Reviewer's report

Title: Analysis of SNP-SNP interactions and bone quantitative ultrasound parameter in early adulthood

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Reviewer: John Loughlin

Reviewer's report:

This is a clearly written manuscript with a very well defined aim. The sample size for SNP-SNP epistatic interaction analysis is modest, and the authors do acknowledge this. They also apply a p-value threshold to avoid false-positives. None of the p-values surpass this threshold, so the conclusion should be that they have not generated robust evidence to support any SNP-SNP epistatic interactions. But that is not the message given in the Abstract or the Discussion. Instead, a reader may leave with the impression that significant effects have been detected.

The authors should be lauded for setting a threshold. After all, the large number of tests performed does mean that p-values <0.05 will be observed by chance; the p-values that they report fall within the range that one would expect when there are no actual genuine effects. But there is a sense that the authors have partly abandoned this objective approach and drawn subjective conclusions from the p-values that are <0.05. In reality, they failed to detect p-values that surpassed their threshold and as such, they should report that no significant SNP-SNP epistatic interactions were observed.

For this manuscript to be publishable, the authors would therefore need to change much of the tone of their conclusions. The issue is that the failure to observe SNP-SNP epistatic interactions may be because none exist for the SNPs tested or that the effects are so weak that the sample size used is much too small to detect them. As such, reporting a negative finding in this regard doesn't really add anything to our current knowledge; does the manuscript therefore merit publication at all?
Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.
Yes

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If not, please specify which controls are required in your comments to the authors.
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