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Letter to the Editor

Effects of school-milk intervention on growth and bone mineral accretion in Chinese girls aged 10–12 years: accounting for cluster randomisation

We have previously reported that dietary supplementation with milk at school for 24 months enhanced growth and bone mineral accretion in Chinese girls aged 10 years at baseline (Du *et al.* 2004). In that study, subjects were randomised into three groups according to their schools because, for both ethical and practical reasons, it was not possible to randomise subjects between supplemented and control groups within the same school. It has been suggested that the impact of a possible intra-cluster correlation should be taken into account in such a cluster-design randomisation trial (Varnell *et al.* 2004).

Therefore, we have further analysed the data using the linear mixed model to allow for clustering by school, with the school defined as a random effect (Murray, 1997). To investigate any proportional effects of discrete variables (i.e. supplementation group), the continuous variables (i.e. bone and anthropometric measures) were subjected to natural log transformation. Outcomes were analysed by adjusting for the baseline value and the intervention group. For size-adjusted bone mineral content, body- and bone-size variables including bone area, weight and height were also adjusted by inclusion in the model as the mean values and also the differences between the baseline values and those at the end of the trial. Menarcheal status as one potential confounding variable was also adjusted in the model for size-adjusted bone mineral content. The regression parameter b_{group} for each intervention group, when multiplied by 100, represents the percentage difference between each of the intervention groups and the control group for each outcome measure (Cole, 2000). The percentage differences between the two intervention groups were calculated in a similar way. Estimates of the strength of a clustering effect within schools are provided by the intra-cluster correlation coefficient. All data were analysed by SAS (SAS for WINDOWS version 9.1; SAS Institute Inc., Chicago, IL, USA).

Compared with analyses made on the pooled individuals, the P values increased in the analyses allowing for clustering by school as degrees of freedom were reduced. However, as shown in Table 1, the significant effects of school-milk supplementation on height, sitting height, and total body bone mineral density remained in both intervention groups ($P = 0{\cdot}003 – 0{\cdot}03$ compared with $P < 0{\cdot}0005$ for analysis made at individual level). For weight, total body bone mineral content and total body size-adjusted bone mineral content, the significant effects remained in the group receiving both Ca- and vitamin D-fortified milk ($P = 0{\cdot}005 – 0{\cdot}03$ compared with $P < 0{\cdot}0005 – P = 0{\cdot}002$ for analysis made at individual level), and a non-significant trend of greater gains was indicated in the group receiving milk fortified with Ca only ($P = 0{\cdot}07 – 0{\cdot}12$ compared with $P < 0{\cdot}0005 – P = 0{\cdot}03$ for analysis made at individual level). The intra-cluster correlation coefficient values were in the range of 0·010–0·025 for anthropometry measurements and 0–0·028 for the bone measurements.

We conclude that the effects of this school-milk intervention study on growth and bone mineral accretion are still evident even after the reduction in the degrees of freedom when taking account of the cluster randomisation design.

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Table 1. Percentage differences between groups in anthropometric and bone measurements after 24 months of milk supplementation allowing for clustering by school*

	(Milk + Ca) − control†				(Milk + Ca + vitD) − control†			(Milk + Ca + vitD) − (milk + Ca)†		
	ICC	Estimate	95 % CI	P	Estimate	95 % CI	P	Estimate	95 % CI	P
Height	0·016	0·8	0·3, 1·3	0·01	0·7	0·1, 1·2	0·02	−0·1	−0·7, 0·4	0·5
Sitting height	0·010	1·2	0·5, 1·8	0·004	0·7	0·1, 1·3	0·03	−0·5	−1·1, 0·2	0·1
Weight	0·025	2·7	−0·2, 5·6	0·07	3·7	0·8, 6·6	0·02	1·0	−1·9, 4·0	0·4
Total body BMC	0·011	1·7	−0·6, 4·1	0·12	2·6	0·3, 5·0	0·03	0·9	−1·5, 3·3	0·4
Size-adjusted BMC	0·012	1·1	−0·2, 2·5	0·09	2·5	1·1, 3·9	0·005	1·4	−0·03, 2·8	0·05
Total body BA	0	−1·0	−3·0, 1·0	0·3	−1·8	−3·8, 0·2	0·07	−0·8	−2·8, 1·3	0·4
Total body BMD	0·028	3·1	0·4, 5·7	0·03	5·4	2·8, 8·1	0·003	2·4	−0·3, 5·1	0·08

Milk + Ca, milk with Ca; milk + Ca + vitD, milk with Ca and vitamin D; ICC, intra-cluster correlation coefficient; BMC, bone mineral content; BA, bone area; BMD, bone mineral density.

* For analysis at individual level, *n* 207, *n* 111 (milk + Ca); *n* 240, *n* 113 (milk + Ca + vitD); *n* 234, *n* 122 (control) for anthropometry and bone measures, respectively. For analysis at cluster level, three per group.

† Analyses were made by linear mixed model. For size-adjusted BMC, adjusted for baseline value, BA, height, weight, menarcheal status at 24 months and clustering by school; for all other variables, adjusted for baseline value and clustering by school.

References

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