2006 IOF+ANZBMS Combined Meeting

Combined Meeting of the
3rd IOF Asia-Pacific Regional Conference on Osteoporosis *and the*
16th Annual Meeting of the ANZ Bone & Mineral Society
~ 22-26 October 2006, Port Douglas, Australia ~
www.anzbms.org.au/asm/asm2006

SESSION TIME: 0930 - 1030, Tuesday 24 Oct 2006

Oral Abstracts

3C (Clinical) - Epidemiology and human genetics

O29

A genome-wide linkage scan of a large twin cohort for QTLs that regulate hip structure phenotypes

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The genetic basis of osteoporotic fracture is only partly explained by bone mineral density (BMD). Hip structural analysis (HSA) is a technique for extracting strength-related structural dimensions of bone cross-sections from two-dimensional hip scan images acquired by dual energy X-ray absorptiometry (DXA) scanners. HSA can be used to provide additional phenotypes for genetic studies which may be independent predictors of osteoporotic fracture risk.

To identify regions of the genome that contain quantitative trait loci (QTL) for hip structure phenotypes of bone, we performed a genome-wide linkage scan (737 highly polymorphic microsatellite markers) on a large cohort of dizygous twin pairs. Unselected female dizygous twins from 1030 pedigrees from the TwinsUK Adult Twin Registry were studied. Univariate multipoint linkage analyses provided maximum evidence of linkage for Femoral Neck Cross Sectional Moment of Inertia (LOD 2.9) to 3p. Linkage for Femoral Neck Section Modulus was also seen to 3p (LOD 2.3). Evidence of linkage in the cohort defined five other possible locations of QTLs (LOD≥2.3) relevant to hip structure on chromosomes 5, 11, 19 and 20.

This study has identified six genomic locations with linkage of LOD ≥2.3 for HSA phenotypes. This data should be of value in assisting researchers to localize genes that regulate hip structure. These results should

complement other genome screens of BMD, HSA and bone structure, and serve to enable further targeted positional candidate and positional cloning studies to advance our understanding of genetic control of bone quality and risk of fracture.

O30

Calcium supplementation in children increases lean mass but has no effect on weight or body fat: a meta-analysis

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Aims: Calcium intake may reduce body weight or weight gain but evidence is conflicting in children. This study aimed to use data from randomised controlled trials (RCTs) to determine whether calcium supplementation in healthy children affects weight or body composition.

Methods: We searched the CENTRAL, MEDLINE, EMBASE, CINAHL, AMED, MANTIS, ISI Web of Science, Food Science and Technology Abstracts and Human Nutrition up until 1st April 2005 and hand-searched relevant conference abstract books. Studies were included if they were placebo-controlled RCTs of at least 3 months of calcium supplementation in healthy children with outcome measures including weight. Meta-analyses were performed using fixed effects models with weighted mean differences for weight and height and standardised mean differences (SMD) for body composition measures.

Results: There were no statistically significant effects of calcium supplementation on weight (+0.14 kg, 95% CI -0.28, +0.57), height (+0.22 cm, 95% CI -0.30, +0.74) or body fat (SMD +0.04, 95% CI -0.08, +0.15). There was a small effect on lean mass (SMD +0.22, 95% CI +0.05, +0.39), equivalent to an approximately 3% greater increase with supplementation.

Conclusion: There is no evidence to support the use of calcium supplementation as a public health intervention to reduce weight gain or body fat in healthy children. The effect on lean mass warrants further investigation to determine possible mechanisms for this effect and its clinical significance.

O31

Five-year and long-term risks of developing osteoporosis: a natural history analysis

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Osteoporosis is defined by BMD which progressively declines with advancing age. Understanding the natural history of osteoporosis is an important step for developing effective intervention. This study sought to estimate the 5-year and long-term risks of developing osteoporosis in men and women.

A cohort of 518 men and 886 women aged 60+ years who had normal or osteopenic BMD (T-scores>-2.5) at baseline (1989). The individuals had subsequently been followed for 15 years with biannually repeated BMD measurements (GE Lunar DPX). Survival analysis was utilized to estimate the 5-year and lifetime risk after adjusting for mortality.

After five years of follow-up, approximately 1% women and 0.4% men of the normal BMD group progressed to osteoporosis. During the same period, 18% of women and 13% of men with baseline osteopenic BMD progressed to osteoporosis.

For long-term risk, approximately 1% of women and 2.5% of men with baseline normal BMD ever developed osteoporosis after adjusting for mortality. Furthermore, in individuals with baseline osteopenic BMD, the mortality-adjusted lifetime risk was 54% in women and 35% in men.

These data show that the public health burden of osteoporosis is more serious than previously thought. In osteopenic individuals, while the short-term risk of developing osteoporosis was comparable between men and women, the long-term risk was greater in women than in men. To alter the course of osteoporosis interventions should target those with osteopenic BMD and high-risk of developing osteoporosis.

Source of financial support: National Health and Medical Research Council, Australia

O32

Impact of the obesity epidemic on bone mineral density: Geelong Osteoporosis Study

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The prevalence of adult obesity has nearly doubled in the past two decades. In this study, body composition was assessed, a decade apart, in two randomly-selected groups of women of the same age (50-59yr) participating in the Geelong Osteoporosis Study (GOS). All women in GOS aged 50-59yr at 10-yr follow-up (2004-6, n=153) were compared with all those aged 50-59yr at baseline (1994-7, n=206). The groups were mutually exclusive. BMD was measured at the PA spine (SP), femoral neck (FN), whole body (WB) and ultradistal forearm (UD) using Lunar DPX-L. For both groups, anthropometric measurements (weight, height, hip and waist circumference) were recorded; fat and lean tissue mass measurements were derived from WB scans.

All indices of adiposity were increased in the 2004-6 group compared to the 1994-7 group: weight +4.7%, body mass index (BMI) +3.3%, fat mass +9.6%, waist circumference +4.6%, waist/hip ratio (WHR) +5.4%. Lean mass (LM) also increased (+2.8%). Unadjusted BMD was greater for women in 2004-6: SP +4.4%, +WB 2.8%; no differences were detected at the FN or UD. This pattern persisted after adjusting for age and BMI: SP (1.207±0.015 vs 1.166±0.012, p=0.03), WB (1.170±0.006 vs 1.152±0.005, p=0.02).

Body composition has changed over the last decade. Whereas increases in adiposity may predispose to metabolic disease, the accompanying increase in BMD is independent of BMI and is non-uniform. The effect of these changes on fracture risk remains unclear.

Body composition (median (IQR) or mean±SE)				**BMD (mean±SE, g/cm²)**			
	2004-7	**1994-7**	**P**		**2004-6**	**1994-7**	**P**
Weight (kg)	74.1 (63.9,84.9)	70.8 (61.0,80.9)	0.00	**SP**	1.220±0.015	1.169±0.013	0.01
BMI (kg/m²)	27.9 (24.3,32.3)	27.0 (23.3,31.4)	0.05	**FN**	0.939±0.012	0.928±0.010	0.51
WHR	0.858±0.005	0.814±0.005	0.00	**WB**	1.187±0.007	1.155±0.006	0.00
Fat (kg)	32.0±1.0	29.2±0.7	0.02	**UD**	0.333±0.005	0.333±0.004	0.99
LM (kg)	40.3±0.4	39.2±0.3	0.03				

O33

Fractures in men: Geelong Osteoporosis Study

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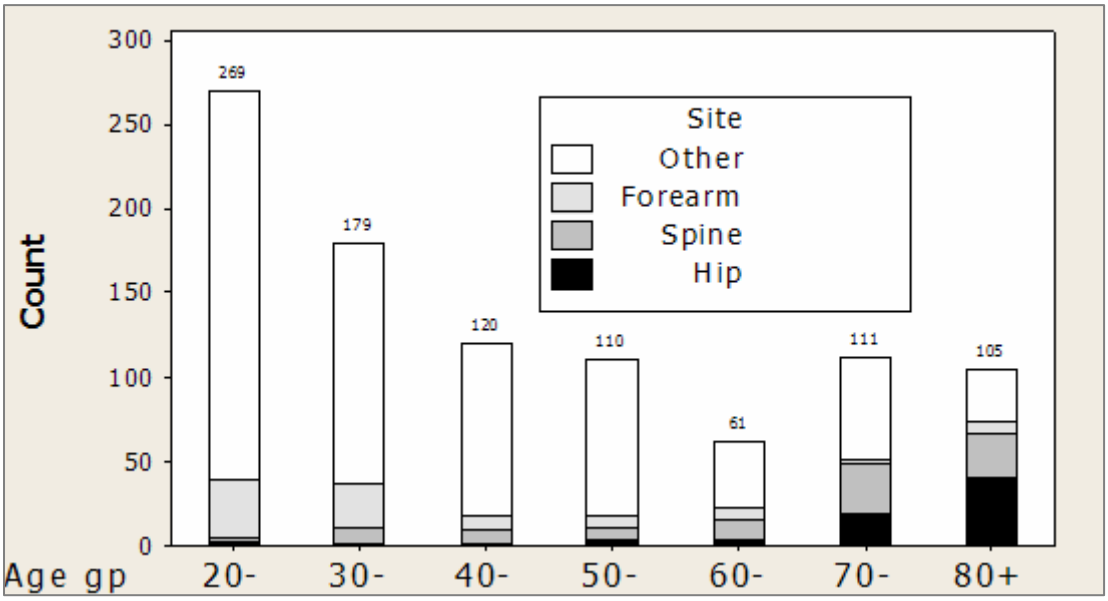
Using radiology reports at the Geelong Hospital, all men aged 20+yr with incident fracture in 2005 were identified; approximately 90% of fractures in the region can be ascertained by this method. We aimed to describe fracture epidemiology by age, fracture site and trauma. Low trauma fracture included spontaneous fracture and those resulting from falls <standing height or unspecified, overexertion, strenuous movement.

We identified 955 men aged 20-96yr sustaining at least one incident fracture (Figure). Trauma level was determined for 591 cases: 223 low and 368 high. Among men aged <60yr, 78% (321/409) of fractures were attributable to high trauma whereas among men aged >60yr only 26% (47/182) were high trauma.

In a subset of fracture cases (n=147, median age 51.1yr, IQR 37.6-64.0), total-hip BMD (Lunar Prodigy) was compared with male controls from a random population-based sample (n=847, 57.2yr IQR 34.9-76.0). Age-

and weight-adjusted BMD for fracture cases (79 high and 68 low trauma) was lower than controls ($p<0.05$) but adjusted BMD for high and low trauma groups did not differ (low trauma 1.021±0.017 vs high trauma 1.044±0.016 vs controls 1.086±0.005 g/cm^2).

One-third of the fracture burden arose from men aged >60yr, with age-related increases in traditional osteoporotic fractures (forearm, spine and hip) and relatively few high trauma. In contrast, high trauma factures at non-osteoporotic sites predominated in younger men. Despite differences in trauma patterns between younger and older men with fracture, BMD was consistently lower for fracture cases compared with controls across all ages.



O34

Metabolic syndrome and bone mineral density in a random sample of Australian men: Geelong Osteoporosis Study

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Components of the metabolic syndrome may have diverse effects on bone, including influences of weight, adipocytokines, hyperglycaemia, dyslipidaemia, hypertension and drug exposures. We examined the association between metabolic syndrome and BMD in an age-stratified random sample of 641 men aged 50-93yr (median 71.6yr, IQR 61.5-79.0). Metabolic syndrome was determined using the new worldwide IDF definition (2004). Medication use and previous fractures during the past 5yr were self-reported. BMD was measured at PA-spine (SP), femoral neck (FN) and whole body (WB); fat and lean mass were determined from WB scans.

215 men had metabolic syndrome; men with and without metabolic syndrome did not differ in age (median (IQR), 70.2 (63.1-77.5) vs 72.4 (60.7-80.8)yr, $p=0.4$). Age-standardised prevalence was 27.5% for men in their fifties, 40.3% sixties, 37.6% seventies and 24.8% for >80yr. Metabolic syndrome was associated with greater weight (mean±SD, 89.1±13.4 vs 79.0±12.7 kg), fat (26.4±7.5 vs 20.8±7.3 kg) and lean mass (58.7±6.4 vs 55.3±6.6 kg)(all $p<0.001$). Age-adjusted BMD was greater by 4% at SP (1.341±0.015 vs 1.287±0.011 g/cm2, $p=0.003$) and 3% at FN (0.954±0.010 vs 0.928±0.007 g/cm2, $p=0.024$) and WB (1.249±0.007 vs 1.216±0.005 g/cm2, $p<0.001$); after weight adjustment, differences were not statistically significant. Based on 36 fractures, fracture risk was not associated with metabolic syndrome (10/215 vs 26/426, OR=0.75, 95%CI 0.36-1.59, $p=0.45$); age-weight-adjustment did not affect this relationship.

Skeletal loading is the dominant effect explaining increased BMD among the 33% of men with metabolic syndrome. Based on limited fracture numbers, the response to loading may be sufficient adaptation for fracture protection.