

## PEER REVIEW HISTORY

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### ARTICLE DETAILS

<b>TITLE (PROVISIONAL)</b>	Methodological quality of public health guideline recommendations on vitamin D and calcium intakes – a systematic review protocol
<b>AUTHORS</b>	Dai, Zhaoli; Kroeger, Cynthia; McDonald, Sally; Page, Matthew; McKenzie, Joanne; Allman-Farinelli, Margaret; Raubenheimer, David; Bero, Lisa

### VERSION 1 – REVIEW

<b>REVIEWER</b>	Mark Bolland University of Auckland, New Zealand I have co-authored systematic reviews on calcium and vitamin D supplementation and repeatedly stated that these supplements are not generally necessary for older people. I have also co-authored papers on the differences between systematic reviews of vitamin D and falls and fractures.
<b>REVIEW RETURNED</b>	19-Jun-2019

<b>GENERAL COMMENTS</b>	<p>The authors propose to systematically review the methodologic quality of public health recommendations related to calcium and vitamin D intake.</p> <p>I have two general comments:</p> <ol style="list-style-type: none"><li>1. The implicit (and sometimes explicit) assumption that calcium and or vitamin D are required for optimum bone health is present throughout the Introduction and presumably underpins the entire protocol development. For example the first sentence states that “Low intakes of vitamin D and calcium are common in older populations.” No value is given for what a low intake of calcium is but intakes that are considered low in Western countries are often high in Asian and African countries where dairy products are not widely consumed. Likewise for most of the world’s population, vitamin D intake is a fairly negligible source of vitamin D compared with sunshine exposure.</li></ol> <p>The last part of the first paragraph then links calcium and vitamin D with osteoporosis. The evidence that dietary calcium intake or vitamin D status is associated with osteoporosis is weak and inconsistent. Most cohort studies do not report associations of calcium intake with fracture risk, and associations with vitamin D status are confounded by ill health but mendelian randomisation analyses do not support causal links. Likewise the evidence that calcium and or vitamin D supplementation prevents fractures is inconsistent, and any effects are, at best, only weak. However, there is clear evidence that prolonged very low vitamin D status causes osteomalacia in adults.</p>
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	<p>I would be interested to see how the protocol would change if the authors did not make any assumptions about the relationship between calcium and vitamin D and bone health.</p> <p>2. Somewhat related to this point, is that there have been numerous systematic reviews of vitamin D and fractures which sometimes come to almost diametrically opposite conclusions. Some reviews conclude that there is strong evidence that vitamin D supplementation prevents fractures in older people, whereas others conclude there is strong evidence that vitamin D supplementation does not prevent fractures. How will the authors deal with that? If the guideline includes or refers to a systematic review, will they assess the review(s) as well? If they don't, is it possible that the guideline could be of exemplary quality but based on an extremely flawed review making its recommendations problematic? In my experience, it often requires an in depth assessment of a systematic review and detailed knowledge of the literature to understand why the reviews on calcium and vitamin D get different results (usually related to choice of studies to include/exclude, ITT vs completers analyses, and/or different combinations of fracture data).</p>
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<b>REVIEWER</b>	Connie Weaver Weaver and Associates Consulting, LLC
<b>REVIEW RETURNED</b>	12-Aug-2019

<b>GENERAL COMMENTS</b>	<p>Abstract line 31 'food sources' rather than 'foods sources'</p> <p>Page 6 lines 36 and 40 How does adherence to guidelines ensure culturally appropriate?</p> <p>Page 6 line 62 WHO guidelines should refer to Table 1 or refer to methods section.</p>
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### VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Reviewer Name

Mark Bolland

Institution and Country : University of Auckland, New Zealand

Please state any competing interests or state 'None declared':

I have co-authored systematic reviews on calcium and vitamin D supplementation and repeatedly stated that these supplements are not generally necessary for older people. I have also co-authored papers on the differences between systematic reviews of vitamin D and falls and fractures. Please leave your comments for the authors below

The authors propose to systematically review the methodologic quality of public health recommendations related to calcium and vitamin D intake.

I have two general comments:

1. The implicit (and sometimes explicit) assumption that calcium and or vitamin D are required for optimum bone health is present throughout the Introduction and presumably underpins the entire protocol development. For example the first sentence states that “Low intakes of vitamin D and calcium are common in older populations.” No value is given for what a low intake of calcium is but intakes that are considered low in Western countries are often high in Asian and African countries where dairy products are not widely consumed. Likewise for most of the world’s population, vitamin D intake is a fairly negligible source of vitamin D compared with sunshine exposure.

The last part of the first paragraph then links calcium and vitamin D with osteoporosis. The evidence that dietary calcium intake or vitamin D status is associated with osteoporosis is weak and inconsistent. Most cohort studies do not report associations of calcium intake with fracture risk, and associations with vitamin D status are confounded by ill health but mendelian randomisation analyses do not support causal links. Likewise the evidence that calcium and or vitamin D supplementation prevents fractures is inconsistent, and any effects are, at best, only weak. However, there is clear evidence that prolonged very low vitamin D status causes osteomalacia in adults.

I would be interested to see how the protocol would change if the authors did not make any assumptions about the relationship between calcium and vitamin D and bone health.

Response: Thank you for the suggestions. We agree with the reviewer that the assumptions about the association of vitamin D and/or calcium with bone health in adults need to be further justified. In fact, it is our intention to conduct this study to evaluate guideline recommendations of these two nutrients and their sources among adults at risk of osteoporosis, precisely because of the inconsistency of the findings in primary studies and systematic reviews.

We have revised the Abstract on page 2 line 2-3, and Introduction to eliminate the assumptions about the benefits of vitamin D and emphasize that the rationale for our study is to investigate inconsistencies in guideline recommendations. Please see page 5-6 line 1-37.

2. Somewhat related to this point, is that there have been numerous systematic reviews of vitamin D and fractures which sometimes come to almost diametrically opposite conclusions. Some reviews conclude that there is strong evidence that vitamin D supplementation prevents fractures in older people, whereas others conclude there is strong evidence that vitamin D supplementation does not prevent fractures. How will the authors deal with that?

If the guideline includes or refers to a systematic review, will they assess the review(s) as well? If they don’t, is it possible that the guideline could be of exemplary quality but based on an extremely flawed review making its recommendations problematic?

In my experience, it often requires an in depth assessment of a systematic review and detailed knowledge of the literature to understand why the reviews on calcium and vitamin D get different results (usually related to choice of studies to include/exclude, ITT vs completers analyses, and/or different combinations of fracture data).

Response: Thanks for raising the important issues and, again, we agree with the reviewer’s concern. In the current protocol, we propose to extract information on the evidence cited to support each included recommendation. This will include categorizing the types of the evidence (e.g., primary study, systematic review, previous guideline report, summary of evidence). See Table 1, section IV. Transparency of Evidence Substantiation. As the focus of this protocol is to appraise the methods used to develop the public health guidelines, assessing the quality of the underlying evidence (i.e. risk of bias assessment) is out of scope. We plan to conduct a separate study (for which we are

developing a separate protocol) to examine the quality of the evidence underpinning the guideline recommendations. We have added this text in Discussion on page 15 line 236-241.

Reviewer: 2

Reviewer Name Connie Weaver

Institution and Country

Weaver and Associates Consulting, LLC

Please state any competing interests or state 'None declared':  
None

Please leave your comments for the authors below

Abstract line 31 'food sources' rather than 'foods sources'

Response: Thank you for pointing out this typographical error. We have removed the wording "food sources" in the Abstract, as there are other sources, including supplement and sunlight (latter for vitamin D) as potential recommendations for vitamin D and calcium.

Page 6 lines 36 and 40 How does adherence to guidelines ensure culturally appropriate?

Response: Thank you for the comment. This sentence has been rewritten and clarified on page 5 – 6, line 21-29. Hence, we hypothesized that adherence to the guideline methods would ensure culturally appropriate recommendations.

Page 6 line 52 WHO guidelines should refer to Table 1 or refer to methods section.

Response: Thank you for the suggestion. We have removed the sentence in Introduction about the WHO methods, and added this in the Methods session under Methodological processes on page 10 – 11, line 139-141.