Reviewer’s report

Title: Differential effects of vitamin D2 and D3 supplements on 25-hydroxyvitamin D level are dose, sex, and time dependent: a randomized controlled trial

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Reviewer: Zaki Hassan-Smith

Reviewer's report:

Review Comments BMC Endocrine Disorders

This paper is robust in its approach to the question of the effect of different vitamin D supplementation regimens on circulating vitamin D levels. It uses a blinded placebo-controlled randomized control trial design, with end-points as registered with ClinicalTrial.org. Multiple dosing regimens arms are compared, including daily, 2 weekly, 4-weekly D2 or D3. Supplements were subjected to in-house analysis. Assessments at levels of compliance were also made. The study is also informative due to the geographical location of the investigating centre. The majority of vitamin D supplementation studies have been carried out in Europe and the US. The manuscript is on the whole well written and clear.

The findings with regards to decreases in D2/D3 levels when treated with the alternative form of vitamin D as shown in Figure 5 are interesting. As a reader it would be interesting to include some speculation on putative mechanisms of this observation.

The headline observation 2-weekly and 4-weekly D3 supplementation are superior in increasing serum vitamin D levels as compared to alternative regimens provides further information in this area.

Study limitations include:

Findings may not be generalizable to every patient group setting (in particular outcomes could vary according to baseline vitamin D status, latitude, age, co-morbidities etc), a comment to this effect would be useful.

In view of the density of data, a potential limitation is in multiple comparisons being made, so the results could be caveated in this way. In particular with regards to secondary end-points of AUC measures at earlier time-points.

The study design did not allow for full assessment of important adverse effects (such as falls risk in the elderly), so superiority/ inferiority of dosing strategies are restricted to commenting on effect on serum levels only and not on general health effects.
Many of the study findings replicate those seen previously.

Action points for authors:

1. Comments on the above raised study limitations
2. A comment on the ethnicity of participants would be informative.
3. There is a discrepancy in the wording of the number of study participants randomized (n=269 vs 279) between the abstract and the first line of results in the manuscript, which is explained by the drop-out rate could this be clarified?

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

Quality of written English
Please indicate the quality of language in the manuscript:

Acceptable

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