LB1 NATURAL HISTORY AND RISK FACTORS OF BONE LOSS IN POSTMENOPAUSAL CAUCASIAN WOMEN: A 15-YEAR FOLLOW-UP POPULATION-BASED STUDY

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The study was to describe the natural history of bone loss over 15 years at femoral neck and lumbar spine and role of environmental factors in postmenopausal women. Bone mineral density (BMD) at the femoral neck (FN) and the lumbar spine (LS) were measured in postmenopausal women from the Chingford Study by DXA. Participants were scanned an average 6 times during the 15-year follow-up from 1989. Height, weight, and HRT status were assessed at each visit. Smoking status and serum dehydroepiandrosterone (DHEAS) levels were assessed at year 1 while serum IGF-I and calcium levels were measured at year 6 and 4, respectively. Osteoarthritis of hip and spine was assessed by X-ray at year 8. A total of 1004 postmenopausal women with an average age of 54 (range 43-68) at baseline were included. Both FN and LS BMD decreased significantly with increasing age ($p<0.0001$). The decline was larger at LS (-0.03 g/cm^2*per year) with a quadratic relationship (0.0002 g/cm^2 per squared age) than at FN (-0.002 g/cm^2*per year) with a linear relationship. Serum DHEAS levels was positively associated with both ΔFN BMD (0.037 g/cm^2 per SD, $p =0.016$) and ΔLS BMD (0.009 g/cm^2 per SD, $p = 0.059$) but the magnitude of the association was reduced significantly with increasing age for ΔFN BMD (-0.0004 g/cm^2 /per year per SD in DHEAS). Serum IGF-I levels were significantly associated with ΔLS BMD (0.01 g/cm^2 per SD, $p = 0.018$)) but not ΔFN BMD. Change in weight was positively associated with both ΔFN and ΔLS BMD (0.002 g/cm^2 per kg increase, $p <0.0001$). Both lean and fat mass measured at year 8 were significantly associated with both ΔFN and ΔLS BMD ($p<0.0001$), but the magnitude of the association was larger for lean mass (0.005-0.008 g/cm^2* per kg increase) than for fat mass (0.002-0.003 g/cm^2* per kg increase). Presence of hip osteophytes was associated with ΔFN BMD ($p = 0.046$) but spine osteophytes were not associated with ΔLS BMD. Smoking status and serum calcium levels were not associated with either ΔFN BMD or ΔLS BMD. All of these associations were independent and adjusted for HRT status which was also significant in the model. This is the largest population-based longitudinal study reporting 15 years of bone loss. The decline of BMD is linear with age for femoral but quadratic for spine. The study confirmed the predictive role of HRT, weight, lean mass, IGF-1, and DHEAS in long term bone loss, which could be valuable in the prevention and treatment of osteoporosis.

LB2 GENOME-WIDE ASSOCIATION (GWA) FOR BMD IN HEALTHY POSTMENOPAUSAL WOMEN

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BMD is a heritable complex trait. Linkage and association studies lack replication. GWA is a powerful hypothesis-free design we used to search loci influencing BMD variation. 500 women (65-75 years) lacking chronic diseases were selected from a population-based study and genotyped for the Affymetrix Mapping 500K array (416,796 SNPs with MAF> 0.01 and in HWE). After exclusions (DNA quality, gender/sample mismatch, admixture) 475 women were studied in relation to DXA BMD. Quality control (IBS clustering) and association testing was done using PLINK. Most significant associations were found in 32 SNPs from 15 novel independent loci associated to BMD (Figure). Four SNPs from an intronic locus on chromosome 21 endured correction (Bonferoni p=0.01)and associated consistently with BMD at several axial sites. Other locus in-between close genes on chromosome 19 associated strongly with femoral neck BMD. Replication will be pursued for this two novel loci influencing variation in BMD.

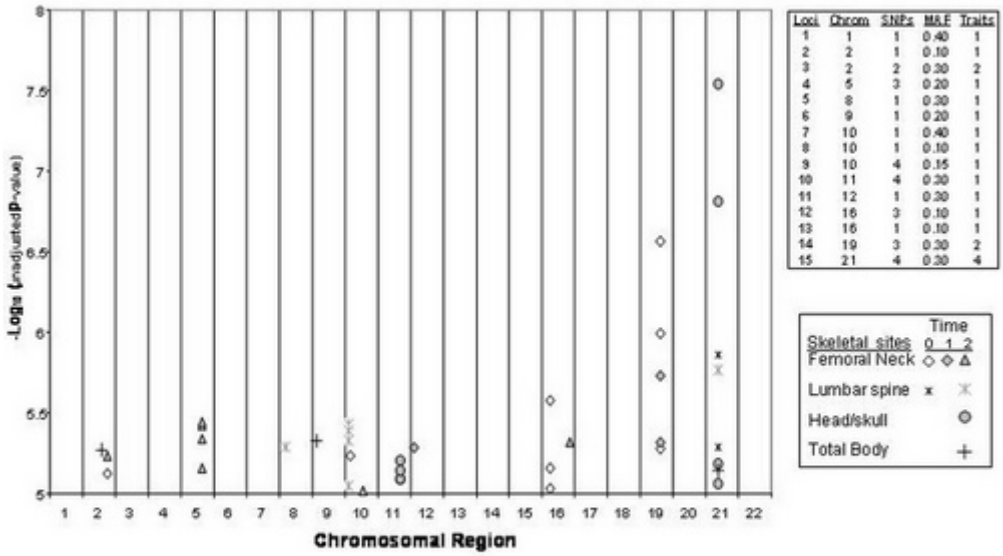

Figure. Most significant SNPs associated to DXA-BMD in 475 non-diseased postmenopausal Caucasian women

LB3 THE EFFECTS OF TIBOLONE IN OLDER WOMEN: RESULTS OF THE LIFT TRIAL SR

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Introduction: Tibolone has estrogenic, antiestrogenic, progestogenic and androgenic effects. It and prevents bone loss but its effects on fractures, cancer, and cardiovascular disease are uncertain.
Methods: 4538 postmenopausal women ages 60 to 85 years with total hip or spine bone mineral density (BMD) T-scores ≤ -2.5 SD or a vertebral fracture and a T-score ≤ 2.0 were randomly assigned to daily Tibolone 1.25 mg or placebo. Vertebral fracture was assessed by annual spine radiographs. Cardiovascular events and breast cancer were adjudicated by expert panels.
Results: The trial was stopped after a median 34 months of follow-up. Women assigned to tibolone group had a decreased risk of vertebral fracture (relative hazard =0.57; 95% confidence interval = 0.42 to 0.78), nonvertebral fracture (RH, 0.74; 95% CI = 0.58 to 0.93) and invasive breast cancer (RH, 0.32; 95% CI = 0.13 to 0.80; P=0.015) and an increased risk of stroke (RH, 2.19; 95% CI = 1.14 to 4.23; P = 0.019). There were no statistically significant differences in risks of coronary heart disease (RH, 1.37; 0.76 to 2.45) or venous thromboembolism (0.57; 0.19 to 1.69). Four women in the tibolone and none in the placebo group developed endometrial cancer (P=0.06) while 4 in the tibolone and 12 in the placebo group had colon cancer (P=0.04).
Conclusion: Tibolone 1.25 mg daily reduces the risk of fractures and breast cancer and, perhaps, colon cancer, but increases the risk of stroke in older women.