1	To the Editor: the effect of genetic factors on the response to vitamin D supplementation
2	may be mediated by vitamin D binding protein concentrations
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15 16	DISCLOSURE STATEMENT: The authors have nothing to disclose
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1 To the Editor: the effect of genetic factors on the response to vitamin D supplementation

2 may be mediated by vitamin D binding protein concentrations

We welcome the paper by Yao et al. (1), presenting the vitamin D binding (DBP) genotype
distribution and concentrations and their influence on the response to vitamin D
supplementation in a large cohort of Chinese adults. There are however several points the
reader should consider in the interpretation of these data.

7 Yao et al. report that supplementation with 2,000IU vitamin D per day failed to correct 8 vitamin D deficiency in 25% of Chinese participants. They used the Endocrine Society (ES) 9 thresholds for vitamin D deficiency for clinical populations (a plasma 25 hydroxy vitamin D 10 (25(OH)D) concentration <50nmol/L) (2). The ES however recommends that for the correction of vitamin D deficiency an 8-week loading schedule of 50,000IU/week followed 11 by a maintenance dose of 1,500-2,000IU/d for adults should be used. However for a study 12 13 amongst healthy community dwelling adults, without conditions that may increase their 14 vitamin D requirements, the use of population guidelines (e.g. that of the Institute of 15 Medicine (3)) would have been more appropriate.

16 The authors appear to suggest that there are major racial differences in the increment of 25(OH)D in the response to vitamin D supplementation. However, the selected papers do 17 not represent the balance of available evidence, which shows a lack of influence of race on 18 the dose-response to vitamin D supplementation, albeit this was mostly based on black and 19 20 white populations (summarised by EFSA (4)). The authors suggest that the low increment in 21 25(OH)D in Chinese participants may be caused by the predominant vitamin D binding protein (DBP) genotypes in this population and the associated differences in the binding 22 23 affinity for 25(OH)D. In support of this statement the authors quote the paper by Arnaud,

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1	1993 (5). However, where Arnaud used vitamin D as a tracer and reported DBP genotype-
2	dependent differences in the affinity for 25(OH)D by extrapolation, other studies using
3	^[3H] 25(OH)D showed small, if any differences (6-8). The DBP genotype-dependent
4	differences in baseline 25(OH)D and the increment in its concentration after
5	supplementation reported by Yao, may be predominantly determined by the genotype-
6	dependent differences in DBP concentrations. Through this mechanism, DBP genotype may
7	influence the fraction of 25(OH)D available for cellular uptake and hydroxylation (9).
8	Finally, the authors suggest that the response to vitamin D supplementation was greater for
9	total 25(OH)D than for 25(OH)D $_{Bio}$ by comparing their respective changes, while ignoring
10	differences in their absolute values. A calculation of their proportional change shows that
11	these are similar (+105 and 107% for total and $25(OH)D_{Bio}$, respectively), a finding that is to
12	be expected since $25(OH)D_{Bio}$ is derived from the concentrations of total $25(OH)D$ and its
13	binding proteins, DBP and albumin. The latter are known not to respond to vitamin D
14	supplementation (10).
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22 The authors report no potential conflict of interest relevant to this letter.

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