



B-vitamins and their interaction with the *MTHFR* C677 T genotype as determinants of bone health in older adults from the TUDA Ageing cohort study

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Osteoporosis, characterised by reduced bone mineral density (BMD) and a high risk of fragility fracture, is increasingly prevalent in today's ageing society⁽¹⁾. Large observational studies support a protective role for certain B-vitamins integral to 1-carbon metabolism (i.e. folate, vitamins B12, B6 and riboflavin) against osteoporosis⁽²⁾. A common polymorphism (C677 T) in the folate metabolising enzyme methylenetetrahydrofolate reductase (*MTHFR*) has also been linked to osteoporosis, with a heightened risk demonstrated in the presence of low B-vitamin status⁽²⁾. However, previous studies exploring the role of this polymorphism have tended to overlook relevant gene-nutrient interactions⁽²⁾. The aim of this investigation was to examine the interaction of relevant B-vitamin biomarkers with the *MTHFR* 677TT genotype as determinants of low BMD.

Older adults (*n* 3,127) recruited to the Trinity Ulster Department of Agriculture (TUDA) Ageing cohort study, and with BMD measured by dual energy X-ray absorptiometry scans, were investigated. Low BMD was defined as a combination of osteopenia (T-Score; between -1 and -2.5 SD) and osteoporosis (T-Score; -2.5 SD or less).

Age ($p < 0.001$), physical inactivity ($p = 0.015$), and parathyroid hormone ($p < 0.001$) were associated with an increased risk of low BMD, while increasing body weight ($p < 0.001$) reduced the risk. The *MTHFR* C677 T genotype was not found to be a significant predictor of low BMD in either males or females. Females with the *MTHFR* 677TT genotype in combination with low biomarker status of riboflavin or folate had a two-fold increased risk of low BMD compared to those with the *MTHFR* 677CC genotype and optimal B-vitamin status, after adjustment for covariates; these associations were not observed in men (Table).

Table. Predictors of low bone mineral density 'BMD' (osteoporosis and osteopenia combined)

B-vitamin biomarker (<i>n</i> 3,127)	OR	95 % CI	P
Males (<i>n</i> 1,056)			
<i>MTHFR</i> 677TT genotype	1.047	0.672–1.631	0.841
Low riboflavin* <i>MTHFR</i> 677TT genotype	0.937	0.476–1.844	0.831
Low folate* <i>MTHFR</i> 677TT genotype	1.905	0.896–4.049	0.094
Females (<i>n</i> 2,071)			
<i>MTHFR</i> 677TT genotype	1.378	0.961–1.976	0.081
Low riboflavin* <i>MTHFR</i> 677TT genotype	2.314	1.237–4.329	0.009
Low folate* <i>MTHFR</i> 677TT genotype	2.007	1.106–3.642	0.022

Analysis by binary logistic regression, comparing lowest tertile of vitamin status to the other tertiles combined. Reference category; *MTHFR* 677CC genotype and highest B-vitamin status. Riboflavin was measured using erythrocyte glutathionine reductase activation coefficient 'EGRac'. Folate was measured in red blood cells by microbiological assay.

These findings suggest that there are important gene-nutrient interactions within 1-carbon metabolism that appear to play an important role in maintaining bone health throughout life.

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1. Strom O, Borgstrom F, Kanis JA *et al.* (2011) *Arch Osteoporos* 6, 59–155.
2. Dai & Koh (2015) *Nutrients*, 7, 3322–3346.