

# OSTEOSCOOP

News on current events in osteoporosis and rheumatology

## How does body fat influence bone mass in childhood?

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**F**at mass may be a causal determinant of bone mass, but the evidence is conflicting, possibly reflecting the influence of confounding factors. The recent identification of common genetic variants related to obesity in children provides an opportunity to implement a Mendelian randomization study of obesity and bone outcomes, which is less subject to confounding and several biases than conventional approaches. Genotyping was retrieved for variants of two loci reliably associated with adiposity (the fat mass and obesity-related gene FTO and that upstream of the MC4R locus) within 7470 children from the Avon Longitudinal Study of Parents and Children (ALSPAC) who had undergone total body DXA scans at a mean of 9.9 yr [1]. Relationships between both fat mass/genotypes and bone measures were assessed in efforts to determine evidence of causality between adiposity and bone mass.

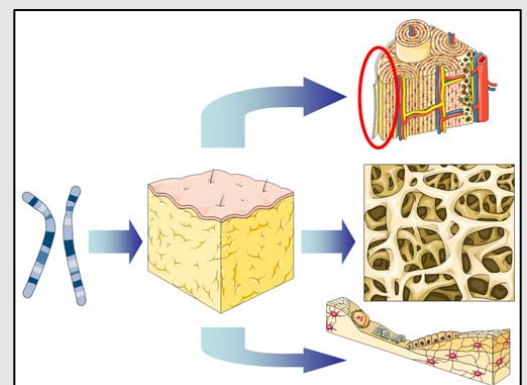
In conventional tests of association, both with and without height adjustment, total fat mass was strongly related to total body, spinal, and upper and lower limb BMC. Equivalent or larger effects were obtained from instrumental variable (IV) regression including the same covariates. Similar results were obtained after adjusting for puberty, when truncal fat mass was used in place of total fat, and when bone area was used instead of bone mass. In analyses where total body BMC adjusted for bone area was the outcome (reflecting volumetric BMD), linear regression with fat mass showed evidence for IV regression also showed a positive effect. When MC4R and FTO markers were used as instruments for fat mass, similar associations with BMC were seen to those with fat mass as measured by DXA.

This suggests that fat mass is on the causal pathway for bone mass in children. In addition, both directly assessed and IV-assessed relationships between fat mass and volumetric density showed evidence for positive effects, supporting a hypothesis that fat effects on bone mass are not entirely accounted for by association with overall bone size.

1. Timpson JN et al. *J Bone Miner Res.* 2009;24:522–533.

### How does body fat influence bone mass in childhood?

Is fat mass a determinant of bone mass? Two independent genetic markers of obesity, related to the FTO and MC4R genes, were used to explore this relationship in 5000 9-y-old children. The results indicate that fat mass is on the causal pathway for bone mass. The relationship between these two genetic markers, fat mass and bone mass largely involved effects on bone size, which represents a stimulatory effect of fat mass on periosteal bone formation. In addition, FTO and MC4R polymorphisms and fat mass were associated with bone mineral density, suggesting that fat mass may also influence bone remodeling.



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