Irish Section Meeting, 19–21 June 2013, Childhood nutrition and obesity: current status and future challenges

## Effect of habitual calcium intake on dietary vitamin D requirements in adults

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If dietary calcium intake is low and serum calcium concentrations decrease, the compensatory metabolic response is the accelerated conversion of 25-hydroxyvitamin D [25(OH)D] to 1,25-dihydroxyvitamin D (via parathyroid hormone), so as to normalize serum calcium levels <sup>(1)</sup>. These interactions between vitamin D and calcium may have implications for the regulation of 25(OH)D production and its catabolism, and consequently for the dietary vitamin D requirement <sup>(2)</sup>. While highlighted as a significant knowledge gap by the North American Institute of Medicine in their recent DRI report for vitamin D and calcium <sup>(1)</sup>, to date this hypothesis has only received limited attention in human studies. The aim of this study was to test this hypothesis using relevant data from our previously published vitamin D intervention studies in 20–40 y olds <sup>(3)</sup> and 64 + y olds <sup>(4)</sup> as well as an updated version of our recent meta-regression analysis <sup>(5)</sup>, all of which up to now have not included dietary calcium intake as a possible additional determinant of vitamin D requirements.

Within the datasets from our two vitamin D intervention studies, baseline serum 25(OH)D and response of serum 25(OH)D to vitamin D<sub>3</sub> intervention (0, 5, 10 or 15 $\mu$ /d) over winter months were stratified by<or ≥ three different cut-offs for dietary calcium intake (550, 700 and 800 mg/d), representing EU estimated average requirement (EAR), UK reference nutrient intake and US EAR for calcium, respectively). Students' paired and unpaired *t*-tests were used to test differences at baseline and response of serum 25(OH)D to intervention in groups stratified according to each cut-off for calcium intake, respectively. Regression models were also run to account for possible confounding effects of sex, age, BMI, habitual vitamin D intake and study centre. In the meta-regression analysis, two new studies published since our original meta-regression in 2011<sup>(5)</sup> were included and habitual calcium intake was reported in each of the 13 studies.

In the meta-regression approach, the relationship between serum 25(OH)D and total vitamin D intake were not significantly different (*P*>0.05) when studies were stratified on the basis of habitual group mean calcium intakes  $\langle o \rangle \ge \sim 1000 \text{ mg/d}$ . Data from our own two intervention studies suggest that while baseline serum 25(OH)D concentrations were significantly lower (*P*<0.05) in the <700 mg/d calcium intakes groups compared to the >700 mg/d in the 64+ y olds, these differences disappeared when data was adjusted for the aforementioned confounding factors. There were no other significant differences (*P*>0.05) in baseline serum 25(OH)D in 20–40 y olds or 64+ y olds when stratified by habitual calcium intake. Upon stratification on the basis of  $\langle or \rangle$  three selected dietary calcium intake cutoffs, there was no significant difference in the response of serum 25(OH)D to vitamin D intervention in 64 y olds stratified by </br/>
Likewise, there was no significant difference in response of serum 25(OH)D to vitamin D intervention in 64 y olds stratified by </br/>  $\langle >550 \text{ mg/d} \text{ or } \langle >800 \text{ mg/d} \text{ but there were lower responses to } 5 \mu/d (12.2 \text{ nmol/L}; P = 0.007), 10 \mu/d (14.6 \text{ nmol/L}; P = 0.008), and 15 \mu/d (9.4 \text{ nmol/L}; P = 0.097) in those 64+ y olds with calcium intakes </br/>
compared to <math>\geq 700 \text{ mg/d}$ . Calcium intake </br/>  $\langle >700 \text{ mg/d} \text{ remained a significant predictor } (P = 0.041)$  of the change in serum 25(OH)D over winter in the regression models that accounted for treatment but also the aforementioned confounding factors.

In conclusion, *post-hoc* analysis seems to suggest that a habitual calcium intake less than 700 mg/d may lead to a more blunted response of winter serum 25(OH)D to increased vitamin D intake in older adults. This may have implications for the dietary vitamin D requirement. *\*The two vitamin D intervention studies were collaborative studies with the University of Ulster, Coleraine. \*\*Current analysis supported by the Department of Health, England.* 

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