



Selección de Resúmenes de Menopausia

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Bone turnover in osteoporotic women during long-term oral bisphosphonates treatment. Implications for treatment failure and "drug holiday" in the real-world.

Liel Y, Plakht Y, Abu-Tailakh M.

Little data exists to support concerns over bone turnover suppression during prolonged oral bisphosphonates treatment and on consequences of the recommended "drug holiday". This study was set to assess bone resorption rates in postmenopausal osteoporotic women on prolonged oral bisphosphonates treatment, and in response to switching to "drug holiday", intravenous bisphosphonate or continuation of oral bisphosphonates. **METHODS:** Frequency distribution of the bone resorption marker urinary deoxypyridinoline cross-links (uDPD), was obtained retrospectively from 211 osteoporotic women attended at an academic hospital endocrine clinic, treated for >2 years with oral bisphosphonates. In some patients uDPD was reassessed following modification or continuation of treatment. **RESULTS:** The mean duration of oral bisphosphonates treatment was 7.2 ± 3.1 years. uDPD was within reference range for premenopausal women in 61.6% of the patients, below in 7.6% of the patients, and above upper limit in 30.8%. uDPD decreased significantly following intravenous zoledronic acid, increased significantly during "drug holiday" and slightly decreased in those continued on oral bisphosphonate treatment. **CONCLUSIONS:** In this real-world study, the majority of women on prolonged oral bisphosphonates maintained bone resorption rates within normal reference range for premenopausal women. Likelihood for inadequate suppression was considerably greater than that of over-suppression. "Drug holiday" resulted in marked increase in bone resorption rates. Additional studies should explore the potential role of bone turnover markers in the evaluation of patients on prolonged oral bisphosphonates and during "drug holiday", in different settings and using additional markers.

PLoS One. 2017 Apr 27;12(4):e0176430. doi: 10.1371/journal.pone.0176430. eCollection 2017.

Circulating leptin and adiponectin are associated with insulin resistance in healthy postmenopausal women with hot flashes.

Huang WY, Chang CC, Chen DR, Kor CT, Chen TY, Wu HM.

INTRODUCTION: Hot flashes have been postulated to be linked to the development of metabolic disorders. This study aimed to evaluate the relationship between hot flashes, adipocyte-derived hormones, and insulin resistance in healthy, non-obese postmenopausal women. **PARTICIPANTS AND DESIGN:** In this cross-sectional study, a total of 151 women aged 45-60 years were stratified into one of three groups according to hot-flash status over the past three months: never experienced hot flashes (Group N), mild-to-moderate hot flashes (Group M), and severe hot flashes (Group S). Variables measured in this study included clinical parameters, hot flash experience, fasting levels of circulating glucose, lipid profiles, plasma insulin, and adipocyte-derived hormones. Multiple linear regression analysis was used to evaluate the associations of hot flashes with adipocyte-derived hormones, and with insulin resistance. **SETTINGS:** The study was performed in a hospital medical center. **RESULTS:** The mean (standard deviation) of body-mass index was 22.8(2.7) for Group N, 22.6(2.6) for Group M, and 23.5(2.4) for Group S, respectively. Women in Group S displayed statistically significantly higher levels of leptin, fasting glucose, and insulin, and lower levels of adiponectin than those in Groups M and N. Multivariate linear regression analysis revealed that hot-flash severity was significantly associated with higher leptin levels, lower adiponectin levels, and higher leptin-to-adiponectin ratio. Univariate linear regression analysis revealed that hot-flash severity was strongly associated with a higher HOMA-IR index (% difference, 58.03%; 95% confidence interval, 31.00-90.64; $p < 0.001$). The association between hot flashes and HOMA-IR index was attenuated after adjusting for leptin or adiponectin and was no longer significant after simultaneously adjusting for leptin and adiponectin. **CONCLUSION:** The present study provides evidence that hot flashes are associated with insulin resistance in postmenopausal women. It further suggests that hot flash association with insulin resistance is dependent on the combination of leptin and adiponectin variables.

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Clinical evaluation of cost efficacy of drugs for treatment of osteoporosis: a meta-analysis.

Albert SG, Reddy S.

OBJECTIVE: To assess the cost efficacy of available regimens for therapy of osteoporosis as defined as the cost time's number need to treat to prevent one fracture. **PATIENTS AND METHODS:** Existing meta-analyses were supplemented through electronic databases SCOPUS and PubMed between 2013 (a date overlapping the latest meta-analyses) and March 2016. Primary references included all randomized controlled trials of anti-osteoporotic drugs versus comparators using search terms "osteoporosis", "random" and "trial". Results There were 43 evaluable randomized double blind placebo controlled trials in 71,809 postmenopausal women comparing fracture frequency. Trials were similar in recruitment age 67.3 (SD±8.1) years, and follow up duration of 25.5 (±12.6) months. Cost comparisons were evaluated for a treatment strategy assuming generic alendronate as first line therapy. Denosumab and teriparatide showed benefits in vertebral fracture reduction over alendronate at incremental costs respectively of \$46,000 and \$455,000 per fracture prevented. Zoledronate, recently released as a generic, would be either less expensive or comparable in cost. None of the alternate medicines were statistically better in preventing hip fractures. Teriparatide was more effective in preventing non-vertebral fractures at an incremental cost of \$1,555,000. **CONCLUSION:** The most cost effective initial therapy of post-menopausal osteoporosis is generic oral alendronate or generic parenteral zoledronate. There is no statistical difference in efficacy of available drugs to prevent hip fractures. There is limited data to suggest switching drugs after sustaining an osteoporotic fracture while on oral alendronate therapy, although generic zoledronate may be considered on the basis of side effects or questions of medication adherence.

Br J Cancer. 2017 Apr 25. doi: 10.1038/bjc.2017.106. [Epub ahead of print]

Comparison of general obesity and measures of body fat distribution in older adults in relation to cancer risk: meta-analysis of individual participant data of seven prospective cohorts in Europe.

Freisling H, Arnold M, Soerjomataram I, O'Doherty MG, Ordóñez-Mena JM, Bamia C, Kampman E9, et al.

BACKGROUND: We evaluated the associations of anthropometric indicators of general obesity (body mass index, BMI), an established risk factor of various cancer, and body fat distribution (waist circumference, WC; hip circumference, HC; and waist-to-hip ratio, WHR), which may better reflect metabolic complications of obesity, with total obesity-related and site-specific (colorectal and postmenopausal breast) cancer incidence. **METHODS:** This is a meta-analysis of seven prospective cohort studies participating in the CHANCES consortium including 18 668 men and 24 751 women with a mean age of 62 and 63 years, respectively. Harmonised individual participant data from all seven cohorts were analysed separately and alternatively for each anthropometric indicator using multivariable Cox proportional hazards models. **RESULTS:** After a median follow-up period of 12 years, 1656 first-incident obesity-related cancers (defined as postmenopausal female breast, colorectal, lower oesophagus, cardia stomach, liver, gallbladder, pancreas, endometrium, ovary, and kidney) had occurred in men and women. In the meta-analysis of all studies, associations between indicators of adiposity, per s.d. increment, and risk for all obesity-related cancers combined yielded the following summary hazard ratios: 1.11 (95% CI 1.02-1.21) for BMI, 1.13 (95% CI 1.04-1.23) for WC, 1.09 (95% CI 0.98-1.21) for HC, and 1.15 (95% CI 1.00-1.32) for WHR. Increases in risk for colorectal cancer were 16%, 21%, 15%, and 20%, respectively per s.d. of BMI, WC, HC, and WHR. Effect modification by hormone therapy (HT) use was observed for postmenopausal breast cancer (Pinteraction<0.001), where never HT users showed an ~20% increased risk per s.d. of BMI, WC, and HC compared to ever users. **CONCLUSIONS:** BMI, WC, HC, and WHR show comparable positive associations with obesity-related cancers combined and with colorectal cancer in older adults. For postmenopausal breast cancer we report evidence for effect modification by HT use.

Climacteric. 2017 Apr 25:1-5. doi: 10.1080/13697137.2017.1315087. [Epub ahead of print]

Relationship between delivery modes and genitourinary syndrome among postmenopausal women.

Yaralizadeh M, Abedi P, Salehinejad P.

OBJECTIVES: Many postmenopausal women suffer from genitourinary syndrome of menopause (GSM) due to the lack of estrogen. This study aimed to evaluate the relationship between mode of delivery and GSM among postmenopausal women. **METHODS:** We performed a case-control study of women who had had either vaginal delivery or Cesarean section. Data were collected through a sociodemographic questionnaire and a check list for assessing signs and symptoms of GSM. Subjective symptoms of vaginal atrophy (dryness, dyspareunia, itching, burning and paleness), pH of the vagina and maturation index were assessed and recorded. Data were analyzed using the χ^2 test and independent t-test. **RESULTS:** A total of 125 postmenopausal women were recruited (65 with a history of normal vaginal delivery (NVD) and 60 with a history of Cesarean section). Vaginal pH was more commonly lower (pH 5-5.49) in the NVD group (50.8% vs. 40%) ($p < 0.001$). The maturation index was also better in the NVD group (42.7 ± 6.34 vs. 24.08 ± 8.2) ($p < 0.001$). All symptoms of vaginal atrophy including paleness, dryness, itching, dyspareunia and burning were significantly less in the NVD group compared to the Cesarean section group ($p < 0.05$).

CONCLUSION: Postmenopausal women with a history of normal vaginal delivery were less likely to have GSM compared to the women with a history of Cesarean section. Other prospective studies can explore this relationship better.

Obesity (Silver Spring). 2017 May;25(5):892-900. doi: 10.1002/oby.21815.

Attenuated Low-Grade Inflammation Following Long-Term Dietary Intervention in Postmenopausal Women with Obesity.

Blomquist C, Alvehus M, Burén J, Ryberg M, Larsson C, Lindahl B, Mellberg C, Söderström I, Chorell E, Olsson T. **OBJECTIVE:** Abdominal fat accumulation after menopause is associated with low-grade inflammation and increased risk of metabolic disorders. Effective long-term lifestyle treatment is therefore needed. **METHODS:** Seventy healthy postmenopausal women (age 60 ± 5.6 years) with BMI 32.5 ± 5.5 were randomized to a Paleolithic-type diet (PD) or a prudent control diet (CD) for 24 months. Blood samples and fat biopsies were collected at baseline, 6 months, and 24 months to analyze inflammation-related parameters. **RESULTS:** Android fat decreased significantly more in the PD group ($P = 0.009$) during the first 6 months with weight maintenance at 24 months in both groups. Long-term significant effects ($P < 0.001$) on adipose gene expression were found for toll-like receptor 4 (decreased at 24 months) and macrophage migration inhibitory factor (increased at 24 months) in both groups. Serum interleukin 6 (IL-6) and tumor necrosis factor α levels were decreased at 24 months in both groups ($P < 0.001$) with a significant diet-by-time interaction for serum IL-6 ($P = 0.022$). High-sensitivity C-reactive protein was decreased in the PD group at 24 months ($P = 0.001$). **CONCLUSIONS:** A reduction of abdominal obesity in postmenopausal women is linked to specific changes in inflammation-related adipose gene expression.

J Transl Med. 2017 Apr 24;15(1):81. doi: 10.1186/s12967-017-1184-x.

Preliminary results demonstrating the impact of Mediterranean diet on bone health.

Savanelli MC, Barrea L, Macchia PE, Savastano S, Falco A, Renzullo A, Scarano E, Nettore I, Colao A, Di Somma C

BACKGROUND: Nutrition is an environmental factor affecting bone health. Nutrition is considered essential to achieve and maintain optimal bone mass. Mediterranean diet (MD) has shown to prevent bone disease. Aim of this study is to investigate the relationship between bone health status and adherence the MD. **METHODS:** Four-hundred eighteen healthy people (105 males and 313 females, age 50 ± 14 years) were recruited in the outdoor hospital of the "Campus Salute Onlus" held in Piazza del Plebiscito in Naples, October 17-20th 2013 and 09-11th October 2014. All subjects underwent clinical assessment, calcaneal quantitative ultrasound (QUS) scanner and PREvención con DIeta MEDiterránea (PREDIMED) questionnaire. **RESULTS:** Globally, prevalence of osteoporosis and osteopenia were 7.7 and 46.0%, respectively. The majority of subjects (60.5%) had an average score (score 6-9) of adherence to MD. The T-score showed positive correlation with PREDIMED score ($r = 0.250$, $p < 0.001$). The higher T-scores were positively associated with a higher consumption of extra-virgin olive oil (EVOO), vegetables, fruits, legumes, and fish and negatively associated with consumption of red meat. The higher T-scores were positively associated with the highest odds of PREDIMED scores (higher adherence) (OR 6.91, IC 6.27-7.61, $p < 0.001$). Multiple regression analysis models indicated that, among the single food items investigated, high T-score can be predicted by

consumption of EVOO ($p < 0.001$), fish ($p < 0.001$) and fruit ($p = 0.002$) intake. A PREDIMED score of 3 was found to be predictive for a low T-score ($\alpha = 0.05$, R-squared index = 0.417). CONCLUSIONS: The results demonstrate a positive correlation between bone health status and adherence to MD, suggesting that a high adherence to MD promotes bone health. The observations here reported confirmed that a specific dietary approach, such as MD, can represent a modifiable environmental factor for osteoporosis' prevention.

J Womens Health (Larchmt). 2017 Feb 28. doi: 10.1089/jwh.2016.5992. [Epub ahead of print]

Lean Mass and Fat Mass as Mediators of the Relationship Between Physical Activity and Bone Mineral Density in Postmenopausal Women.

Xiang J, Chen Y, Wang Y, Su S, Wang X, Xie B, Zhang Q, Liu M.

BACKGROUND: The relationship between physical activity (PA) and bone health is well known, but the role of lean mass (LM) and fat mass (FM) in this relationship remains uncertain. Therefore, the aim of this study was to examine the mediating effect of LM and FM on the relationship between PA and bone mineral density (BMD) in postmenopausal women. MATERIALS AND METHODS: This cross-sectional study involved 282 postmenopausal women aged between 50 and 65 year, who were randomly selected from Hongqi community of Harbin City in China. PA was measured using an International PA Questionnaire. Body composition, BMD of the lumbar spine, hip, and total body were measured using dual-energy X-ray absorptiometry. Mediation analysis was performed to investigate the mediating effect of LM and FM on the relationship between PA and BMD. RESULTS: In partial correlation analysis, PA, LM, and FM were positively related to BMD. Positive correlation was found between PA and LM. There were significant differences in BMD between different categories of PA, but the differences disappeared after adjusting for LM. Mediation analysis showed that LM and FM played a mediating role in the relationship between PA and BMD. LM appeared to mediate the effect of BMD in the spine, hip, and total body by 26.91%, 19.55% and 47.98%, respectively; and FM was 22.23%, 27.97%, and 33.02%, respectively. CONCLUSION: LM and FM affected the relationship between PA and BMD as mediator. Postmenopausal women with high LM and FM had more BMD.

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Bone mineral density and fractures after surgical menopause: a systematic review and meta-analysis.

Fakkert IE, Teixeira N, Abma EM, Slart RHJA, Mourits MJE, de Bock GH.

BACKGROUND: Oophorectomy is recommended to women at increased ovarian cancer risk. When performed at premenopausal age oophorectomy induces acute surgical menopause, with unwanted consequences. OBJECTIVE: To investigate bone mineral density (BMD) and fracture prevalence after surgical menopause. SEARCH STRATEGY: A literature search on PubMed, Embase and Cochrane library through March 2016. SELECTION CRITERIA: Primary studies reporting on BMD, T-scores or fracture prevalence in women with surgical menopause and age-matched reference groups. DATA COLLECTION AND ANALYSIS: Data was extracted on BMD (grams/cm²), T-scores and fracture prevalence in women with surgical menopause and reference groups. Quality was assessed by an adaptation of Downs and Black's checklist. Random effects models were used to meta-analyse results of studies reporting on BMD or fracture rates. MAIN RESULTS: Seventeen studies were included, comprising 43,386 women with surgical menopause. Ten studies provided sufficient data for meta-analysis. BMD after surgical menopause was significantly lower compared to premenopausal age-matched women (mean difference lumbar spine: -0.15 g/cm², 95% CI: -0.19 - -0.11; femoral neck: -0.17 g/cm², 95% CI: -0.23 - -0.11) but not to women with natural menopause (lumbar spine: -0.02 g/cm², 95% CI: -0.04 - 0.00; femoral neck: 0.04 g/cm², 95% CI: -0.09 - 0.16). Hip fracture rate was not increased after surgical menopause compared to natural menopause (HR: 0.85, 95% CI: 0.70 - 1.04). CONCLUSIONS: No evident effect of surgical menopause was observed on BMD and fracture prevalence compared to natural menopause. However, available studies are prone to bias and need to be interpreted with caution.