Reviewer's report

Title: Implications of standardization of serum 25-hydroxyvitamin D data for the evaluation of vitamin D status in Germany, including a temporal analysis

Version: 0 Date: 22 Apr 2018

Reviewer: Patricia Lee

Reviewer's report:

The study is informative and has a great value of using large population data to evaluate standardized measurements to determine vitamin D status. The methods and analysis were appropriate. However there are many concerns that require attention. Specific comments are detailed below.

Background

P4, Lines 66-69: The systematic review (no convincing evidence for a causal relationship between 25(OH)D and non-skeletal diseases) doesn't seem to be relevant to the study topic. Did the systematic review suggest any issues with measurement of serum Vitamin D?

Lines 88-89: the sentence "...comparable over time, location, and laboratory procedure..." is not clear.

P5, Line 94 ("As part of..."): delete 'one of'.

Lines 109-110: a comparison of data from two cross-sectional surveys

p.6, Line 130: delete 'also'

Materials and Methods

Discuss potential sources of selection bias in the following population data:

* GNHIE98 data: selection bias due to low availability of 25(OH)D data (initial number: 7124 →4030 →3917). The number of available serum samples from the survey was 3917.

* DEGS1: "the persons who already participated in the GNHIE98…response rate 42%”. Does this mean 1645 (3917x42%=1645) of the 6995 serum samples from GNHIE98 survey?

* KiGGS data: selection bias due to availability of serum samples (57%=10015/17641).
Please describe in brief how the subset of serum samples for re-analysis was selected. Were the samples considered representative for population standardization? As the sample sizes for the three subset samples to establish standardization of 25(OH)D measurements were small, the sampling of the subset samples is crucial and needs to be well justified.

In 2.2 data collection, are 'All surveys comprised self-administered questionnaires, a physician-administered personal interview, physical examinations,…' relevant to this study?

p. 8, Lines 173-177: "Simple linear…to create standardize data sets" should be placed in 'Statistical analyses' section.

Results
Please provide interpretation of Table 1. Include group totals and grand total in the table. There were discrepancies in the population structures between GNHIES98 and DEGS1 data, as well as between men and women. Were they consistent with the structure of the entire German population (according to official population data)?

Please provide a brief interpretation of Table 2. Explain why in the last column of "Rval ≤ value" (In Table 2) is X12 (a squared value). Was a curvilinear model used?

Figures 4 and 6: explain why the standardized 25(OH)D distributions have two distinct peaks.

Tables 4-6: The authors stated that the previous VDSP program "did not provide a deeper insight into potential differences among age-groups within the wider population groups". To fill this gap, please compare the differences between male and female populations as well as age differences in means and prevalence of 25(OH)D levels. Please also comment on the impact of standardization on specific sex and age groups.

Table 4, please explain why the standardized prevalence (7.3 (4.4-11.8)) of <30 nmol/l in women aged 60-69 was significantly lower than all other age groups, same aged male group and the original 25(OH)D data of the same aged group?
p.12, Lines: 258-249: Is it valid to compare prevalence of vitamin D deficiency between adults and children?

Discussion

p.12, Lines 268-270: please reference the information source.

p. 15, Lines 321-322: "the development and establishment of evidence-based reference values for the evaluation of vitamin D status, especially deficiency and sufficiency, is challenging." Please provide 1-2 examples for this statement.

**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.

No

**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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