

Invited Commentary

Commentary on ‘dietary magnesium intake and fracture risk: data from a large prospective study’

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In recent years there has been increasing acknowledgement of the influence of nutritional factors on bone health. In our ageing population osteoporotic bone fractures are a leading cause of disability and a consequent major burden on health and social care systems. Simple dietary strategies focusing on nutrition for optimal bone health may offer an acceptable universal option to help reduce fracture risk. Research studies on this topic have previously mainly focused on Ca and vitamin D intakes, but there has been a growing interest in the role of other nutrients including dietary Mg, for which there is a mechanistic rationale for epidemiological investigation. Bone represents the major body store of Mg, and experimental studies have shown Mg to be involved in bone metabolism, including having nitric-oxide dependent effects on osteoblast activity and osteoclast number, and affecting hydroxyapatite crystal formation and consequent bone stiffness⁽¹⁾. Ca homeostasis, highly relevant to bone health, is modulated by Mg through parathyroid hormone and vitamin D, and Mg deficiency in animal models promotes pro-inflammatory cytokine secretion and oxidative stress which both stimulate osteoclastic bone resorption⁽¹⁾.

In this issue of the *British Journal of Nutrition*, Veronese *et al.*⁽²⁾ present exciting new findings from a large USA-based cohort study (the Osteoarthritis Initiative; OAI) of middle to older-age men and women at high risk of knee osteoarthritis. Fracture occurrence, at the three most common osteoporotic fracture sites (hip, spine and forearm), was analysed for 3765 participants over a follow-up period of 8 years. Dietary Mg data were derived from FFQ completed at baseline and have been converted into sex-specific intake quintiles for analysis. During the follow-up period, 560 individuals reported the occurrence of a fracture. Regression analyses, with adjustment for relevant confounders, showed that the highest dietary Mg intake quintiles for both men and women were associated with significantly lower risk of fracture, compared with the lowest intake quintiles. Furthermore, the magnitude of these effects is particularly noteworthy with the highest Mg quintiles in men and women associated with 53 and 62% lower risk of fracture, respectively.

It is pertinent to consider that only 27% of the study cohort reached the USA RDA for Mg of 420 mg for men and 320 mg for women over 30 years of age (the UK reference nutrient intake (RNI) is 300 and 270 mg, respectively⁽³⁾), but that risk of fracture for women in this subgroup was significantly lower than in

those not achieving the RDA. Low prevalence of individuals consuming recommended dietary Mg intakes has been described previously for Western population cohorts^(4–6), and is thought to have been exacerbated in recent years as a consequence of increased consumption of processed foods lacking Mg and depletion of soil Mg concentrations through intensive farming practices resulting in food produce with reduced Mg content⁽⁷⁾. Differing national reference values complicate direct comparison of prevalence. For example, only 17% in the UK-based European Prospective Investigation into Cancer and Nutrition (EPIC)-Norfolk cohort of 25 639 men and women would meet the USA RDA, but 49% meet the UK RNI, and 81% meet the UK estimated average requirement of 250 and 200 mg which may be more appropriate for population-level assessment⁽⁸⁾. Nevertheless, from the findings of Veronese *et al.*⁽²⁾, one might speculate that increased compliance with Mg intake recommendations has the potential to reduce risk of fracture, at least in women.

Few studies have investigated fracture risk and dietary Mg intake in men and none has previously shown any association^(9–11). Veronese *et al.*⁽²⁾ have highlighted a negative association in the OAI cohort, but the magnitude of differences in fracture risk between upper and lower Mg quintiles for men was smaller than that seen for women. The physiology of ageing differs in a number of respects between the sexes, and further investigation will be required to decipher the interplay of hormonal and inflammatory responses, body composition and nutritional differences which may be contributing to the sex differences seen with Mg and bone health.

Despite mounting epidemiological evidence of the positive association of Mg intake and bone mineral density, data showing an association between dietary Mg intake and fracture risk has until now been unconvincing⁽¹²⁾. The study described by Veronese *et al.*⁽²⁾ thus provides a useful addition to the literature supporting the relevance of dietary intake of Mg to osteoporotic fracture risk and, once reinforced by clinical trial data, raises the prospect of exploiting this relationship in nutritional public health strategies to improve bone health at a population level.

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