Author’s response to reviews

Title: Vitamin D, parathyroid hormone and metabolic syndrome - the PORMETS study

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Author’s response to reviews:

Rebuttal letter – response to each point raised by the Academic Editor and Reviewers.

Editor Comments

Comment #1

It has come to our attention that throughout the manuscript there is significant text overlap with other publications. While we understand that you may wish to express some of the same ideas contained in these publications, please be aware that we cannot condone the use of text from previously published work. We would therefore be grateful if you could provide a justification for the overlap in text between your manuscript and other sources. Please be informed that we cannot proceed with handling your manuscript before this issue is resolved, and the sections of text in question have been reformulated. The report has been attached to further help your revisions.

Please note that the software used to detect overlaps is imperfect and highlights two or more consecutive matching words, therefore, please just focus on those whole sentences/paragraphs highlighted. If this study uses methodology from a previously published work, please provide a summarizing statement in the methodology together with a citation to the original paper.

Response to comment #1

According to the Editor’s recommendations, the authors provide a justification for the text overlap between the manuscript and other sources, and only focused on the whole sentences/paragraphs highlighted within.
The authors would like to draw attention to the inclusion of the text “response to the reviewers” in the overlap count.

Overlap 1

The most significant overlap was with a previously published paper by the authors that described the recruitment procedures and methodology of PORMETS study, from which this sample was selected. As such, these procedures, as the Editor can understand, are the same and, consequently, it is very difficult not to overlap expressions or ways of describing the same methodological procedure. Nevertheless, the authors included a statement referring this in the beginning of the methods section (lines 104-105 of the manuscript), as well as the proper reference:


Overlap 2

Regarding the second overlap (www.ncbi.nlm.nih.gov), with 278 words (3%), the manuscript only presents 5 text sections with said overlap (line 87 -10 words; line 173 - 6 words; line 206 -4 words; line 241 -15 words; line 397 -10 words). In all these positions, the authors believe the overlap is negligible as they refer to very common statements as “were included” or “the metabolic syndrome which represents a cluster”.

Overlap 3

“drug treatment for elevated glucose; systolic …130 …/or diastolic … 85 mmHg or antihypertensive drug treatment in a patient with a history of hypertension; triglycerides …mg/dL (1.7 mmol/L) or drug treatment for elevated triglycerides; HDL … (1.3 mmol/L) … and … mg/dL (1.0 mmol/L) … or drug treatment for reduced HDL…” (Methods section, line 177)

The sentence presents the metabolic syndrome criteria according to the Joint Interim Statement (JIS) of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity. According to the software program, an overlap was found with a website (file.scirp.org) that was not previously consulted by the authors. The authors admit that other authors may have used
similar phrases since the JIS criteria are rigid and the criteria have to be presented in the same way as in the original article.

Overlap 11

“…represent a distinct state of… against bone loss. Dysfunction of the parathyroid glands, may be a potential cause …13” (Discussion section, line 285)

In fact part of the phrase was inspired by the Sahota article properly identified in reference 13. Although the authors wished to express the same ideas contained in this publication, some changes were made to the sentence taking into account the Editor’s recommendations.

The above sentence was replaced by: “The “blunted PTH response” may correspond to a protective mechanism of bone mass, through the development of a functional hypoparathyroidism 13. In addition to parathyroid dysfunction, other factors may contribute to the modification of the PTH response to low VitD levels…” (Discussion section, lines 285-287 of the manuscript).

Overlap 18

“Insulin resistance was estimated according to the homeostatic model assessment (HOMA) as the product of fasting glucose (mmol/L) and insulin (μU/mL) divided by a constant of 22.5” (Methods section, line 164)

The estimate of insulin resistance by Homeostatic Model Assessment (HOMA) was first described by Matthews and collaborators in “Homeostasis model assessment: insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. Diabetologia, 1985;28(7):412-9”.

According to the software program, the authors found some overlap with their definition in a thesis dissertation of Maria Manuela Cabral (https://repositorio-aberto.up.pt/bitstream/10216/71104/2/29221.pdf), a Portuguese investigator. Although this overlap was involuntary the authors decided to slightly modify the phrase: “Insulin resistance was estimated by the Homeostatic Model Assessment (HOMA), from fasting glucose (mmol/L) and insulin (μU/mL), as the product of the two divided by 22.5” (Methods section, lines 167-169 of the manuscript)
“Calcidiol has low biological activity, but is the major circulating form of VitD in the blood stream and best indicator of VitD status.” (Introduction section, line 78)

This phrase bears some resemblance to a phrase found in the cited article (Prasad P, Kochhar A. Interplay of vitamin D and metabolic syndrome: A review. Diabetes Metab Syndr. 2016;10 (2):105-12. doi: 10.1016/j.dsx.2015.02.014).

We propose replacing the phrase by another:

“Calcidiol has low bioactivity, but is the main form of VitD in the blood stream and best indicator of VitD status.” (Introduction section, lines 78-79 of the manuscript)

“A bi-directional Mendelian randomization analysis 36 provided evidence for the role of obesity as a causal risk factor for the development of VitD deficiency” (Discussion section, line 350)

In fact, part of the phrase was inspired by Vimaleswaran´s article properly identified by reference 36. Although the authors wished to express the same ideas contained in this publication, some changes were made to the sentence taking into account the Editor’s recommendations.

The above sentence was replaced by: “A bi-directional Mendelian randomization analysis 36 suggested a causal role of obesity for the risk of hypovitaminosis D” ((Discussion section, lines 352-353 of the manuscript)

The authors did not consult the publication: Barreto Silva MI, Cavalieri VV, Lemos CC, Klein MR, Bregman R. Body adiposity predictors of vitamin D status in nondialyzed patients with chronic kidney disease: A cross-sectional analysis in a tropical climate city. Nutrition 2017;33:240-247. In this article, the sentence “A meta-analysis including 21 adult cohorts provided evidence for the role of obesity as a causal risk factor for the development of vitamin D deficiency” is presented and identified by the same reference (Vimaleswarn).

“Previous studies have reported that low 25(OH) levels were associated with insulin resistance, glucose intolerance, obesity…5” (Discussion section, line 342)
In fact, part of the phrase was inspired by Ju’s article properly identified by the reference 5. Although the authors wished to express the same ideas contained in this publication, some changes were made to the sentence taking into account the Editor’s recommendations. The above sentence was replaced by: “Low levels of vitamin D have been reported to be associated not only with obesity and insulin resistance but also with glucose intolerance, dyslipidemia, increased renin gene transcription, endothelial dysfunction, proliferation of vascular smooth muscle cells, thrombogenicity and inflammation” (Discussion section, lines 344-346 of the manuscript)

Overlap 49

“In addition, hypovitaminosis D is highly prevalent in adults with CVD, particularly in those with coronary heart disease and heart failure” (Discussion section, line 337)

In fact, part of the phrase was inspired by Kim’s article properly identified by reference 34. Although the authors wished to express the same conclusions contained in this publication, some changes were made to the sentence taking into account the Editor’s recommendations. The above sentence was replaced by: “In addition, the prevalence of hypovitaminosis D is generally increased in adults with CVD, namely in coronary heart disease and heart failure” (Discussion section, lines 340-341 of the manuscript)

Overlap 58

“a recent meta-analysis demonstrated an inverse association between the 25(OH)D levels and increased risk of type 2 diabetes” (Discussion section, line 358; lines 361-363 of the manuscript)

In the article by Afza,l properly identified by reference 38, the authors’s hypothesis was: “low plasma 25-hydroxyvitamin D[25(OH)D] is associated with increased risk of type 2 diabetes in the general population”. Our sentence, as it stands, is not reproduced in the article. However, the term “increased risk of type 2 diabetes” is used. It would have been difficult to use another term, taking into account the purpose of the article.

The authors did not consult the publication: Epstein D, Kvanta A, Lindqvist. Seasonality and incidence of central retinal vein occlusion in Sweden: a 6-year study. Ophthalmic Epidemiol.2015;22(2):94-7. In addition, the scope of this article is completely different.
“low 25(OH)D levels are associated with an increased risk of ischemic heart disease, myocardial infarction, …and premature death 4” (Discussion section, line 338; lines 341-343 of the manuscript)

In fact, in the article by Brøndum-Jacobsen, properly identified by reference 4, ischemic heart disease, myocardial infarction and early death were the end points. Therefore, it will not be possible to change the sentence without changing the end points defined by the authors of the article.

Comment #2

Please amend the Introduction heading to Background.

Response to comment #2

According to the Editor’s recommendations, the term “Introduction” was replaced by “Background”.

Comment #3

Please remove any supplementary files which you do not want published as they are no longer needed at this stage.

Response to comment #3

According to the Editor’s recommendations, supplementary files that are not intended to be published will be removed.

Comment #4

At this stage, please upload your manuscript as a single, final, clean version that does not contain any tracked changes, comments, highlights, strikethroughs or text in different colours. All relevant tables/figures/additional files should also be clean versions. Figures (and additional files) should remain uploaded as separate files.

Response to comment #4

According to the Editor’s recommendations, will be uploaded a single, final and clean version of the manuscript
Reviewer reports

Rachel Crowley (Reviewer 1)

Comment #1

The authors have considered the reviewers' comments in detailed and provided a measured response. The manuscript is suitable for publication - I would suggest a last proofread eg line 335 Lost rather than lot, and references to weight should be spelled out in full rather than using Wt in the Discussion (eg lines 324 and 356).

Response to comment #1

Thank you for the constructive comments on how to improve the readability of the manuscript. According to the reviewer's suggestions, the text was amended at the indicated locations.

Zaki Hassan-Smith (Reviewer 2)

The authors thank the reviewer for the contribution to the improvement of their manuscript.