ [$p = 0.11$], respectively) outcomes. Analyses limited to BP trials gave similar results. For all fracture types, relationships were weaker and nonsignificant for bone resorption markers. We conclude that short-term AR

treatment-related changes in bone ALP and PINP strongly predict vertebral fracture treatment efficacy, but not nonvertebral or hip fracture treatment efficacy. Change in bone formation markers might be useful to predict the anti-vertebral fracture efficacy of new A R compounds or novel dosing regiments with approved AR drugs.

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Calcium and vitamin D supplementation are not associated with risk of incident ischaemic cardiac events or death: findings from the UK Biobank cohort.

Harvey NC, D'Angelo S, Paccou J, Curtis EM, Edwards M, Raisi-Estabragh Z, Walker-Bone K, Petersen S, Cooper C

We investigated associations between calcium/vitamin D supplementation and incident cardiovascular events/deaths in a UK population-based cohort. UK Biobank is a large prospective cohort comprising 502,637 men and women aged 40-69 years at recruitment. Supplementation with calcium/vitamin D was self-reported, and information on incident hospital admission (ICD-10) for ischaemic heart disease (IHD), myocardial infarction (MI) any cardiovascular event, and subsequent death, was obtained from linkage to national registers. Cox Proportional Hazards models were used to investigate longitudinal relationships between calcium/vitamin D supplementation and hospital admission for men/women, controlling for covariates. 475,255 participants (median age 58years, 55.8% women) had complete data on calcium/vitamin D supplementation. 33,437 participants reported taking calcium supplements; 19,089 vitamin D; 10,007 both. In crude and adjusted analyses, there were no associations between use of calcium supplements and risk of incident hospital admission with either IHD, MI or any cardiovascular event, or subsequent death. Thus, for example, in unadjusted models, the hazard ratio (HR) for admission with myocardial infarction was 0.97 (95%CI:0.79,1.20; p = 0.79) amongst women taking calcium supplementation. Corresponding HR for men: 1.16 (95%CI:0.92,1.46;p = 0.22). After full adjustment, HR(95%CI) were 0.82 (0.62,1.07), p = 0.14 amongst women and 1.12 (0.85,1.48), p = 0.41 amongst men. Adjusted HR(95%CI) for admission with IHD were 1.05 (0.92,1.19), p = 0.50 amongst women and 0.97 (0.82,1.15), p = 0.77 amongst men. Results were similar for any cardiovascular admission and for vitamin D and combination supplementation. There were no associations with death, and in women, further adjustment for HRT use did not alter the associations. In this very large prospective cohort, there was no evidence that use of calcium/vitamin D supplementation was associated with increased risk of hospital admission or death following ischaemic or non-ischaemic cardiovascular events.