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Methodological quality of public health guideline recommendations on vitamin D and calcium intakes – a systematic review protocol

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Abstract

Introduction Recommended intakes of vitamin D and calcium from food and supplements for bone health vary by public health guidelines among countries and professional organizations. It is unknown whether the methods used to develop these recommendations followed a rigorous process and how the differences in methods and processes used may affect the recommended intakes of vitamin D and calcium. The objectives of this study include 1) collate and compare recommendations for vitamin D and calcium across guidelines, 2) appraise methodological quality of the guideline recommendations, and 3) identify methodological factors that may affect the recommended intakes for vitamin D and calcium. This study will make a significant contribution to the knowledge base of methodological rigor in public health guidelines for vitamin D and calcium recommendation.

Methods and analysis We will conduct a systematic review to evaluate recommendations for vitamin D and calcium intakes and their foods sources for osteoporosis prevention in generally healthy middle-aged and older adults. Methodological assessment will be performed for each guideline against those outlined in the 2014 World Health Organization (WHO) Handbook for Guideline Development. Systematic search strategy will be applied to locate food-based dietary guidelines and bone health guidelines indexed in various electronic databases, guideline repositories and gray literature from 1 January 2009 to 28 February 2019. Descriptive statistics will be used to summarize the data on intake recommendation and on fraction of guidelines in compliance with the WHO criteria. Logistic regression, if feasible, will be used to assess the relationships between the methodological factors and the recommendation intakes.

Ethics and dissemination Ethics approval is not required as we will only extract published data or information from the published guidelines. Results of this review will be disseminated through conference presentations and peer-reviewed publications.

Protocol registration number PROSPERO, CRD42019126452.

Keywords: vitamin D, calcium, public health guideline, guideline development methods

Strengths and limitations of this study

- To the best of our knowledge, this will be the first study that critically appraises the methodological quality of guideline recommendations for dietary and supplemental vitamin D and calcium intakes.
- *A priori* systematic review methods will be used in the screening, data extraction, data synthesis and sub-group analysis.
- Eligible guidelines published in English only may potentially limit the sample size of and regional coverage of guideline recommendations included in our analysis.
- Information required to assess methodological quality of guidelines may be missing, particularly when other guideline development standards (e.g. the Institute of Medicine standards for trustworthy clinical guidelines) rather than the WHO handbook for guideline development were used to develop public health guidelines.

Introduction

Low intakes of vitamin D and calcium are common in older populations. Such insufficiency of vitamin D and calcium is partly due to ageing, which impairs food intake, mobility, efficiency of skin synthesis of vitamin D and biological absorption and retention of calcium.[1 2] Due to global ageing, incidence of osteoporosis and fractures are rising rapidly worldwide.[3] The burdens associated with osteoporosis in disability, premature mortality, and economics are substantial, particularly fractures at the hip. For example, global deaths and disability-adjusted life years (DALYs) attributable to low bone mineral density had risen from 103,000 and 3,125,000 in 1990 to 188,000 and 5, 216,000 in 2010, respectively with one third of falls-related deaths were attributable to low bone mineral density.[4] Because vitamin D and calcium play a significant role in bone health maintenance,[2] it is important to study factors in guideline recommendation development that may contribute to the appropriate recommended intakes for vitamin D, calcium, their food sources and beneficial diet for adults at risk of osteoporosis.

Public health guidelines provide guidance in maintaining well-being and disease prevention. However, current recommendations for vitamin D and calcium in the dietary guidelines and bone health guidelines vary significantly among countries and even among professional organizations.[5 6 7 8] Several factors may have contributed to such variation: limited rich food sources of vitamin D and calcium; recommended reference intakes focused at the nutrient level with little consideration at the food level; and minimal or no recommendation for sun UVB exposure for vitamin D synthesis because of various concerns such as geographic location, seasons, health risk, etc. As a result, people may seek to take dietary supplements to increase their vitamin D and calcium intake levels. Further, conflicting results of the efficacy of

vitamin D and/or calcium supplementation[7 9-16] in the prevention of osteoporosis and their adverse effects in cardiac risks[17 18] and compromised renal function[14 16] can further complicate the appropriate amount recommended in the public health guidelines. This may lead to uncertainty in the health benefits of adequate intakes of vitamin D and / or calcium supplementation in falls and osteoporosis prevention.

Findings from the previous review of food-based dietary guidelines have suggested that inconsistencies exist in the methodological processes used to retrieve, appraise and synthesize relevant evidence in national dietary guidelines.[19] However, it remains unclear whether the discordance in the recommended intakes of vitamin D and calcium may be related to the methods and processes used to develop these recommendations in public health guidelines. For example, findings from a global review of food-based dietary guidelines suggest that social-economic equity and cultural factors are still issues that need to be incorporated in guideline development for the appropriate food intakes among populations with different backgrounds and that there are significant regional differences in dairy representation and recommendations.[20]. In this study, we hypothesize that high adherence to guideline development criteria which span from representation of guideline development group to external review process would be more likely to formulate higher scientific rigour and culturally/ethnically appropriateness of public health guideline recommendations.

The objective of this study is to compare the methods and processes used in formulating public health guideline recommendations for vitamin D and calcium among middle-aged and older adults for the prevention of osteoporosis, and to assess whether they comply with the criteria outlined in the 2014 World Health Organization Handbook for Guideline Development.[21] We will further assess whether the similarity or differences in the vitamin D and calcium intake

recommendations can be explained by the methodological quality of the guidelines in the following domains, including characteristics of the guideline development group, conflicts of interest disclosure and management, whether systemic review methods are used to synthesize the evidence, types and quality of the evidence substantiating the recommendations, methods used to determine the direction and strength of the recommendations, and external peer review process. Findings from this study will illustrate methodological rigor and potential limitations in current public health guidelines for vitamin D and calcium intakes.

Methods

Overview

We will include public health guidelines or policy statements related to vitamin D/ calcium intake and bone health for generally healthy adults aged 40 years and above. Because middle-aged and older adults are individuals at risk to develop osteoporosis, we intend to include those who may experience menopause as young as 40 years to ensure the coverage of all age groups at risk across guidelines. We will include both food-based dietary guidelines and health guidelines for osteoporosis (including fracture) prevention. We will use the definition described in the 2014 WHO handbook for guideline development to define guidelines and recommendations, i.e. "any document containing recommendations for clinical practice or public health policy. A recommendation tells the intended end-user of the guideline what he or she can or should do in specific situations to achieve the best health outcomes possible, individually or collectively."[21]

Inclusion criteria

- Most recent version of national food-based dietary guidelines

- Most recent version of national guidelines, policy statements or standards for osteoporosis prevention

We will only include national guidelines that have been developed by a nationally or internationally recognised government authority or by a medical/academic society or organization. This is to ensure consistency between the food-based dietary guidelines and the bone health guidelines at country (state) level, as food-based dietary guidelines are typically a state government document. In addition to the guideline documents, we will include supporting documents such as those provide details for the methodology used and evidence underpinning the recommendations. For instance, guideline committee's reports, in which we can locate methodology and supporting evidence will be included. An example is the "Scientific Report of the 2015 Dietary Guidelines Advisory Committee," which describes the development of the dietary guideline and supporting evidence for the "Dietary Guidelines for Americans 2015-2020." Similarly, "A review of the evidence to address targeted questions to inform the revision of the Australian Dietary Guidelines" [22] as well as the Nutrient Reference Values (NRV) document for Australia and New Zealand are companion documents with evidence substantiating the recommendations for the "Australian Dietary Guidelines 2013."[23] If there are multiple versions of a national guideline from the same country or authority, only the most recent version will be included. Similarly, if an updated bone health guideline is based on the previous documents that describe the processes of the recommendation development, these documents will be included to locate the information on methods and evidence used to support the recommendations.

Exclusion criteria

- Food guides such as food pyramids, food plates, or simple designed pictorial or graphic representation
- Bone health guidelines regarding vitamin D and calcium recommendations in the management of osteoporosis, secondary osteoporosis (e.g. osteoporosis due to rheumatoid arthritis) or for a particular group of population (e.g. pregnant women) or those with health condition (e.g. patients with cancer, cirrhosis, etc.)

We will not include food guides, because they lack substantial materials to document the guideline development process. Guideline recommendations on clinical treatment of any bone disorders, or guidelines targeted to a particular group of populations such as those with HIV or cancer patients or pregnant or lactating women or a particular type of osteoporosis (e.g. glucocorticoid-induced osteoporosis) will be excluded. This is because the focus of this study is to review recommended vitamin D and calcium intakes for generally healthy populations to maintain bone health or to prevent osteoporosis.

Search strategy

We will search guidelines or policy statements that are published from 1 January 2009 until 28 February 2019 in the following electronic databases: MEDLINE (via OVID), EMBASE (via OVID), CINAHL (via EBSCO), and Practice Based Evidence in Nutrition. Additionally, the following sources which include guidelines specifically will be searched: National Guideline Clearinghouse, National Institute for Health and Care Excellence, and Guidelines International Network. We will only include documents published in English but no geographic regions are restricted. We will use a combination of controlled vocabulary and free-text terms for vitamin D, sunlight, calcium, dairy, vegetable, seafood, fortified food (as these are the good dietary sources for vitamin D and / or calcium), dietary patterns, osteoporosis/fracture and guideline. The search

strategy for Medline via Ovid is described in **Appendix A**. Similar search strategies with appropriate syntax will be applied to EMBASE and CINAHL. We will also search the gray literature via the Food and Agricultural Organization (FAO) website for relevant food-based dietary guidelines[24] and the International Osteoporosis Foundation[25] for bone health guidelines from national government agencies or organizations. Additionally, we will consult leading experts in the field of bone health to avoid any oversights.

Data extraction process

Recommendations for vitamin D and calcium

Verbatim text of qualitative and quantitative recommendations on dietary intake of vitamin D/calcium, vitamin D/calcium containing foods, a healthy dietary pattern beneficial to bone health, supplementation dosage for vitamin D/calcium, nutrient reference intakes for vitamin D and calcium, and timing and length of sun exposure for vitamin D synthesis will be extracted from each included guideline. Because there is no standard for wording of recommendation across and within guidelines,[26 27] we will adopt the criteria described in the report by Woolf and colleagues for the presentation and formulation of recommendations.[28] These criteria include "consistent semantic and formatting indicators," "a summary section to facilitate identification of recommendations," "decidable and executable wording" and "avoiding embedding recommendation text within long paragraphs." We will not adopt "evidence quality and recommendation strength in proximity to each recommendation," as an objective in this review is to assess the quality of evidence underpinning the recommendations. For example, in bone health public guidelines, the following would be considered as eligible recommendations: "General practitioners should recommend that postmenopausal women and older men maintain a diet high in calcium to meet the Australian recommended dietary intake," or "General practitioners should recommend the following important lifestyle choices for all postmenopausal

women and older men: adequate but safe exposure to sunlight as a source of vitamin D."[29] Statements or text mentioning vitamin D or calcium as knowledge-based information or as a rationale to support an argument will be excluded as a recommendation. For example, "Soy beverages fortified with calcium, vitamin A, and vitamin D, are included as part of the dairy group, because they are similar to milk based on nutrient composition and in their use in meals."[30]

We will use a pilot-tested data extraction form to capture vitamin D and calcium recommendation intakes and categorize as "Yes" or "No" according to criteria described above.[28] Verbatim text will be extracted, if rated as "Yes," including numerical values and/or recommendations without numerical values. Data extraction will be conducted by ZD, CMK/SM independently via REDCap (Research Electronic Data Capture), an electronic data capture tools hosted at the University of Sydney.[31] Any discrepancies in the data extracted will be resolved through discussion with the other reviewer (CMK/SM); otherwise, further discussion with the senior author (LB) will be carried out to resolve the disagreement through consensus. Additionally, we will contact the guideline authors to obtain all relevant materials during the data extraction to avoid missing documents.

Methodological processes

We will appraise guideline recommendation development processes against the criteria outlined in the 2nd edition of the 2014 WHO Handbook for Guideline Development,[21] a "gold standard" for public health guideline development. The reasons we have chosen the 2014 WHO handbook for guideline development include: it was developed by the primary international public health agency; it is more recent compared with other standards; and it incorporates the most comprehensive domains and elements for a rigorous guideline development.[32 33] Compared

with the Appraisal of Guidelines for Research and Evaluation II (AGREE II),[34] the WHO handbook criteria cover the same domains with more extensive details regarding the guideline development processes. For example, for conflicts of interest, the 2014 WHO guideline handbook includes both disclosure and management of conflicts of interest among the guideline development group members and funders,[21] while the AGREE II instrument addresses conflicts of interest among the guideline development group members only.[34]

The items outline in the WHO handbook with description of the criteria are described in **Table 1**, which includes the following domains: Guideline development group, Conflicts of interest, Review methods, Transparency of evidence substantiation, Recommendation development, and Peer review process. We will record whether each included guideline recommendation is compliant with each of the WHO criteria and classify as Yes, No, or Unclear. If "Yes" is rated, verbatim text will be extracted from the guideline to substantiate per the recommended item. "No" is referred to those which explicitly state none for the items to be appraised. "Unclear" is referred to those that neither explicitly state none nor those with relevant statements supporting the criterion. Three reviewers (ZD, CMK/SM) will perform the critical appraisal and data extraction independently. Discrepancies will be first discussed and resolved through consensus among the reviewers, and with the senior author (LB) if it remains unresolved after the first attempt.

Other information to be extracted

Guideline title, country of origin, guideline developing authority or organization, publication year, age group of the population, gender of the population (men, women, or both), and funding body will be extracted. Further, we will extract the information of the evidence underpinning the recommendations including the types of evidence (primary research, systematic

review, or summary of evidence table: see details in "Transparency of evidence substantiation" in Table 1) and their citation information.

Main outcomes

As mentioned earlier, a binary outcome will be created based on whether a recommendation exists in a public health guideline for the following: vitamin D intakes, vitamin D containing food consumption (such as fortified dairy or other fortified beverage and seafood), a healthy diet for bone health, sun exposure for vitamin D synthesis, supplement use of vitamin D, calcium reference intakes, calcium containing food consumption (such as dairy and dark-green leafy vegetables,), and supplement use of calcium. If quantitative recommendations (those with amount per day) are available, we will categorize the numerical values into different groups and present the distribution of the recommended intake values.

Analysis

We will use descriptive statistics (e.g. frequency and proportion for categorical variables) to summarize the characteristics of each included guideline. This will include age group of the population, gender of the population, conflict of interest disclosed and managed, and cultural/ethnic consideration. Across the included guidelines, we will summarize the recommendation (those with values or recommendation text) for vitamin D and calcium, their food sources, dietary patterns and sun exposure for vitamin D by types of guidelines (food-based dietary guidelines versus bone health guidelines), by continent (Asia, Australia, Europe, North America, South America, and Africa), by gross national income per capita (low, middle and high), and by disclosure of conflict of interest (yes, no). Also, we will present the fractions of the guidelines that are compliant with each of the criteria outlined in the WHO handbook for all

guidelines, food-based dietary guidelines and bone health guidelines. Finally, if feasible, we will perform logistic regression analysis to examine the associations between each methodological factor [Yes versus None (combining No and Unclear)] in the six domains of guideline development methods (see Table 1) and a positive recommendation (defined as "yes" for the recommendation) for dietary vitamin D/calcium, supplemental vitamin D/calcium, a healthy diet for bone health, and sun exposure (for vitamin D synthesis), where each of the recommendations will be considered as a binary outcome. Also, we may perform a multinomial logistic regression analysis for the association between each of the methodological factors (those in Table 1) and categories of the recommended values for vitamin D / calcium (i.e. dietary intake values/supplemental intake values on an ordinal scale), after adjustment for guideline characteristics. The reason that a multinomial logistic regression is proposed is because that recommended intakes for vitamin D/ calcium in public health guidelines are often clustered or provided as a range. For example, vitamin D recommendation in a guideline could be 400-800 IU/d, 600-800 IU/d, 800-1000 IU/d, 1500-2000 IU/D; and calcium recommendation could be 600 mg/d, 700-800 mg/d, 1000 mg/d, 1000-1200 mg/d, >=1000mg/d, etc. Therefore, a logistic regression analysis is likely more suitable in these analyses.

Analysis of subgroups or subsets

We will further perform subgroup analyses by continent (North America, South/Central America, Africa, Australia, Asia, Europe), by gross national income per capita regarding country's development levels (low, middle and high), by guideline types (food-based dietary guidelines versus osteoporosis prevention guidelines), by conflicts of interest (disclosed versus non-disclosed; and funded by not-for-profit organization versus for-profit organization if feasible) to summarize the proportion of compliance with the WHO criteria.

Discussion and dissemination

To the best of our knowledge, this will be the first study to critically appraise methodological quality regarding guideline recommendations for dietary and supplemental vitamin D and calcium intakes, their food sources, a healthy diet pattern and sun exposure for vitamin D synthesis. This review will advance our knowledge on how guideline development methodology and processes may affect the similarity or differences of the intake recommendations. These findings will further address potential limitations in public health guidelines for the recommended intakes of vitamin D, calcium, and the relevant food sources (sun exposure) for bone health.

As we will only include guidelines or statements published in English, this may reduce sample size and limit the coverage of non-English speaking countries if their guidelines/statement reports are not published in English. Although we believe that the criteria outlined in the 2014 WHO handbook for guideline development cover the most comprehensive processes for guideline recommendation development, we understand that some guideline authorities may adopt other standards. For example, the Institute of Medicine standards are commonly used to develop trustworthy clinical guidelines.[32] Therefore, we might experience guidelines with missing data regarding our stringent and comprehensive methodological criteria according to the WHO handbook for guideline development. Further, recent concerns have been raised about possible over consumption of phosphorous from meat and dairy sources and highly processed foods. Because the amount of phosphorus additives in processed food products are generally not accounted for, current nutrition databases assume that phosphorous level remains similar for the same types of foods (e.g. natural beef and processed beef products), this would potentially underestimate the actual intake of phosphorous in the populations[35 36] and result in a

lower recommended intake of calcium in the guidelines.[37] Due to the scope and feasibility of this study, we will not further account for such underestimation of phosphorous intake at the population level, which could be a potential limitation of this review to address the appropriate recommendations for calcium intake in the included guidelines.

We will seek to present our findings at international academic conferences and report our findings in a peer-reviewed medical journal article. We also plan to present our findings to key stakeholders in public health authorities and with public health advocates for bone health and osteoporosis prevention.

Conclusions

Currently, there are no studies that have comprehensively appraised methodological rigor in guideline development methods and processes used to develop vitamin D and calcium recommendations. Due to global ageing and a rapid rise of osteoporosis, this review will be timely to assess guideline recommendations for vitamin D and calcium and help to address potential limitations and identify areas for improvement in developing future guideline recommendations for vitamin D and calcium to maintain bone health.

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Authors' contributions

Study Design: ZD, LB, CMK;
Data Collection: ZD, CMK, SM;
Coding: ZD, CMK, SM;
Methods and Stats: ZD, MP, JM;
Analysis: ZD, MP, JM;
Writing: ZD (first draft);
Revising and editing: all authors;
Guarantor: ZD, LB

Competing interests statement: None disclosed.

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Table 1. Appraisal of the processes and methods used in the recommendations for vitamin D and calcium in public health guidelines

Process and Method domains	Process and Method criteria	Description	Examples where to look
I. Guideline development group (GDG, including members of steering group, research team and individuals involved formulating the final recommendations)			
Were each of the following considered in the formation of the guideline development group?	1. Discipline representation	Information about the composition, discipline, and relevant expertise of the guideline development group should be provided.	Information can be located in methods, guideline panel member list, acknowledgements, and appendices.
	2. Diversity representation	Information about gender, diversity, across the life-course, subject to different gender norms, and belonging to different income and education groups of the guideline development group.	
	3. Stakeholder input	Stakeholders such as nongovernmental organizations, advocacy groups, funders, target audiences, and service-users may be invited to ensure transparency of the processes and facilitate implementation.	
II. Conflicts of interest			
Were each of the following steps addressed regarding conflicts of interest?	4. Disclosure of conflicts of interest obtained (extract verbatim text of COI for each member)	Is there an explicit statement that all group members have declared whether they have any competing interests?	Paragraphs/chapters describing the guideline development group or
	5. Conflicts of interest managed	Members declaration of interests must be reported to the steering group. Potential candidates for membership who have major conflicts of interest, be they financial or nonfinancial, cannot be appointed to the GDG. Minor conflicts of interest can be managed at the individual	

		level (e.g. by restricting participation in parts of the GDG meeting) or at the group level.	acknowledgements section in methods, conflicts of interest, guideline panel, and appendix
	6. Disclosure of funders of the guideline obtained and disclose funder's role in influencing the guideline development process and recommendations	Is there an explicit statement of funder of the guideline and the role of funders in the final guideline recommendations?	
III. Systematic review methods			
Were methods for each of the following addressed in the guideline?	7. Formulation of key questions for the evidence review in PICO, PICOT, or PEO format (also extract the key questions in such format)	Key questions are framed in a way that enables a systematic search of the literature and delineates inclusion and exclusion criteria for the body of evidence to formulate the research questions for the recommendations in such format.	Examine the paragraphs/chapters describing the guideline development process in methods, literature search strategy and appendices.
	8. Choosing (finalizing) priority outcomes for systematic review	List high-priority key questions and the outcomes to formulate recommendations.	
	9. Systematic methods to search for evidence	Details of the strategy used to search for evidence should be provided including search terms used, sources consulted, and dates of the literature covered. Sources may include electronic databases, hand searching journals, reviewing conference proceedings, and other guidelines.	
	10. Evidence retrieval (screening and selection of eligible studies)	Process of data from eligible studies are extracted and search strategy and results should be carefully documented.	
	11. Evidence quality assessment	Each study included in a systematic review should be assessed for risk of bias (e.g. use the Cochrane risk of bias tool, Quality assessment tolls project report, etc.)	

	12. Evidence synthesis	The findings of the systematic review may be synthesized in a narrative manner or quantitatively in a meta-analysis. The review should describe how data were handled and why a given approach to synthesis was taken for each outcome.	
IV. Transparency of evidence substantiation			
If evidence was explicitly linked to recommendation, what type of evidence was reported?	13. Are recommendations explicitly linked to substantiating evidence?	An explicit link between the recommendations and the evidence on which they are based should be included in the guideline. The guideline user should be able to identify the components of the body of evidence relevant to each recommendation.	Define and examine the recommendations in the guideline and the text describing the body of evidence that underpins them. Examples of commonly labeled sections or chapters in a guideline where this information can be found include: recommendations and key evidence.
	a. Primary research	Primary individual studies	
	b. Systematic reviews	Systematic reviews of clinical trials / observational studies	
	c. Summary table of the evidence	Summary of evidence table	
	d. GRADE evidence profiles	GRADE summary of evidence table	
	e. Evidence to decision table		
	f. If evidence is explicitly linked to recommendation, what is the citation information, if applicable?	List the citations of the studies underlying the recommendations	
V. Recommendation development: Factors that determine the direction and strength of a recommendation			
Was each of the following items considered when developing the recommendation? (also communicate	14. Was a consensus process clearly described for developing recommendations	A description of the methods used to formulate the recommendations and how final decisions were arrived at should be provided. For example, methods may include a voting system, informal consensus, and formal consensus	

authority whether other documentation may provide such information if they cannot be located in the main guideline reports)		techniques. Areas of disagreement and methods of resolving them should be specified.	Examples of commonly labeled sections or chapters in a guideline where this information can be found include methods and guideline development process or in appendices.
	15. Was a method employed to determine strength and/or certainty of the recommendation?	Is there a method provided to influence the direction and strength of a recommendation (e.g. use GRADE framework and others)	
	16. Priority of the problem: Is the problem a burden of disease?	The problem's priority is determined by its importance and frequency (i.e. burden of disease, disease prevalence or baseline risk). The greater the importance of the problem, the greater the likelihood of a strong recommendation.	
	17. Quality of the evidence: Is higher quality of the body of evidence included to support the recommendation?	Is there a method provided to grade the quality of body of evidence to assess the strength of the recommendation (e.g. GRADE and others)	
	18. Certainty of evidence: Does the recommendation include consistent body of evidence (e.g. confidence in effect estimates)?	The quality of the evidence – the degree of confidence in the estimates of effect. This is a key factor in determining the strength of a recommendation.	
	19. Benefits and harms: Are evaluations performed on the net benefit or net harm associate with an intervention or exposure?	The balance between an intervention's or exposure's benefits and harms. Did the guideline development group consider the magnitude of the effects and the relative importance of the outcomes, including any disadvantages or inconveniences associated with the intervention.	
	20. Balance: Does the balance between desirable and undesirable effects support the recommendation?	Does the balance between desirable and undesirable effects favour the intervention or the comparison?	

	21. Outcome importance: Is there important uncertainty about or variability in how much people value the main outcome?	Is there important uncertainty about or variability in how much people value the main outcomes, including adverse effects and burden of the test and downstream outcomes of clinical management that is guided by the test results?	
	22. Equity: Does the evidence used reduce inequalities, improve equity or contribute to the realization of one of several human rights defined under the international legal framework?	What would be the impact on health equity?	
	23. Acceptability: Is the option acceptable to key stakeholders?	A strategy to address concerns about acceptability during implementation will be included in the guideline with the recommendations. Acceptability is affected by several factors, such as who benefits from an intervention and who is harmed by it; who pays for it or saves money on account of it; and when the benefits, harms and costs occur.	
	24. Feasibility: Is the option feasible to implement?	Feasibility is influenced by the resources available, programmatic considerations, the existing and the necessary infrastructure and training, etc.	
VI. Peer review process			
	25. Was the guideline/recommendation reviewed by an external review group?	Is there an explicit statement about the peer review of the draft final guideline? The external review group is composed of persons interested in the subject of the guideline as well as individuals who will be affected by the recommendations.	Information can be located in methods, guideline panel member list, acknowledgements, and appendices.

Appendix A. Medline search strategy via Ovid

1. Vitamin D/
2. Cholecalciferol/
3. Ergocalciferols/
4. Vitamin D Deficiency/
5. Sunlight/
6. Ultraviolet Rays/
7. Vit* D.tw.
8. Ergocalciferol.tw.
9. Calciferol.tw.
10. Cholecalciferol.tw.
11. Sunlight.tw.
12. (Light adj3 expos*).tw.
13. UV.tw.
14. Ultraviolet.tw.
15. or/1-14
16. exp Calcium/
17. Calcium, Dietary/
18. calcium.mp.
19. or/16-18
20. 15 or 19
21. Diet/
22. "Diet, Food, and Nutrition"/
23. Diet, Vegetarian/
24. Diet, Vegan/
25. Diet, Western/
26. Diet Therapy/
27. Healthy Diet/

28. Food, Fortified/
29. Dietary supplements/
30. exp Dairy Products/
31. Shellfish/
32. Fishes/
33. exp Seafood/
34. Vegetables/
35. exp Vegetable Products/
36. Agaricales/
37. Diet*.tw.
38. (Diet* adj3 supplement*).tw.
39. (Fortified adj3 food*).tw.
40. Vegetable*.tw.
41. Mushroom*.tw.
42. Dairy.tw.
43. Milk.tw.
44. Cheese.tw.
45. Yog?urt.tw.
46. Seafood.tw.
47. Fish.tw.
48. Shellfish.tw.
49. or/21-48
50. 20 or 49
51. 20 and 49
52. exp clinical pathway/
53. exp clinical protocol/
54. exp consensus/
55. exp consensus development conference/

56. exp consensus development conferences as topic/

57. critical pathways/

58. exp guideline/

59. guidelines as topic/

60. exp practice guideline/

61. practice guidelines as topic/

62. health planning guidelines/

63. (guideline or practice guideline or consensus development conference or consensus development conference, NIH).pt.

64. (position statement* or policy statement* or practice parameter* or best practice*).ti,ab,kf,kw.

65. (standards or guideline or guidelines).ti,kf,kw.

66. ((practice or treatment* or clinical) adj guideline*).ab.

67. (CPG or CPGs).ti.

68. consensus*.ti,kf,kw.

69. consensus*.ab. /freq=2

70. ((critical or clinical or practice) adj2 (path or paths or pathway or pathways or protocol*)).ti,ab,kf,kw.

71. recommendat*.ti,kf,kw.

72. (care adj2 (standard or path or paths or pathway or pathways or map or maps or plan or plans)).ti,ab,kf,kw.

73. (algorithm* adj2 (screening or examination or test or tested or testing or assessment* or diagnosis or diagnoses or diagnosed or diagnosing)).ti,ab,kf,kw.

74. or/52-73

75. Osteoporosis/

76. Fractures, Bone/

77. Bone Density/

78. osteoporosis.tw.

79. fracture*,bone.tw.

80. bone density.tw.

81. bone health.mp.

82. 75 or 76 or 77 or 78 or 79 or 80 or 81

83. Adult/

84. Aged/

85. Middle Aged/

86. adult*.tw.

87. aged.tw.

88. middle aged.tw.

89. 83 or 84 or 85 or 86 or 87 or 88

90. 74 and 82 and 89

91. 50 and 90

PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol*

Section and topic	Item No	Checklist item	(Page No.#)
ADMINISTRATIVE INFORMATION			
Title:			
Identification	1a	Identify the report as a protocol of a systematic review	1
Update	1b	If the protocol is for an update of a previous systematic review, identify as such	
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number	3
Authors:			
Contact	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author	1
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	16
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	n/a
Support:			
Sources	5a	Indicate sources of financial or other support for the review	15
Sponsor	5b	Provide name for the review funder and/or sponsor	15
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	16
INTRODUCTION			
Rationale	6	Describe the rationale for the review in the context of what is already known	4-5
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	5
METHODS			
Eligibility criteria	8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review	6-7
Information sources	9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage	8
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	26-29
Study records:			

Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	9-10
Selection process	11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)	10
Data collection process	11c	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	10 and 11
Data items	12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications	9-11
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	12
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	10-11
Data synthesis	15a	Describe criteria under which study data will be quantitatively synthesised	12
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as I^2, Kendall's τ)	12-13
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)	13
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	12
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)	n/a
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)	n/a

*** It is strongly recommended that this checklist be read in conjunction with the PRISMA-P Explanation and Elaboration (cite when available) for important clarification on the items. Amendments to a review protocol should be tracked and dated. The copyright for PRISMA-P (including checklist) is held by the PRISMA-P Group and is distributed under a Creative Commons Attribution Licence 4.0.**

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Methodological quality of public health guideline recommendations on vitamin D and calcium intakes – a systematic review protocol

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Abstract

Introduction Current recommendations for vitamin D and calcium in dietary guidelines and bone health guidelines vary significantly among countries and professional organizations. It is unknown whether the methods used to develop these recommendations followed a rigourous process and how the differences in methods used may affect the recommended intakes of vitamin D and calcium. The objectives of this study are 1) collate and compare recommendations for vitamin D and calcium across guidelines, 2) appraise methodological quality of the guideline recommendations, and 3) identify methodological factors that may affect the recommended intakes for vitamin D and calcium. This study will make a significant contribution to enhancing the methodological rigour in public health guidelines for vitamin D and calcium recommendations.

Methods and analyses We will conduct a systematic review to evaluate vitamin D and calcium recommendations for osteoporosis prevention in generally healthy middle-aged and older adults. Methodological assessment will be performed for each guideline against those outlined in the 2014 World Health Organization (WHO) Handbook for Guideline Development. A systematic search strategy will be applied to locate food-based dietary guidelines and bone health guidelines indexed in various electronic databases, guideline repositories and gray literature from 1 January 2009 to 28 February 2019. Descriptive statistics will be used to summarize the data on intake recommendation and on proportion of guidelines consistent with the WHO criteria. Logistic regression, if feasible, will be used to assess the relationships between the methodological factors and the recommendation intakes.

Ethics and dissemination Ethics approval is not required as we will only extract published data or information from the published guidelines. Results of this review will be disseminated through conference presentations and peer-reviewed publications.

Protocol registration number PROSPERO, CRD42019126452.

Keywords: vitamin D, calcium, public health guidelines, guideline development methods

Strengths and limitations of this study

- To the best of our knowledge, this will be the first study that critically appraises the methodological quality of guideline recommendations for vitamin D and calcium intakes.
- This study will provide insights to address potential limitations in guideline development and identify areas for improvement in developing vitamin D and calcium recommendations.
- Eligible guidelines published in English only may potentially limit the sample size of and regional coverage of the guideline recommendations included in our analysis.
- Information required to assess methodological quality of guidelines may be missing, particularly when other guideline development standards (e.g. the Institute of Medicine standards for trustworthy clinical guidelines) rather than the WHO Handbook for Guideline Development were used to develop public health guidelines.

Introduction

Current recommendations for vitamin D and calcium in dietary guidelines and bone health guidelines vary significantly among countries and professional organizations.[1 2 3 4] Several factors may have contributed to such variation: dietary sources of vitamin D and calcium are different among countries and regions, with some but not all fortifying the nutrients in the food products as an example; some guidelines may consider supplement use as part of the recommendations, while others recommend sunlight exposure as a source of vitamin D. For the latter, race and skin tone also contribute to the appropriate length of time of sun exposure to achieve certain vitamin D levels. Another possible reason for these varied recommendations is that evidence on the efficacy of vitamin D and/or calcium supplementation[3 5-14] in the prevention of osteoporosis, particularly in fracture prevention, is conflicting; and their adverse effects in cardiac risks[15 16] and compromised renal function[10 12] must also be taken into account. Further, what defines vitamin D deficiency measured by serum 25(OH)D is debatable and varies among the general populations.[14 17-19] This variation of optimal vitamin D level further contributes to the inconsistent findings in randomized control trials testing the effects of different dosages of vitamin D and/or calcium supplementation in fracture prevention.[13 14]

Additionally, inconsistencies exist in the guideline development processes used to retrieve, appraise and synthesize relevant evidence, as well as in reporting conflicts of interest and funding sources in national dietary guidelines.[20] This can potentially further affect the discordance in the recommended intakes of vitamin D and calcium in guideline recommendations. For example, findings from a global review of food-based dietary guidelines suggest that social and economic equity and cultural factors need to be incorporated in guideline development in order to recommend appropriate food intakes among populations with different

backgrounds. Further, there are significant regional differences in dairy intake recommendations across different dietary guidelines.[21] As dairy is the main source of dietary calcium and vitamin D in some but not all populations,[22 23] recommendations about dietary sources need to consider the ethnic and cultural contexts. Taken together, guideline development methods should include, but be not limited to, evidence identification, evaluation, and synthesis; as well as incorporating stakeholders' positions, feasibility and acceptability of the recommendations.

The objective of this study is to compare recommendations for vitamin D and calcium intakes and their associated parameters [e.g. sun exposure for vitamin D synthesis and serum 25(OH)D level to define vitamin D status], and the methods used in formulating these recommendations for middle-aged and older adults in public health guidelines. We will further assess whether the similarity or differences in the vitamin D and calcium intake recommendations can be explained by the guidelines' methodological quality. Findings from this study will illustrate methodological rigour and potential limitations in current public health guidelines for vitamin D and calcium recommended intakes.

Methods

Overview

We will include public health guidelines or policy statements related to vitamin D/ calcium intake and bone health for generally healthy adults aged 40 years and above. Because middle-aged and older adults are individuals at risk to develop osteoporosis, we intend to include those who may experience menopause as young as 40 years to ensure the coverage of all age groups at risk in the included guidelines. We will include both food-based dietary guidelines and health guidelines for osteoporosis (including fracture) prevention. We will use the definition described in the 2014 World Health Organization (WHO) Handbook for Guideline Development to define guidelines and recommendations, i.e. "any document containing recommendations for

clinical practice or public health policy. A recommendation tells the intended end-user of the guideline what he or she can or should do in specific situations to achieve the best health outcomes possible, individually or collectively."[24]

Inclusion criteria

- Most recent version of national food-based dietary guidelines
- Most recent version of national guidelines, policy statements or standards for osteoporosis prevention

We will only include national guidelines that have been developed by a nationally or internationally recognised government authority or by a medical/academic society or organization. This is to ensure consistency between the food-based dietary guidelines and the bone health guidelines at country (state) level, as food-based dietary guidelines are typically a state government document. In addition to the guideline documents, we will include supporting documents such as those provide details for the methodology used and evidence underpinning the recommendations. For instance, guideline committee's reports, in which we can locate methodology and supporting evidence will be included. An example is the "Scientific Report of the 2015 Dietary Guidelines Advisory Committee," which describes the development of the dietary guideline and supporting evidence for the "Dietary Guidelines for Americans 2015-2020." Similarly, "A review of the evidence to address targeted questions to inform the revision of the Australian Dietary Guidelines" [25] as well as the Nutrient Reference Values (NRV) document for Australia and New Zealand are companion documents with evidence substantiating the recommendations for the "Australian Dietary Guidelines 2013."[26] If there are multiple versions of a national guideline from the same country or authority, only the most recent version will be included. Similarly, if an updated bone health guideline is based on the previous

documents that describe the processes of the recommendation development, these documents will be included to locate the information on methods and evidence used to support the recommendations.

Exclusion criteria

- Food guides such as food pyramids, food plates, or simple designed pictorial or graphic representation
- Bone health guidelines regarding vitamin D and calcium recommendations in the management of osteoporosis, secondary osteoporosis (e.g. osteoporosis due to rheumatoid arthritis) or for a particular group of population (e.g. pregnant women) or those with health condition (e.g. patients with cancer, cirrhosis, etc.)

We will not include food guides, because they lack substantial materials to document the guideline development process. Guideline recommendations on clinical treatment of any bone disorders, or guidelines targeted to a particular group of populations such as those with HIV or cancer patients or pregnant or lactating women or a particular type of osteoporosis (e.g. glucocorticoid-induced osteoporosis) will be excluded. This is because the focus of this study is to review recommended vitamin D and calcium intakes for generally healthy populations to maintain bone health or to prevent osteoporosis.

Search strategy

We will search guidelines or policy statements that are published from 1 January 2009 until 28 February 2019 in the following electronic databases: MEDLINE (via OVID), EMBASE (via OVID), CINAHL (via EBSCO), and Practice Based Evidence in Nutrition. Additionally, the following sources which include guidelines specifically will be searched: National Guideline Clearinghouse, National Institute for Health and Care Excellence, and Guidelines International

Network. We will only include documents published in English but no geographic regions are restricted. We will use a combination of controlled vocabulary and free-text terms for vitamin D, sunlight, calcium, dairy, vegetable, seafood, fortified food (as these are the good dietary sources for vitamin D and / or calcium), dietary patterns, osteoporosis/fracture and guideline. The search strategy for Medline via Ovid is described in **Supplemental material.** Similar search strategies with appropriate syntax will be applied to EMBASE and CINAHL. We will also search the gray literature via the Food and Agricultural Organization (FAO) website for relevant food-based dietary guidelines[27] and the International Osteoporosis Foundation[28] for bone health guidelines from national government agencies or organizations. Additionally, we will consult leading experts in the field of bone health to avoid any oversights.

Data extraction process

Recommendations for vitamin D and calcium

Verbatim text of qualitative and quantitative recommendations on dietary intake of vitamin D/calcium, vitamin D/calcium containing foods, a healthy dietary pattern beneficial to bone health, supplementation dosage for vitamin D/calcium, nutrient reference intakes for vitamin D and calcium, timing and length of sun exposure for vitamin D synthesis, and serum 25(OH)D level to define vitamin D status will be extracted from each included guideline. Because there is no standard for wording of recommendation across and within guidelines,[29 30] we will adopt the criteria described in the report by Woolf and colleagues for the presentation and formulation of recommendations.[31] These criteria include "consistent semantic and formatting indicators," "a summary section to facilitate identification of recommendations," "decidable and executable wording" and "avoiding embedding recommendation text within long paragraphs." We will not adopt "evidence quality and recommendation strength in proximity to each recommendation," as an objective in this review is to assess the quality of evidence

underpinning the recommendations. For example, in bone health public guidelines, the following would be considered as eligible recommendations: "General practitioners should recommend that postmenopausal women and older men maintain a diet high in calcium to meet the Australian recommended dietary intake," or "General practitioners should recommend the following important lifestyle choices for all postmenopausal women and older men: adequate but safe exposure to sunlight as a source of vitamin D."[32] Statements or text mentioning vitamin D or calcium as knowledge-based information or as a rationale to support an argument will be excluded as a recommendation. For example, "Soy beverages fortified with calcium, vitamin A, and vitamin D, are included as part of the dairy group, because they are similar to milk based on nutrient composition and in their use in meals."[33]

We will use a pilot-tested data extraction form to capture vitamin D and calcium recommendation intakes and categorize as "Yes" or "No" according to criteria described above.[31] Verbatim text will be extracted, if rated as "Yes," including numerical values and/or recommendations without numerical values. Data extraction will be conducted by ZD, CMK/SM independently via REDCap (Research Electronic Data Capture), an electronic data capture tools hosted at the University of Sydney.[34] Any discrepancies in the data extracted will be resolved through discussion with the other reviewer (CMK/SM); otherwise, further discussion with the senior author (LB) will be carried out to resolve the disagreement through consensus. Additionally, we will contact the guideline authors to obtain all relevant materials during the data extraction to avoid missing documents.

Methodological processes

We will appraise the guideline recommendation development processes against the criteria outlined in the 2nd edition of the 2014 WHO Handbook for Guideline Development,[24] a

"gold standard" for public health guideline development. The reasons we have chosen the 2014 WHO Handbook for Guideline Development include: it was developed by the primary international public health agency; it is more recent compared with other standards; and it incorporates the most comprehensive domains and elements for a rigorous guideline development.[35 36] Compared with the Appraisal of Guidelines for Research and Evaluation II (AGREE II),[37] the WHO handbook criteria cover the same domains with more extensive details regarding the guideline development processes. For example, for conflicts of interest, the 2014 WHO guideline handbook includes both disclosure and management of conflicts of interest among the guideline development group members and funders,[24] while the AGREE II instrument addresses conflicts of interest among the guideline development group members only.[37]

The items outline in the WHO handbook with description of the criteria are described in **Table 1**, which includes the following domains: Guideline development group, Conflicts of interest, Review methods, Transparency of evidence substantiation, Recommendation development, and Peer review process. We will record whether each included guideline recommendation is consistent with each of the WHO criteria and classify as Yes, No, or Unclear. If "Yes" is rated, verbatim text will be extracted from the guideline to substantiate per the recommended item. "No" is referred to those which explicitly state none for the items to be appraised. "Unclear" is referred to those that neither explicitly state none nor those with relevant statements supporting the criterion. Three reviewers (ZD, CMK/SM) will perform the critical appraisal and data extraction independently. Discrepancies will be first discussed and resolved through consensus among the reviewers, and with the senior author (LB) if it remains unresolved after the first attempt.

Other information to be extracted

Guideline title, country of origin, guideline developing authority or organization, publication year, age group of the population, gender of the population (men, women, or both), and funding body will be extracted. Further, we will extract the information of the evidence underpinning the recommendations including the types of evidence (primary research, systematic review, or summary of evidence table: see details in "Transparency of evidence substantiation" in Table 1) and their citation information.

Patient and public involvement

No patient involved.

Main outcomes

As mentioned earlier, a binary outcome will be created based on whether a recommendation exists in a public health guideline for the following: vitamin D intakes, vitamin D containing food consumption (such as fortified dairy or other fortified beverage and seafood), a healthy diet for bone health, sun exposure for vitamin D synthesis, supplement use of vitamin D, serum 25(OH)D level to define vitamin D status, calcium reference intakes, calcium containing food consumption (such as dairy and dark-green leafy vegetables,), and supplement use of calcium. If quantitative recommendations (those with amount per day) are available, we will categorize the numerical values into different groups and present the distribution of the recommended intake values.

Data synthesis

Using the information extracted from the included guidelines, we will summarize the recommendation (those with values or recommendation text) for vitamin D and calcium, their food sources, dietary patterns and sun exposure for vitamin D, as well as serum level of

25(OH)D to define vitamin D status, by types of guidelines (food-based dietary guidelines versus bone health guidelines), by continent (Asia, Australia, Europe, North America, South America, and Africa), by gross national income per capita (low, middle and high), and by disclosure of conflict of interest (yes, no). Also, we will present the proportions of the guidelines that are consistent with each of the criteria outlined in the WHO handbook for all guidelines, and separately for the dietary guidelines and bone health guidelines. We will also use descriptive statistics (e.g. frequency and proportion for categorical variables) to summarize the characteristics of each included guideline.

If feasible, we will perform logistic regression analysis to examine the associations between each methodological factor [Yes versus None (combining No and Unclear)] in the six domains of guideline development methods (see Table 1) and a positive recommendation (defined as "yes" for the recommendation) for dietary vitamin D/calcium, supplemental vitamin D/calcium, a healthy diet for bone health, sun exposure (for vitamin D synthesis), and optimal vitamin D level, where each of the recommendations will be considered as a binary outcome. Also, we may perform a multinomial logistic regression analysis for the association between each of the methodological factors (those in Table 1) and categories of the recommended values for vitamin D / calcium (i.e. dietary intake values/supplemental intake values and optimal 25(OH)D level on an ordinal scale), after adjustment for key guideline characteristics. The reason that a multinomial logistic regression is proposed is because that recommended intakes for vitamin D/ calcium and optimal vitamin D level in public health guidelines are often clustered or provided as a range. For example, vitamin D recommendation in a guideline could be 400-800 IU/d, 600-800 IU/d, 800-1000 IU/d, 1500-2000 IU/d; and calcium recommendation

could be 600 mg/d, 700-800 mg/d, 1000 mg/d, 1000-1200 mg/d, >=1000 mg/d, etc. Therefore, a logistic regression analysis is likely more suitable in these analyses.

Discussion and dissemination

To the best of our knowledge, this will be the first study to critically appraise methodological quality regarding guideline recommendations for dietary and supplemental vitamin D and calcium intakes, their food sources, a healthy diet pattern and sun exposure for vitamin D synthesis. This review will advance our knowledge on how guideline development methodology and processes may affect the similarity or differences of the intake recommendations. These findings will further address potential limitations in public health guidelines for the recommended intakes of vitamin D and calcium in middle-aged and older adults.

As we will only include guidelines or statements published in English, this may reduce sample size and limit the coverage of non-English speaking countries if their guidelines/statement reports are not published in English. Although we believe that the criteria outlined in the 2014 WHO handbook for guideline development cover the most comprehensive processes for guideline recommendation development, we understand that some guideline authorities may adopt other standards. For example, the Institute of Medicine standards are commonly used to develop trustworthy clinical guidelines.[35] Therefore, we might experience guidelines with missing data regarding our stringent and comprehensive methodological criteria according to the WHO handbook for guideline development. Further, recent concerns have been raised about possible over consumption of phosphorous from meat and dairy sources and highly processed foods. Because the amount of phosphorus additives in processed food products are generally not accounted for, current nutrition databases assume that phosphorous level remains

similar for the same types of foods (e.g. natural beef and processed beef products), this would potentially underestimate the actual intake of phosphorous in the populations,[38 39] and result in a lower recommended intake of calcium in the guidelines.[40] Due to the scope and feasibility of this study, we will not further account for such underestimation of phosphorous intake at the population level, which could be a potential limitation of this review to address the appropriate recommendations for calcium intake in the included guidelines.

Also, assessment of the quality of the evidence underpinning the recommendations for vitamin D and calcium is out of the scope in this study protocol, as the focus here is to appraise the methods used to develop the public health guidelines. However, we will extract information about the types of evidence cited to support each included recommendation. In a follow-up study, we will further assess the evidence quality (e.g. risk of bias) of the cited studies and systematic reviews.

We will seek to present our findings at international academic conferences and report our findings in a peer-reviewed medical journal article. We also plan to present our findings to key stakeholders in public health authorities and with public health advocates for bone health and osteoporosis prevention.

Conclusions

Currently, there are no studies that have comprehensively appraised methodological rigour in guideline development methods and processes used to develop vitamin D and calcium recommendations. Due to global ageing and a rapid rise of osteoporosis, this review will provide a timely assessment of guideline recommendations for vitamin D and calcium, and help to address potential limitations and identify areas for improvement in developing future guideline recommendations for vitamin D and calcium.

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Authors' contributions

Study Design: ZD, LB, CMK;
Data Collection: ZD;
Coding: ZD, CMK, SM;
Methods and Stats: ZD, MJP, JEM;

Writing: ZD (first draft);

Revising and editing: ZD, CMK, SM, MJP, JEM, MAF, DR, LB;

Guarantor: ZD, LB

Competing interests statement: None disclosed.

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Table 1. Appraisal of the processes and methods used in the recommendations for vitamin D and calcium in public health guidelines

Process and Method domains	Process and Method criteria	Description	Examples where to look
I. Guideline development group (GDG, including members of steering group, research team and individuals involved formulating the final recommendations)			
Were each of the following considered in the formation of the guideline development group?	1. Discipline representation	Information about the composition, discipline, and relevant expertise of the guideline development group should be provided.	Information can be located in methods, guideline panel member list, acknowledgements, and appendices.
	2. Diversity representation	Information about gender, diversity, across the life-course, subject to different gender norms, and belonging to different income and education groups of the guideline development group.	
	3. Stakeholder input	Stakeholders such as nongovernmental organizations, advocacy groups, funders, target audiences, and service-users may be invited to ensure transparency of the processes and facilitate implementation.	
II. Conflicts of interest			
Were each of the following steps addressed regarding conflicts of interest?	4. Disclosure of conflicts of interest obtained (extract verbatim text of COI for each member)	Is there an explicit statement that all group members have declared whether they have any competing interests?	Paragraphs/chapters describing the guideline development group or
	5. Conflicts of interest managed	Members declaration of interests must be reported to the steering group. Potential candidates for membership who have major conflicts of interest, be they financial or nonfinancial, cannot be appointed to the GDG. Minor conflicts of interest can be managed at the individual	

		level (e.g. by restricting participation in parts of the GDG meeting) or at the group level.	acknowledgements section in methods, conflicts of interest, guideline panel, and appendix
	6. Disclosure of funders of the guideline obtained and disclose funder's role in influencing the guideline development process and recommendations	Is there an explicit statement of funder of the guideline and the role of funders in the final guideline recommendations?	
III. Systematic review methods			
Were methods for each of the following addressed in the guideline?	7. Formulation of key questions for the evidence review in PICO, PICOT, or PEO format (also extract the key questions in such format)	Key questions are framed in a way that enables a systematic search of the literature and delineates inclusion and exclusion criteria for the body of evidence to formulate the research questions for the recommendations in such format.	Examine the paragraphs/chapters describing the guideline development process in methods, literature search strategy and appendices.
	8. Choosing (finalizing) priority outcomes for systematic review	List high-priority key questions and the outcomes to formulate recommendations.	
	9. Systematic methods to search for evidence	Details of the strategy used to search for evidence should be provided including search terms used, sources consulted, and dates of the literature covered. Sources may include electronic databases, hand searching journals, reviewing conference proceedings, and other guidelines.	
	10. Evidence retrieval (screening and selection of eligible studies)	Process of data from eligible studies are extracted and search strategy and results should be carefully documented.	
	11. Evidence quality assessment	Each study included in a systematic review should be assessed for risk of bias (e.g. use the Cochrane risk of bias tool, Quality assessment tolls project report, etc.)	

	12. Evidence synthesis	The findings of the systematic review may be synthesized in a narrative manner or quantitatively in a meta-analysis. The review should describe how data were handled and why a given approach to synthesis was taken for each outcome.	
IV. Transparency of evidence substantiation			
If evidence was explicitly linked to recommendation, what type of evidence was reported?	13. Are recommendations explicitly linked to substantiating evidence?	An explicit link between the recommendations and the evidence on which they are based should be included in the guideline. The guideline user should be able to identify the components of the body of evidence relevant to each recommendation.	Define and examine the recommendations in the guideline and the text describing the body of evidence that underpins them. Examples of commonly labeled sections or chapters in a guideline where this information can be found include: recommendations and key evidence.
	a. Primary research	Primary individual studies	
	b. Systematic reviews	Systematic reviews of clinical trials / observational studies	
	c. Summary table of the evidence	Summary of evidence table	
	d. GRADE evidence profiles	GRADE summary of evidence table	
	e. Evidence to decision table		
	f. If evidence is explicitly linked to recommendation, what is the citation information, if applicable?	List the citations of the studies underlying the recommendations	
V. Recommendation development: Factors that determine the direction and strength of a recommendation			
Was each of the following items considered when developing the recommendation? (also communicate	14. Was a consensus process clearly described for developing recommendations	A description of the methods used to formulate the recommendations and how final decisions were arrived at should be provided. For example, methods may include a voting system, informal consensus, and formal consensus	

authority whether other documentation may provide such information if they cannot be located in the main guideline reports)		techniques. Areas of disagreement and methods of resolving them should be specified.	Examples of commonly labeled sections or chapters in a guideline where this information can be found include methods and guideline development process or in appendices.
	15. Was a method employed to determine strength and/or certainty of the recommendation?	Is there a method provided to influence the direction and strength of a recommendation (e.g. use GRADE framework and others)	
	16. Priority of the problem: Is the problem a burden of disease?	The problem's priority is determined by its importance and frequency (i.e. burden of disease, disease prevalence or baseline risk). The greater the importance of the problem, the greater the likelihood of a strong recommendation.	
	17. Quality of the evidence: Is higher quality of the body of evidence included to support the recommendation?	Is there a method provided to grade the quality of body of evidence to assess the strength of the recommendation (e.g. GRADE and others)	
	18. Certainty of evidence: Does the recommendation include consistent body of evidence (e.g. confidence in effect estimates)?	The quality of the evidence – the degree of confidence in the estimates of effect. This is a key factor in determining the strength of a recommendation.	
	19. Benefits and harms: Are evaluations performed on the net benefit or net harm associate with an intervention or exposure?	The balance between an intervention's or exposure's benefits and harms. Did the guideline development group consider the magnitude of the effects and the relative importance of the outcomes, including any disadvantages or inconveniences associated with the intervention.	
	20. Balance: Does the balance between desirable and undesirable effects support the recommendation?	Does the balance between desirable and undesirable effects favour the intervention or the comparison?	

	21. Outcome importance: Is there important uncertainty about or variability in how much people value the main outcome?	Is there important uncertainty about or variability in how much people value the main outcomes, including adverse effects and burden of the test and downstream outcomes of clinical management that is guided by the test results?	
	22. Equity: Does the evidence used reduce inequalities, improve equity or contribute to the realization of one of several human rights defined under the international legal framework?	What would be the impact on health equity?	
	23. Acceptability: Is the option acceptable to key stakeholders?	A strategy to address concerns about acceptability during implementation will be included in the guideline with the recommendations. Acceptability is affected by several factors, such as who benefits from an intervention and who is harmed by it; who pays for it or saves money on account of it; and when the benefits, harms and costs occur.	
	24. Feasibility: Is the option feasible to implement?	Feasibility is influenced by the resources available, programmatic considerations, the existing and the necessary infrastructure and training, etc.	
VI. Peer review process			
	25. Was the guideline/recommendation reviewed by an external review group?	Is there an explicit statement about the peer review of the draft final guideline? The external review group is composed of persons interested in the subject of the guideline as well as individuals who will be affected by the recommendations.	Information can be located in methods, guideline panel member list, acknowledgements, and appendices.

Supplemental material: Medline search strategy via Ovid

1. Vitamin D/
2. Cholecalciferol/
3. Ergocalciferols/
4. Vitamin D Deficiency/
5. Sunlight/
6. Ultraviolet Rays/
7. Vit* D.tw.
8. Ergocalciferol.tw.
9. Calciferol.tw.
10. Cholecalciferol.tw.
11. Sunlight.tw.
12. (Light adj3 expos*).tw.
13. UV.tw.
14. Ultraviolet.tw.
15. or/1-14
16. exp Calcium/
17. Calcium, Dietary/
18. calcium.mp.
19. or/16-18
20. 15 or 19
21. Diet/
22. "Diet, Food, and Nutrition"/
23. Diet, Vegetarian/
24. Diet, Vegan/
25. Diet, Western/
26. Diet Therapy/
27. Healthy Diet/

28. Food, Fortified/
29. Dietary supplements/
30. exp Dairy Products/
31. Shellfish/
32. Fishes/
33. exp Seafood/
34. Vegetables/
35. exp Vegetable Products/
36. Agaricales/
37. Diet*.tw.
38. (Diet* adj3 supplement*).tw.
39. (Fortified adj3 food*).tw.
40. Vegetable*.tw.
41. Mushroom*.tw.
42. Dairy.tw.
43. Milk.tw.
44. Cheese.tw.
45. Yog?urt.tw.
46. Seafood.tw.
47. Fish.tw.
48. Shellfish.tw.
49. or/21-48
50. 20 or 49
51. 20 and 49
52. exp clinical pathway/
53. exp clinical protocol/
54. exp consensus/
55. exp consensus development conference/

56. exp consensus development conferences as topic/

57. critical pathways/

58. exp guideline/

59. guidelines as topic/

60. exp practice guideline/

61. practice guidelines as topic/

62. health planning guidelines/

63. (guideline or practice guideline or consensus development conference or consensus development conference, NIH).pt.

64. (position statement* or policy statement* or practice parameter* or best practice*).ti,ab,kf,kw.

65. (standards or guideline or guidelines).ti,kf,kw.

66. ((practice or treatment* or clinical) adj guideline*).ab.

67. (CPG or CPGs).ti.

68. consensus*.ti,kf,kw.

69. consensus*.ab. /freq=2

70. ((critical or clinical or practice) adj2 (path or paths or pathway or pathways or protocol*)).ti,ab,kf,kw.

71. recommendat*.ti,kf,kw.

72. (care adj2 (standard or path or paths or pathway or pathways or map or maps or plan or plans)).ti,ab,kf,kw.

73. (algorithm* adj2 (screening or examination or test or tested or testing or assessment* or diagnosis or diagnoses or diagnosed or diagnosing)).ti,ab,kf,kw.

74. or/52-73

75. Osteoporosis/

76. Fractures, Bone/

77. Bone Density/

78. osteoporosis.tw.

79. fracture*,bone.tw.

80. bone density.tw.

81. bone health.mp.

82. 75 or 76 or 77 or 78 or 79 or 80 or 81

83. Adult/

84. Aged/

85. Middle Aged/

86. adult*.tw.

87. aged.tw.

88. middle aged.tw.

89. 83 or 84 or 85 or 86 or 87 or 88

90. 74 and 82 and 89

91. 50 and 90

PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol*

Section and topic	Item No	Checklist item	(Page No.#)
ADMINISTRATIVE INFORMATION			
Title:			
Identification	1a	Identify the report as a protocol of a systematic review	1
Update	1b	If the protocol is for an update of a previous systematic review, identify as such	
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number	3
Authors:			
Contact	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author	1
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	16
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	n/a
Support:			
Sources	5a	Indicate sources of financial or other support for the review	15
Sponsor	5b	Provide name for the review funder and/or sponsor	15
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	16
INTRODUCTION			
Rationale	6	Describe the rationale for the review in the context of what is already known	4-5
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	5
METHODS			
Eligibility criteria	8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review	6-7
Information sources	9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage	8
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	26-29
Study records:			

Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	9-10
Selection process	11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)	10
Data collection process	11c	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	10 and 11
Data items	12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications	9-11
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	12
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	10-11
Data synthesis	15a	Describe criteria under which study data will be quantitatively synthesised	12
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as I^2, Kendall's τ)	12-13
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)	13
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	12
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)	n/a
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)	n/a

*** It is strongly recommended that this checklist be read in conjunction with the PRISMA-P Explanation and Elaboration (cite when available) for important clarification on the items. Amendments to a review protocol should be tracked and dated. The copyright for PRISMA-P (including checklist) is held by the PRISMA-P Group and is distributed under a Creative Commons Attribution Licence 4.0.**

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Methodological quality of public health guideline recommendations on vitamin D and calcium intakes – a systematic review protocol

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Abstract

Introduction Current recommendations for vitamin D and calcium in dietary guidelines and bone health guidelines vary significantly among countries and professional organizations. It is unknown whether the methods used to develop these recommendations followed a rigourous process and how the differences in methods used may affect the recommended intakes of vitamin D and calcium. The objectives of this study are 1) collate and compare recommendations for vitamin D and calcium across guidelines, 2) appraise methodological quality of the guideline recommendations, and 3) identify methodological factors that may affect the recommended intakes for vitamin D and calcium. This study will make a significant contribution to enhancing the methodological rigour in public health guidelines for vitamin D and calcium recommendations.

Methods and analyses We will conduct a systematic review to evaluate vitamin D and calcium recommendations for osteoporosis prevention in generally healthy middle-aged and older adults. Methodological assessment will be performed for each guideline against those outlined in the 2014 World Health Organization (WHO) Handbook for Guideline Development. A systematic search strategy will be applied to locate food-based dietary guidelines and bone health guidelines indexed in various electronic databases, guideline repositories and gray literature from 1 January 2009 to 28 February 2019. Descriptive statistics will be used to summarize the data on intake recommendation and on proportion of guidelines consistent with the WHO criteria. Logistic regression, if feasible, will be used to assess the relationships between the methodological factors and the recommendation intakes.

Ethics and dissemination Ethics approval is not required as we will only extract published data or information from the published guidelines. Results of this review will be disseminated through conference presentations and peer-reviewed publications.

Protocol registration number PROSPERO, CRD42019126452.

Keywords: vitamin D, calcium, public health guidelines, guideline development methods

Strengths and limitations of this study

- To the best of our knowledge, this will be the first study that critically appraises the methodological quality of guideline recommendations for vitamin D and calcium intakes.
- This study will provide insights to address potential limitations in guideline development and identify areas for improvement in developing vitamin D and calcium recommendations.
- Eligible guidelines published in English only may potentially limit the sample size of and regional coverage of the guideline recommendations included in our analysis.
- Information required to assess methodological quality of guidelines may be missing, particularly when other guideline development standards (e.g. the Institute of Medicine standards for trustworthy clinical guidelines) rather than the WHO Handbook for Guideline Development were used to develop public health guidelines.

Introduction

Current recommendations for vitamin D and calcium in dietary guidelines and bone health guidelines vary significantly among countries and professional organizations.[1 2 3 4] Several factors may have contributed to such variation: dietary sources of vitamin D and calcium are different among countries and regions, with some but not all fortifying the nutrients in the food products as an example; some guidelines may consider supplement use as part of the recommendations, while others recommend sunlight exposure as a source of vitamin D. For the latter, race and skin tone also contribute to the appropriate length of time of sun exposure to achieve certain vitamin D levels. Another possible reason for these varied recommendations is that evidence on the efficacy of vitamin D and/or calcium supplementation[3 5-14] in the prevention of osteoporosis, particularly in fracture prevention, is conflicting; and their adverse effects in cardiac risks[15 16] and compromised renal function[10 12] must also be taken into account. Further, what defines vitamin D deficiency measured by serum 25(OH)D is debatable and varies among the general populations.[14 17-19] This variation of optimal vitamin D level further contributes to the inconsistent findings in randomized control trials testing the effects of different dosages of vitamin D and/or calcium supplementation in fracture prevention.[13 14]

Additionally, inconsistencies exist in the guideline development processes used to retrieve, appraise and synthesize relevant evidence, as well as in reporting conflicts of interest and funding sources in national dietary guidelines.[20] This can potentially further affect the discordance in the recommended intakes of vitamin D and calcium in guideline recommendations. For example, findings from a global review of food-based dietary guidelines suggest that social and economic equity and cultural factors need to be incorporated in guideline development in order to recommend appropriate food intakes among populations with different

backgrounds. Further, there are significant regional differences in dairy intake recommendations across different dietary guidelines.[21] As dairy is the main source of dietary calcium and vitamin D in some but not all populations,[22 23] recommendations about dietary sources need to consider the ethnic and cultural contexts. Taken together, guideline development methods should include, but be not limited to, evidence identification, evaluation, and synthesis; as well as incorporating stakeholders' positions, feasibility and acceptability of the recommendations.

The objective of this study is to compare recommendations for vitamin D and calcium intakes and their associated parameters [e.g. sun exposure for vitamin D synthesis and serum 25(OH)D level to define vitamin D status], and the methods used in formulating these recommendations for middle-aged and older adults in public health guidelines. We will further assess whether the similarity or differences in the vitamin D and calcium intake recommendations can be explained by the guidelines' methodological quality. Findings from this study will illustrate methodological rigour and potential limitations in current public health guidelines for vitamin D and calcium recommended intakes.

Methods

Overview

We will include public health guidelines or policy statements related to vitamin D/ calcium intake and bone health for generally healthy adults aged 40 years and above. Because middle-aged and older adults are individuals at risk to develop osteoporosis, we intend to include those who may experience menopause as young as 40 years to ensure the coverage of all age groups at risk in the included guidelines. We will include both food-based dietary guidelines and health guidelines for osteoporosis (including fracture) prevention. We will use the definition described in the 2014 World Health Organization (WHO) Handbook for Guideline Development to define guidelines and recommendations, i.e. "any document containing recommendations for

clinical practice or public health policy. A recommendation tells the intended end-user of the guideline what he or she can or should do in specific situations to achieve the best health outcomes possible, individually or collectively."[24]

Inclusion criteria

- Most recent version of national food-based dietary guidelines
- Most recent version of national guidelines, policy statements or standards for osteoporosis prevention

We will only include national guidelines that have been developed by a nationally or internationally recognised government authority or by a medical/academic society or organization. This is to ensure consistency between the food-based dietary guidelines and the bone health guidelines at country (state) level, as food-based dietary guidelines are typically a state government document. In addition to the guideline documents, we will include supporting documents such as those provide details for the methodology used and evidence underpinning the recommendations. For instance, guideline committee's reports, in which we can locate methodology and supporting evidence will be included. An example is the "Scientific Report of the 2015 Dietary Guidelines Advisory Committee," which describes the development of the dietary guideline and supporting evidence for the "Dietary Guidelines for Americans 2015-2020." Similarly, "A review of the evidence to address targeted questions to inform the revision of the Australian Dietary Guidelines" [25] as well as the Nutrient Reference Values (NRV) document for Australia and New Zealand are companion documents with evidence substantiating the recommendations for the "Australian Dietary Guidelines 2013."[26] If there are multiple versions of a national guideline from the same country or authority, only the most recent version will be included. Similarly, if an updated bone health guideline is based on the previous

documents that describe the processes of the recommendation development, these documents will be included to locate the information on methods and evidence used to support the recommendations.

Exclusion criteria

- Food guides such as food pyramids, food plates, or simple designed pictorial or graphic representation
- Bone health guidelines regarding vitamin D and calcium recommendations in the management of osteoporosis, secondary osteoporosis (e.g. osteoporosis due to rheumatoid arthritis) or for a particular group of population (e.g. pregnant women) or those with health condition (e.g. patients with cancer, cirrhosis, etc.)

We will not include food guides, because they lack substantial materials to document the guideline development process. Guideline recommendations on clinical treatment of any bone disorders, or guidelines targeted to a particular group of populations such as those with HIV or cancer patients or pregnant or lactating women or a particular type of osteoporosis (e.g. glucocorticoid-induced osteoporosis) will be excluded. This is because the focus of this study is to review recommended vitamin D and calcium intakes for generally healthy populations to maintain bone health or to prevent osteoporosis.

Search strategy

We will search guidelines or policy statements that are published from 1 January 2009 until 28 February 2019 in the following electronic databases: MEDLINE (via OVID), EMBASE (via OVID), CINAHL (via EBSCO), and Practice Based Evidence in Nutrition. Additionally, the following sources which include guidelines specifically will be searched: National Guideline Clearinghouse, National Institute for Health and Care Excellence, and Guidelines International

Network. We will only include documents published in English but no geographic regions are restricted. We will use a combination of controlled vocabulary and free-text terms for vitamin D, sunlight, calcium, dairy, vegetable, seafood, fortified food (as these are the good dietary sources for vitamin D and / or calcium), dietary patterns, osteoporosis/fracture and guideline. The search strategy for Medline via Ovid is described in **Supplemental material.** Similar search strategies with appropriate syntax will be applied to EMBASE and CINAHL. We will also search the gray literature via the Food and Agricultural Organization (FAO) website for relevant food-based dietary guidelines[27] and the International Osteoporosis Foundation[28] for bone health guidelines from national government agencies or organizations. Additionally, we will consult leading experts in the field of bone health to avoid any oversights.

Data extraction process

Recommendations for vitamin D and calcium

Verbatim text of qualitative and quantitative recommendations on dietary intake of vitamin D/calcium, vitamin D/calcium containing foods, a healthy dietary pattern beneficial to bone health, supplementation dosage for vitamin D/calcium, nutrient reference intakes for vitamin D and calcium, timing and length of sun exposure for vitamin D synthesis, and serum 25(OH)D level to define vitamin D status will be extracted from each included guideline. Because there is no standard for wording of recommendation across and within guidelines,[29 30] we will adopt the criteria described in the report by Woolf and colleagues for the presentation and formulation of recommendations.[31] These criteria include "consistent semantic and formatting indicators," "a summary section to facilitate identification of recommendations," "decidable and executable wording" and "avoiding embedding recommendation text within long paragraphs." We will not adopt "evidence quality and recommendation strength in proximity to each recommendation," as an objective in this review is to assess the quality of evidence

underpinning the recommendations. For example, in bone health public guidelines, the following would be considered as eligible recommendations: "General practitioners should recommend that postmenopausal women and older men maintain a diet high in calcium to meet the Australian recommended dietary intake," or "General practitioners should recommend the following important lifestyle choices for all postmenopausal women and older men: adequate but safe exposure to sunlight as a source of vitamin D."[32] Statements or text mentioning vitamin D or calcium as knowledge-based information or as a rationale to support an argument will be excluded as a recommendation. For example, "Soy beverages fortified with calcium, vitamin A, and vitamin D, are included as part of the dairy group, because they are similar to milk based on nutrient composition and in their use in meals."[33]

We will use a pilot-tested data extraction form to capture vitamin D and calcium recommendation intakes and categorize as "Yes" or "No" according to criteria described above.[31] Verbatim text will be extracted, if rated as "Yes," including numerical values and/or recommendations without numerical values. Data extraction will be conducted independently via REDCap (Research Electronic Data Capture), an electronic data capture tools hosted at the University of Sydney.[34] Any discrepancies in the data extracted will be resolved through discussion with the other reviewer; otherwise, further discussion with the senior author will be carried out to resolve the disagreement through consensus. Additionally, we will contact the guideline authors to obtain all relevant materials during the data extraction to avoid missing documents.

Methodological processes

We will appraise the guideline recommendation development processes against the criteria outlined in the 2nd edition of the 2014 WHO Handbook for Guideline Development,[24] a

"gold standard" for public health guideline development. The reasons we have chosen the 2014 WHO Handbook for Guideline Development include: it was developed by the primary international public health agency; it is more recent compared with other standards; and it incorporates the most comprehensive domains and elements for a rigorous guideline development.[35 36] Compared with the Appraisal of Guidelines for Research and Evaluation II (AGREE II),[37] the WHO handbook criteria cover the same domains with more extensive details regarding the guideline development processes. For example, for conflicts of interest, the 2014 WHO guideline handbook includes both disclosure and management of conflicts of interest among the guideline development group members and funders,[24] while the AGREE II instrument addresses conflicts of interest among the guideline development group members only.[37]

The items outline in the WHO handbook with description of the criteria are described in **Table 1**, which includes the following domains: Guideline development group, Conflicts of interest, Review methods, Transparency of evidence substantiation, Recommendation development, and Peer review process. We will record whether each included guideline recommendation is consistent with each of the WHO criteria and classify as Yes, No, or Unclear. If "Yes" is rated, verbatim text will be extracted from the guideline to substantiate per the recommended item. "No" is referred to those which explicitly state none for the items to be appraised. "Unclear" is referred to those that neither explicitly state none nor those with relevant statements supporting the criterion. Three reviewers will perform the critical appraisal and data extraction independently. Discrepancies will be first discussed and resolved through consensus among the reviewers, and with the senior author if it remains unresolved after the first attempt.

Other information to be extracted

Guideline title, country of origin, guideline developing authority or organization, publication year, age group of the population, gender of the population (men, women, or both), and funding body will be extracted. Further, we will extract the information of the evidence underpinning the recommendations including the types of evidence (primary research, systematic review, or summary of evidence table: see details in "Transparency of evidence substantiation" in Table 1) and their citation information.

Patient and public involvement

No patient involved.

Main outcomes

As mentioned earlier, a binary outcome will be created based on whether a recommendation exists in a public health guideline for the following: vitamin D intakes, vitamin D containing food consumption (such as fortified dairy or other fortified beverage and seafood), a healthy diet for bone health, sun exposure for vitamin D synthesis, supplement use of vitamin D, serum 25(OH)D level to define vitamin D status, calcium reference intakes, calcium containing food consumption (such as dairy and dark-green leafy vegetables,), and supplement use of calcium. If quantitative recommendations (those with amount per day) are available, we will categorize the numerical values into different groups and present the distribution of the recommended intake values.

Data synthesis

Using the information extracted from the included guidelines, we will summarize the recommendation (those with values or recommendation text) for vitamin D and calcium, their food sources, dietary patterns and sun exposure for vitamin D, as well as serum level of

25(OH)D to define vitamin D status, by types of guidelines (food-based dietary guidelines versus bone health guidelines), by continent (Asia, Australia, Europe, North America, South America, and Africa), by gross national income per capita (low, middle and high), and by disclosure of conflict of interest (yes, no). Also, we will present the proportions of the guidelines that are consistent with each of the criteria outlined in the WHO handbook for all guidelines, and separately for the dietary guidelines and bone health guidelines. We will also use descriptive statistics (e.g. frequency and proportion for categorical variables) to summarize the characteristics of each included guideline.

If feasible, we will perform logistic regression analysis to examine the associations between each methodological factor [Yes versus None (combining No and Unclear)] in the six domains of guideline development methods (see Table 1) and a positive recommendation (defined as "yes" for the recommendation) for dietary vitamin D/calcium, supplemental vitamin D/calcium, a healthy diet for bone health, sun exposure (for vitamin D synthesis), and optimal vitamin D level, where each of the recommendations will be considered as a binary outcome. Also, we may perform a multinomial logistic regression analysis for the association between each of the methodological factors (those in Table 1) and categories of the recommended values for vitamin D / calcium (i.e. dietary intake values/supplemental intake values and optimal 25(OH)D level on an ordinal scale), after adjustment for key guideline characteristics. The reason that a multinomial logistic regression is proposed is because that recommended intakes for vitamin D/ calcium and optimal vitamin D level in public health guidelines are often clustered or provided as a range. For example, vitamin D recommendation in a guideline could be 400-800 IU/d, 600-800 IU/d, 800-1000 IU/d, 1500-2000 IU/d; and calcium recommendation

could be 600 mg/d, 700-800 mg/d, 1000 mg/d, 1000-1200 mg/d, ≥1000mg/d, etc. Therefore, a logistic regression analysis is likely more suitable in these analyses.

Discussion

To the best of our knowledge, this will be the first study to critically appraise methodological quality regarding guideline recommendations for dietary and supplemental vitamin D and calcium intakes, their food sources, a healthy diet pattern and sun exposure for vitamin D synthesis. This review will advance our knowledge on how guideline development methodology and processes may affect the similarity or differences of the intake recommendations. These findings will further address potential limitations in public health guidelines for the recommended intakes of vitamin D and calcium in middle-aged and older adults.

As we will only include guidelines or statements published in English, this may reduce sample size and limit the coverage of non-English speaking countries if their guidelines/statement reports are not published in English. Although we believe that the criteria outlined in the 2014 WHO handbook for guideline development cover the most comprehensive processes for guideline recommendation development, we understand that some guideline authorities may adopt other standards. For example, the Institute of Medicine standards are commonly used to develop trustworthy clinical guidelines.[35] Therefore, we might experience guidelines with missing data regarding our stringent and comprehensive methodological criteria according to the WHO handbook for guideline development. Further, recent concerns have been raised about possible over consumption of phosphorous from meat and dairy sources and highly processed foods. Because the amount of phosphorus additives in processed food products are generally not accounted for, current nutrition databases assume that phosphorous level remains

similar for the same types of foods (e.g. natural beef and processed beef products), this would potentially underestimate the actual intake of phosphorous in the populations,[38 39] and result in a lower recommended intake of calcium in the guidelines.[40] Due to the scope and feasibility of this study, we will not further account for such underestimation of phosphorous intake at the population level, which could be a potential limitation of this review to address the appropriate recommendations for calcium intake in the included guidelines.

Also, assessment of the quality of the evidence underpinning the recommendations for vitamin D and calcium is out of the scope in this study protocol, as the focus here is to appraise the methods used to develop the public health guidelines. However, we will extract information about the types of evidence cited to support each included recommendation. In a follow-up study, we will further assess the evidence quality (e.g. risk of bias) of the cited studies and systematic reviews.

Ethics and dissemination

Ethics approval is not required as we will only extract published data or information from the published guidelines. We will seek to present our findings at international academic conferences and report our findings in a peer-reviewed medical journal article. We also plan to present our findings to key stakeholders in public health authorities and with public health advocates for bone health and osteoporosis prevention.

Conclusions

Currently, there are no studies that have comprehensively appraised methodological rigour in guideline development methods and processes used to develop vitamin D and calcium recommendations. Due to global ageing and a rapid rise of osteoporosis, this review will provide a timely assessment of guideline recommendations for vitamin D and calcium, and help to

address potential limitations and identify areas for improvement in developing future guideline recommendations for vitamin D and calcium.

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Authors' contributions

Study Design: ZD, LB, CMK;

Data Collection: ZD;

Methods and Stats: ZD, MJP, JEM;

Writing: ZD (first draft);

Revising and editing: ZD, CMK, SM, MJP, JEM, MAF, DR, LB;

Guarantor: ZD, LB

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Table 1. Appraisal of the processes and methods used in the recommendations for vitamin D and calcium in public health guidelines

Process and Method domains	Process and Method criteria	Description	Examples where to look
I. Guideline development group (GDG, including members of steering group, research team and individuals involved formulating the final recommendations)			
Were each of the following considered in the formation of the guideline development group?	1. Discipline representation	Information about the composition, discipline, and relevant expertise of the guideline development group should be provided.	Information can be located in methods, guideline panel member list, acknowledgements, and appendices.
	2. Diversity representation	Information about gender, diversity, across the life-course, subject to different gender norms, and belonging to different income and education groups of the guideline development group.	
	3. Stakeholder input	Stakeholders such as nongovernmental organizations, advocacy groups, funders, target audiences, and service-users may be invited to ensure transparency of the processes and facilitate implementation.	
II. Conflicts of interest			
Were each of the following steps addressed regarding conflicts of interest?	4. Disclosure of conflicts of interest obtained (extract verbatim text of COI for each member)	Is there an explicit statement that all group members have declared whether they have any competing interests?	Paragraphs/chapters describing the guideline development group or
	5. Conflicts of interest managed	Members declaration of interests must be reported to the steering group. Potential candidates for membership who have major conflicts of interest, be they financial or nonfinancial, cannot be appointed to the GDG. Minor conflicts of interest can be managed at the individual	

		level (e.g. by restricting participation in parts of the GDG meeting) or at the group level.	acknowledgements section in methods, conflicts of interest, guideline panel, and appendix
	6. Disclosure of funders of the guideline obtained and disclose funder's role in influencing the guideline development process and recommendations	Is there an explicit statement of funder of the guideline and the role of funders in the final guideline recommendations?	
III. Systematic review methods			
Were methods for each of the following addressed in the guideline?	7. Formulation of key questions for the evidence review in PICO, PICOT, or PEO format (also extract the key questions in such format)	Key questions are framed in a way that enables a systematic search of the literature and delineates inclusion and exclusion criteria for the body of evidence to formulate the research questions for the recommendations in such format.	Examine the paragraphs/chapters describing the guideline development process in methods, literature search strategy and appendices.
	8. Choosing (finalizing) priority outcomes for systematic review	List high-priority key questions and the outcomes to formulate recommendations.	
	9. Systematic methods to search for evidence	Details of the strategy used to search for evidence should be provided including search terms used, sources consulted, and dates of the literature covered. Sources may include electronic databases, hand searching journals, reviewing conference proceedings, and other guidelines.	
	10. Evidence retrieval (screening and selection of eligible studies)	Process of data from eligible studies are extracted and search strategy and results should be carefully documented.	
	11. Evidence quality assessment	Each study included in a systematic review should be assessed for risk of bias (e.g. use the Cochrane risk of bias tool, Quality assessment tolls project report, etc.)	

	12. Evidence synthesis	The findings of the systematic review may be synthesized in a narrative manner or quantitatively in a meta-analysis. The review should describe how data were handled and why a given approach to synthesis was taken for each outcome.	
IV. Transparency of evidence substantiation			
If evidence was explicitly linked to recommendation, what type of evidence was reported?	13. Are recommendations explicitly linked to substantiating evidence?	An explicit link between the recommendations and the evidence on which they are based should be included in the guideline. The guideline user should be able to identify the components of the body of evidence relevant to each recommendation.	Define and examine the recommendations in the guideline and the text describing the body of evidence that underpins them. Examples of commonly labeled sections or chapters in a guideline where this information can be found include: recommendations and key evidence.
	a. Primary research	Primary individual studies	
	b. Systematic reviews	Systematic reviews of clinical trials / observational studies	
	c. Summary table of the evidence	Summary of evidence table	
	d. GRADE evidence profiles	GRADE summary of evidence table	
	e. Evidence to decision table		
	f. If evidence is explicitly linked to recommendation, what is the citation information, if applicable?	List the citations of the studies underlying the recommendations	
V. Recommendation development: Factors that determine the direction and strength of a recommendation			
Was each of the following items considered when developing the recommendation? (also communicate	14. Was a consensus process clearly described for developing recommendations	A description of the methods used to formulate the recommendations and how final decisions were arrived at should be provided. For example, methods may include a voting system, informal consensus, and formal consensus	

authority whether other documentation may provide such information if they cannot be located in the main guideline reports)		techniques. Areas of disagreement and methods of resolving them should be specified.	Examples of commonly labeled sections or chapters in a guideline where this information can be found include methods and guideline development process or in appendices.
	15. Was a method employed to determine strength and/or certainty of the recommendation?	Is there a method provided to influence the direction and strength of a recommendation (e.g. use GRADE framework and others)	
	16. Priority of the problem: Is the problem a burden of disease?	The problem's priority is determined by its importance and frequency (i.e. burden of disease, disease prevalence or baseline risk). The greater the importance of the problem, the greater the likelihood of a strong recommendation.	
	17. Quality of the evidence: Is higher quality of the body of evidence included to support the recommendation?	Is there a method provided to grade the quality of body of evidence to assess the strength of the recommendation (e.g. GRADE and others)	
	18. Certainty of evidence: Does the recommendation include consistent body of evidence (e.g. confidence in effect estimates)?	The quality of the evidence – the degree of confidence in the estimates of effect. This is a key factor in determining the strength of a recommendation.	
	19. Benefits and harms: Are evaluations performed on the net benefit or net harm associate with an intervention or exposure?	The balance between an intervention's or exposure's benefits and harms. Did the guideline development group consider the magnitude of the effects and the relative importance of the outcomes, including any disadvantages or inconveniences associated with the intervention.	
	20. Balance: Does the balance between desirable and undesirable effects support the recommendation?	Does the balance between desirable and undesirable effects favour the intervention or the comparison?	

	21. Outcome importance: Is there important uncertainty about or variability in how much people value the main outcome?	Is there important uncertainty about or variability in how much people value the main outcomes, including adverse effects and burden of the test and downstream outcomes of clinical management that is guided by the test results?	
	22. Equity: Does the evidence used reduce inequalities, improve equity or contribute to the realization of one of several human rights defined under the international legal framework?	What would be the impact on health equity?	
	23. Acceptability: Is the option acceptable to key stakeholders?	A strategy to address concerns about acceptability during implementation will be included in the guideline with the recommendations. Acceptability is affected by several factors, such as who benefits from an intervention and who is harmed by it; who pays for it or saves money on account of it; and when the benefits, harms and costs occur.	
	24. Feasibility: Is the option feasible to implement?	Feasibility is influenced by the resources available, programmatic considerations, the existing and the necessary infrastructure and training, etc.	
VI. Peer review process			
	25. Was the guideline/recommendation reviewed by an external review group?	Is there an explicit statement about the peer review of the draft final guideline? The external review group is composed of persons interested in the subject of the guideline as well as individuals who will be affected by the recommendations.	Information can be located in methods, guideline panel member list, acknowledgements, and appendices.

Supplemental material: Medline search strategy via Ovid

1. Vitamin D/
2. Cholecalciferol/
3. Ergocalciferols/
4. Vitamin D Deficiency/
5. Sunlight/
6. Ultraviolet Rays/
7. Vit* D.tw.
8. Ergocalciferol.tw.
9. Calciferol.tw.
10. Cholecalciferol.tw.
11. Sunlight.tw.
12. (Light adj3 expos*).tw.
13. UV.tw.
14. Ultraviolet.tw.
15. or/1-14
16. exp Calcium/
17. Calcium, Dietary/
18. calcium.mp.
19. or/16-18
20. 15 or 19
21. Diet/
22. "Diet, Food, and Nutrition"/
23. Diet, Vegetarian/
24. Diet, Vegan/
25. Diet, Western/
26. Diet Therapy/
27. Healthy Diet/

28. Food, Fortified/
29. Dietary supplements/
30. exp Dairy Products/
31. Shellfish/
32. Fishes/
33. exp Seafood/
34. Vegetables/
35. exp Vegetable Products/
36. Agaricales/
37. Diet*.tw.
38. (Diet* adj3 supplement*).tw.
39. (Fortified adj3 food*).tw.
40. Vegetable*.tw.
41. Mushroom*.tw.
42. Dairy.tw.
43. Milk.tw.
44. Cheese.tw.
45. Yog?urt.tw.
46. Seafood.tw.
47. Fish.tw.
48. Shellfish.tw.
49. or/21-48
50. 20 or 49
51. 20 and 49
52. exp clinical pathway/
53. exp clinical protocol/
54. exp consensus/
55. exp consensus development conference/

56. exp consensus development conferences as topic/

57. critical pathways/

58. exp guideline/

59. guidelines as topic/

60. exp practice guideline/

61. practice guidelines as topic/

62. health planning guidelines/

63. (guideline or practice guideline or consensus development conference or consensus development conference, NIH).pt.

64. (position statement* or policy statement* or practice parameter* or best practice*).ti,ab,kf,kw.

65. (standards or guideline or guidelines).ti,kf,kw.

66. ((practice or treatment* or clinical) adj guideline*).ab.

67. (CPG or CPGs).ti.

68. consensus*.ti,kf,kw.

69. consensus*.ab. /freq=2

70. ((critical or clinical or practice) adj2 (path or paths or pathway or pathways or protocol*)).ti,ab,kf,kw.

71. recommendat*.ti,kf,kw.

72. (care adj2 (standard or path or paths or pathway or pathways or map or maps or plan or plans)).ti,ab,kf,kw.

73. (algorithm* adj2 (screening or examination or test or tested or testing or assessment* or diagnosis or diagnoses or diagnosed or diagnosing)).ti,ab,kf,kw.

74. or/52-73

75. Osteoporosis/

76. Fractures, Bone/

77. Bone Density/

78. osteoporosis.tw.

79. fracture*,bone.tw.

80. bone density.tw.

81. bone health.mp.

82. 75 or 76 or 77 or 78 or 79 or 80 or 81

83. Adult/

84. Aged/

85. Middle Aged/

86. adult*.tw.

87. aged.tw.

88. middle aged.tw.

89. 83 or 84 or 85 or 86 or 87 or 88

90. 74 and 82 and 89

91. 50 and 90

PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol*

Section and topic	Item No	Checklist item	(Page No.#)
ADMINISTRATIVE INFORMATION			
Title:			
Identification	1a	Identify the report as a protocol of a systematic review	1
Update	1b	If the protocol is for an update of a previous systematic review, identify as such	
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number	3
Authors:			
Contact	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author	1
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	16
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	n/a
Support:			
Sources	5a	Indicate sources of financial or other support for the review	15
Sponsor	5b	Provide name for the review funder and/or sponsor	15
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	16
INTRODUCTION			
Rationale	6	Describe the rationale for the review in the context of what is already known	4-5
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	5
METHODS			
Eligibility criteria	8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review	6-7
Information sources	9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage	8
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	26-29
Study records:			

Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	9-10
Selection process	11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)	10
Data collection process	11c	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	10 and 11
Data items	12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications	9-11
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	12
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	10-11
Data synthesis	15a	Describe criteria under which study data will be quantitatively synthesised	12
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as I^2, Kendall's τ)	12-13
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)	13
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	12
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)	n/a
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)	n/a

*** It is strongly recommended that this checklist be read in conjunction with the PRISMA-P Explanation and Elaboration (cite when available) for important clarification on the items. Amendments to a review protocol should be tracked and dated. The copyright for PRISMA-P (including checklist) is held by the PRISMA-P Group and is distributed under a Creative Commons Attribution Licence 4.0.**

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