Vitamin D recommendations in nutritional guidelines: A systematic quality evaluation using AGREE-2 and analysis of potential predictors

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Abstract

Background Vitamin D has been widely promoted for bone health through supplementation and fortification of the general population. However, there is growing evidence that does not support these strategies. Our aim is to review the quality and recommendations on vitamin D nutritional and clinical practice guidelines and explore predictive factors for their direction and strength. Methods We searched Medline, TRIP, G-I-N and guidelines.gov databases for guidelines from January 2010 to January 2018. We performed a descriptive analysis, a quality appraisal using AGREE II scores (Appraisal of Guidelines Research and Evaluation) and a bivariate analysis evaluating the association between direction and strength of recommendations, three AGREE II domains' scores (Rigor of development, Applicability and Editorial Independence) and pre-specified characteristics. Results We included 24 guidelines in our review. Nine recommended supplementations, eight suggested its use, and seven did not recommend it. AGREE II mean scores were 40.1% for "Rigor of development", 34.5% for "Applicability, and 39.6% for "Editorial independence". Guidelines with higher scores in these domains were less likely to recommend or suggest vitamin D supplementation (64% recommending against vs 29% suggesting for, and 27% recommending for; $p=0.002$, 52% vs 26% and 25%; $p=0.003$, 61% vs 35% and 24%; $p=0.001$, respectively). Guidelines with potential conflicts of interest were more likely to recommend or suggest vitamin D supplementation (likelihood ratio: $p=0.018$). Conclusions Policy makers, clinicians and patients should be aware that lower quality guidelines, and those reporting conflicts of interest are more likely to promote vitamin D supplementation. Guideline organizations should improve the quality of their recommendations' development, and the management of conflicts of interest. Users and editors should be aware of these findings when using and appraising guidelines.

Background

Vitamin D plays a vital role in several physiological processes(1–4). The best understood of these functions is calcium regulation, counter regulating parathyroid hormone secretion to maintain calcium serum levels(5) and fixing calcium absorption. It is predominantly synthesized via direct sunlight (ultraviolet B radiation) exposure(6), as it is limited to only a few natural sources(7) in human diet. Severe deficiency leads to rickets in children and osteomalacia in adults; its deficit has been associated with low bone mineral density(8), and increased risk of fractures(9).

Public health concerns about suboptimal vitamin D intake have led to the development of dietary and supplementation recommendations(10) in nutritional guidelines. However, the link between vitamin D intake and fracture risk is controversial(11). These recommendations were initially addressed to populations at risk of low sun exposure, particularly in northern latitudes(12). Early systematic reviews(13–15) showed a decrease in fractures among older institutionalized women, while more recent ones have demonstrated the absence of beneficial effect(16–22). Of note is the absence of randomized clinical trials in the general population to evaluate outcomes such as fractures, with only surrogate outcomes (e.g. bone mineral density and 25-hydroxycholecalciferol (25-OH-D)(23) being available. Vitamin D supplementation has not shown any effect in preventing cardiovascular disease or cancer(24–26), and high doses paradoxically, have been associated with an increase in falls in the elderly(27).

Another subject of debate is what constitutes vitamin D deficiency. While some studies declared epidemic proportions of deficiency(28), others have not confirmed these claims(10). Typically assessed with 25-OH-D serum levels, the threshold to maintain adequate bone health is also disputed(10).

Our aim is to review and analyze Vitamin D recommendations present in nutritional and clinical practice guidelines (CPGs) as well as potential related factors for these recommendations.

Methods

We searched Medline via PubMed, Guidelines.gov, the Guidelines International Network (G-I-N), and Trip Database. We conducted our search for CPGs published between January 2010 and January 2018. The full search strategy can be found in the **Supplementary File 1**.

Eligibility criteria

We included guideline publications, following the definition of the Institute of Medicine(29). We included guidelines that formulated recommendations for vitamin D intake, and/or screening for the general, healthy population. We excluded guidelines addressed to pediatric population (to prevent rickets), guidelines on specific conditions (e.g. chronic corticoid users), guidelines addressed to osteoporotic patients exclusively, or for secondary prevention of osteoporotic fractures.

Data extraction

We collected: year of publication, institution, region, target population, proposed vitamin D levels, calcium advice (if given), sun exposure advice, screening advice, fortification advice, suggested methods for vitamin D obtention, and supplementation recommendations. Three reviewers (DF, EN and JK) conducted screening, data extraction, and quality assessment. We resolved disagreements through discussion or with the help of another reviewer (PA). We classified the recommendations following the distinction that the Grading of Recommendations Assessment, Development and Evaluation (GRADE) provides(30) in three categories: "Recommends in favor", for unequivocal, strong recommendations; "Suggests in favor", for weak or conditional recommendations; and "Does not recommend", for guidelines which did not provided advice in favor or recommended against supplementation.

We also collected information concerning authors' potential conflicts of interest (COIs) and how these were managed. We focused on evaluating individual COIs reporting and the potential Institutional COIs in accordance with methodology implemented in previous evaluations(31,32). We recorded if organizations

addressed affiliation, financial and intellectual COIs in their report. We also collected the type of organization that formulated the recommendations and, if available, the institution's potential financial or advocacy COIs(32). Two reviewers (DF and CC) collected this data independently. In case of disagreement, we solved it by discussion and the help of a third reviewer (PA).

Quality appraisal

We used the AGREE II (Appraisal of Guidelines Research and Evaluation version 2)(33) instrument. This tool evaluates the methodological rigor and transparency with which a guideline is developed. We restricted our assessment to the Rigor of Development, Applicability, and Editorial Independence domains (**Supplementary Box 1**). AGREE II does not provide a “general” score of the guideline quality, hence, given the scope of our review, we focused on three specific subdomains for our quality appraisal. “Rigor of development” provides a rationale of the methodological strength of the guideline. “Applicability” addresses issues regarding the advice given on its recommendations’ implementation. Finally, besides our specific analysis of conflicts of interest, “Editorial independence” provided us additional information on this matter. After calibration, two researchers evaluated publications independently. We calculated the percentage of the maximum possible score for each domain, and its standardized range (from 0% to 100%).

Data analysis

We performed a descriptive analysis for each included guideline. We assessed the reproducibility of quantitative measurements made by different observers by calculating the intra-class correlation coefficients (ICC), and the associated 95% confidence intervals (CI) for each AGREE II domain. We conducted a bivariate analysis to evaluate the potential association between recommendations and AGREE II scores with the following factors: region, type of organization, target population, suggested method to obtain Vitamin D, advice on sun exposure, advice on fortifying strategies, and conflicts of interest. We included in our logistic regression model the results that remained significant in the bivariate analysis.

Results

The initial search yielded 491 references. Forty-five guidelines were selected for full text review and 24 guidelines were finally included in our analysis (**Figure 1**). Nine (38%) guidelines were from the USA or Canada, seven (29%) from Europe, four (16%) from Asia, two (8%) from Australia and New Zealand, and two (8%) from international organizations. By type of society: fourteen (56%) guidelines were developed by scientific societies, two (8%) by international governmental organizations, and nine (36%) by national governmental organizations.

Thirteen (54%) guidelines targeted general adult population, ten (42%) addressed older populations (≥ 50 years old), and one (4%) targeted pregnant women. Regarding vitamin D screening, eight (33%) guidelines recommended vitamin D screening to individuals with risk factors (e.g. dark skin or low sun exposure) (**Table 1** and **Table 2**).

Nine (38%) guidelines recommended in favor of some form of supplementation of vitamin D at some stage in life, seven (29%) suggested it, and eight (33%) did not recommend or recommended against supplementation. By population, eleven (46%) guidelines recommended or suggested supplementation for the general population, eight (33%) recommended supplementation for pediatric population, six (25%) recommended or suggested supplementation in pregnant women, and twenty-three (96%) recommended it for the elderly and institutionalized patients. The daily intake recommended varied from 400 International Units (IU) to 4000 IU (SD 621.33), the mode being 800 IU. (**Table 1** and **Table 2** and **Supplementary Table 1**).

With respect to vitamin D obtention, six guidelines (25%) highlighted the importance of sun exposure to achieve enough vitamin D levels. Twenty guidelines (83%) recommended supplementation as the favored method to obtain adequate vitamin D levels, two (8%) recommended sun exposure, and two guidelines (8%) did not provide a specific method. Five guidelines (21%) recommended vitamin D fortification strategies, either mandatory or voluntary. Regarding vitamin D screening, eight (33%) guidelines recommended vitamin D screening for individuals with risk factors.

In the subdomains of AGREE II evaluated (**Figure 2** and **Supplementary Table 1**), the mean score was 40.1% for Rigor of Development (range 10.4%-90.9%; Standard Deviation (SD): 23.5%), 34.5% for Applicability (range 12.5%-77.1%; SD: 18.1%), and 39.6% for Editorial Independence (range 8.3%-80.6%; SD: 19.8%). Six (25%) guidelines reached a score over 50% for Rigor of Development, Applicability, and Editorial Independence domains. The ICC was 0.954 (CI95% 0.887-0.980) for Rigor of Development, 0.91 (CI95% 0.815-0.96) for Applicability and 0.854 (CI95% 0.682-0.938) for Editorial Independence. See **Supplementary File 2** for the detailed score of the guidelines included.

Regarding conflicts of interest (COI) reporting, 19 out of 24 (79%) guidelines reported an explicit process to manage them, in two (8%) the process was unclear and four (17%) did not report any related information. Twenty three out of 24 (96%) reported affiliations, whereas 2 (8%) did not. In 19 out of 24 (79%) reported financial ties, two (8%) did not reported them clearly and four (17%) did not report them at all. Intellectual COI were reported in seven out of 24 guidelines (29%), with 18 (75%) not providing any information. Regarding institutional financial ties five guidelines (21%) reported them, thirteen (54%) did not provide any information, and seven (29%) were unclear. When examining if the institution potentially played an advocacy role favoring intervention, we detected this in five cases (21%), eight (33%) being unclear. Overall, we considered 15 out of 24 guidelines (63%) to have potential COIs (**Table 3**).

The guidelines that do not recommend vitamin D supplementation (compared with those that suggested or recommended it) scored significantly higher in the Rigor of Development domain (64% recommending against vs 29% suggesting, and 27% recommending for; $p=0.002$), Applicability (52% vs 26% and 25%;

p=0.003) and Editorial Independence (61% vs 35% and 24%; p=0.001) respectively. A post-hoc analysis showed no significant differences between the “suggest” and “recommend” categories.

Guidelines that provided recommendations in favor of vitamin D supplementation were associated with conflicts of interest, either detected or declared (likelihood ratio p=0.018). In the logistic regression model, Rigor of Development and Applicability were independent predictors of recommending vitamin D supplementation; the higher the score, the less likely supplementation was recommended Odds Ratio (OR) 1.11; CI95% 1.02-1.19 and OR 1.15; CI95% 1.03-1.28 respectively. With respect to vitamin D screening, we found a significant association between recommending screening and lower AGREE II scores for Rigor of Development, Applicability and Editorial Independence (50% vs 24% p=0.002; 41% vs 24% p=0.007; 46% vs 31% p=0.05).

Finally, guidelines that declared no conflicts of interest, and guidelines in which no conflicts of interest were detected scored significantly higher in “Rigor of Development”, “Applicability” and “Editorial independence” domains, compared to those guidelines that did not, or for which conflicts of interest were detected (54% vs 32% p=0.033; 48% vs 27% p=0.022, and; 51% vs 33% p=0.024). We did not find any other associations with respect to the rest of predefined variables.

Discussion

Our systematic assessment of vitamin D recommendations shows that despite the lack of conclusive evidence, most organizations recommend vitamin D supplementation for the general population. With a few exceptions, the guidelines included were generally of low quality. More importantly, those with lower scores or with conflicts of interest were more likely to recommend wider supplementation.

In general, our results resonate with previous AGREE II evaluations where low scores were reported for the majority of guideline topics(34–39). This finding could suggest that guideline development is not directly related to the quality of the underlying evidence. While the guidelines identified recommended population supplementation, the Institute of Medicine (IOM) landmark systematic report, recognized the low quality of the available evidence about vitamin D supplementation, favoring supplementation only in specific situations with minimum sun exposure(10). Paradoxically, this report is cited in most of the guidelines evaluated, to support strong recommendations towards supplementation. Furthermore, the IOM report acknowledged that the thresholds proposed by some organizations amplify the sense of an “epidemic of deficiency that does not correlate with epidemiological data”(10). By contrast, renowned organizations evaluated in our study, such as the National Osteoporosis Foundation, do not rate the quality of the evidence, nor the strength of the recommendations for populations with very different baseline risk (institutionalized vs community), and extrapolate effectiveness evidence from women to men. GRADE contemplates five exceptional situations in which a strong recommendation may be warranted in the face of low-quality evidence. For example, when it suggests benefit in a life-threatening situation(40). None of these apply for the situation we described.

Our results are also in agreement with previously reported ties between industry, advocacy and academia in this field(41,42). We provide much needed empirical observational evidence illustrating that conflicts of interest are associated with more interventionist recommendations. According to one systematic review about conflicts of interest in practice guidelines, the authors were not able to identify studies informing about the effect of COI on recommendations(43). Although our assessment is an indirect measure, the observed signal is significant, and is consistent with the expected direction(41,42).

Although we did not focus on pediatric guidelines, we detected population-level vitamin D supplementation recommendations for children, even when the incidence of rickets continues to be rare in the developed world, despite some reports of an increase(44,45). In developing countries, given that most of them are situated relatively close to the equator, which grants enough UVB sun exposure all year-round, putting emphasis on vitamin D rather than on correct nutrition seems a futile approach to child health care. Similarly, the World Health Organization, in their publication on vitamin D supplementation in pregnant women, acknowledges that adequate nutrition in pregnant women is best achieved through a healthy balanced diet(46). Supplementation or fortification may be justified in northern latitudes, especially in higher risk sub-populations such as dark-skinned individuals, people who do not spend enough time outdoors, and women who fully cover themselves for religious or cultural reasons(10).

Some additional concerns in the recommendations we evaluated were mostly based on the use of surrogate markers, such as bone mineral density or serum levels of 25-OH-D for defining vitamin D deficiency. This is problematic given that the correlation between intake, desirable serum levels and preventive effects is unclear(10). Also, despite the fact that there might be a potential beneficial effect of supplementation with calcium and vitamin D in specific subgroups, such as institutionalized elderly women(13), extrapolating supplementation to the general population is not necessarily straight forward. Especially when the certainty of evidence is low. Finally, there is also the potential risk for medicalization and the economic implications of testing and clinical appointments(47).

We encourage end users of recommendations to remain cautious when using recommendations in this field, especially those developed with unclear methods, those with potential conflicts of interest, and those targeting the general population. Recommendation developers should adhere to rigorous methods and use actionable, standardized language. We urge scientific societies and governmental organizations to adopt a cautionary approach when recommending preventive or screening interventions addressed to the general population. Lastly, organizations and journals should address conflicts of interest more transparently.

Limitations

We restricted our literature search to guideline repositories and Medline. However, most of the relevant guidelines are likely to have been captured, given how representative of published guidelines MEDLINE and the searched databases are. We did not perform a full AGREE II evaluation, but the direction and scoring of the domains analyzed were. However, this study had several strengths. To our knowledge, is the first systematic assessment of published guidelines that

inform about the effect of COI on recommendations. We performed our analysis using rigorous and transparent methods. The evaluation of the relationship of several pre-specified factors with more interventionist recommendations provides relevant information for developers, and users, including policy makers.

Conclusions

Vitamin D has been one of the most widely studied topics in medicine. Nonetheless, high quality, conclusive evidence about a net beneficial effect with its supplementation is lacking. The scientific community should probably start recognizing that vitamin D is not the “magic bullet” it appeared to be, and that its implication in physiological processes is likely to be tangential, rather than causal. Future research should probably be directed to improving lifestyles(48) rather than medicalizing healthy populations.

Abbreviations

AGREE II: Appraisal of Guidelines Research and Evaluation / Appraisal of Guidelines Research and Evaluation version 2

25-OH-D: 25-hydroxycholecalciferol

CPGs: Clinical Practice Guidelines

G-I-N: Guidelines International Network

GRADE: Grading of Recommendations Assessment, Development and Evaluation

COI: Conflicts of interest

ICC: Intra-class correlation coefficient

CI: Confidence interval

IU: International Units

SD: Standard deviation

OR: Odds Ratio

IOM: Institute of Medicine

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Availability and data material

All data generated or analyzed during this study are included in this published article (and its supplementary information files).

Competing interests:

The authors declare that they have no competing interests.

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Authors' contributions

DF contributed to design, data extraction, data analysis and wrote this manuscript. AL collaborated in design, helped with data analysis and collaborated in manuscript redaction. EN and EP collaborated in data extraction and manuscript redaction. CC and JK collaborated in data extraction. IG collaborated in data analysis and statistical advice. PA collaborated in design, data analysis and manuscript redaction.

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Tables

Table 1: Vitamin D recommendations in guidelines

GUIDELINE NAME, INSTITUTION	REGION	YEAR	TARGET POPULATION	VITAMIN D SUPPLEMENTATION	VITAMIN D SCREENING ADVICE	CALCIUM ADVICE	FAVOURED METHOD FOR VITAMIN D	SUN EXPOSITION ADVICE	FORTIF ADVI GIVEN VITAM
VITAMIN D FOR PREVENTION OF FALLS AND THEIR CONSEQUENCES IN OLDER ADULTS ¹ , AMERICAN GERIATRICS SOCIETY BUILDING HEALTHY BONES THROUGHOUT LIFE AN EVIDENCE-INFORMED STRATEGY TO PREVENT OSTEOPOROSIS IN AUSTRALIA ² , AUSTRALIA AND NEW ZEALAND BONE AND MINERAL SOCIETY & OSTEOPOROSIS AUSTRALIA OSTEOPOROSIS: DIAGNOSIS, TREATMENT, AND FRACTURE PREVENTION ³ , BRITISH COLUMBIA MEDICAL ASSOCIATION TAIWAN OSTEOPOROSIS PRACTICE GUIDELINES ⁴ , BUREAU OF HEALTH PROMOTION TAIWAN DUTCH DIETARY GUIDELINES 2015 / EVALUATION OF DIETARY REFERENCE VALUES FOR VITAMIN D ^{5,6} , HEALTH COUNCIL OF THE NETHERLANDS EVALUATION, TREATMENT, AND PREVENTION OF VITAMIN D DEFICIENCY: AN ENDOCRINE SOCIETY CLINICAL PRACTICE GUIDELINE ⁷ , ENDOCRINE SOCIETY VITAMIN D SUPPLEMENTATION IN ELDERLY OR POSTMENOPAUSAL WOMEN: A 2013 UPDATE OF THE 2008 RECOMMENDATIONS ⁸ , EUROPEAN SOCIETY FOR CLINICAL AND ECONOMIC ASPECTS OF OSTEOPOROSIS AND OSTEOARTHRITIS (ESCEO) DIETARY REFERENCE INTAKES FOR CALCIUM AND VITAMIN D ⁹ , INSTITUTE OF MEDICINE IOF POSITION STATEMENT: VITAMIN D RECOMMENDATIONS FOR OLDER ADULTS ¹⁰ , INTERNATIONAL OSTEOPOROSIS FOUNDATION OSTEOPOROSIS/FRACTURE PREVENTION NATIONAL GUIDELINE SUMMARY ¹¹ , KAISER PERMANENTE EVIDENCE-BASED GUIDELINES FOR FALL PREVENTION IN KOREA ¹² , KOREAN ASSOCIATION OF INTERNAL MEDICINE CALCIUM AND VITAMIN D SUPPLEMENTATIONS: 2015 POSITION STATEMENT OF THE KOREAN SOCIETY FOR BONE AND MINERAL RESEARCH ¹³ , KOREAN BONE SOCIETY FALLS: ASSESSMENT AND PREVENTION OF FALLS IN OLDER PEOPLE ¹⁴ , NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE (NICE) CLINICIAN'S GUIDE TO	North America	2014	Population older than 65	Recommends	With risk factors	No	Supplementation	No	No
	Oceania	2013	General population	Does not recommend*	With risk factors	Yes	Sun exposure	Yes	No
	North America	2011	General population	Recommends	No	No	Supplementation	No	No
	Asia	2011	General and older population	Suggests	No	Yes	Supplementation	No	No
	Europe	2015	General population	Suggests	No	Yes	Supplementation	Yes	No
	North America	2011	General population	Suggests	With risk factors	No	Supplementation	No	No
	Europe	2013	General population	Suggests	With risk factors	Yes	Supplementation	No	No
	North America	2011	General population	Does not recommend **	No	Yes	No method favoured	No	No
	International	2013	Population older than 60	Recommends	With risk factors	Yes	Supplementation	No	Yes:
	North America	2014	Population older than 50 and women	Recommends	No	Yes	Supplementation	No	No
	Asia	2017	Older population	Suggests	No	Yes	Supplementation	No	No
	Asia	2015	Population older than 50	Recommends	No	Yes	Supplementation	No	Yes:
	Europe	2013	Population older than 65	Does not recommend ***	No	Yes	No method favoured	No	Yes:

<p>PREVENTION AND TREATMENT OF OSTEOPOROSIS¹⁵, NATIONAL OSTEOPOROSIS FOUNDATION</p> <p>THE NATIONAL OSTEOPOROSIS FOUNDATION'S POSITION STATEMENT ON PEAK BONE MASS DEVELOPMENT AND LIFESTYLE FACTORS: A SYSTEMATIC REVIEW AND IMPLEMENTATION RECOMMENDATIONS¹⁶, NATIONAL OSTEOPOROSIS FOUNDATION</p> <p>OSTEOPOROSIS CLINICAL GUIDELINE FOR PREVENTION AND TREATMENT EXECUTIVE SUMMARY¹⁷, NATIONAL OSTEOPOROSIS GUIDELINE GROUP</p> <p>NORDIC NUTRITION RECOMMENDATIONS 2012: INTEGRATING NUTRITION AND PHYSICAL ACTIVITY¹⁸, NORDIC NUTRITION RECOMMENDATIONS</p> <p>VITAMIN D IN ADULT HEALTH AND DISEASE: A REVIEW AND GUIDELINE STATEMENT FROM OSTEOPOROSIS CANADA¹⁹, OSTEOPOROSIS CANADA</p> <p>PREVENTIVE ACTIVITIES IN WOMEN²⁰, PROGRAM OF PREVENTIVE ACTIVITIES IN PRIMARY CARE (PAPPS), SPANISH SOCIETY OF FAMILY MEDICINE</p> <p>CLINICAL GUIDELINE FOR THE PREVENTION AND TREATMENT OF OSTEOPOROSIS IN POSTMENOPAUSAL WOMEN AND OLDER MEN AND TREATMENT OF OSTEOPOROSIS IN POSTMENOPAUSAL WOMEN AND OLDER MEN²¹, ROYAL AUSTRALIAN COLLEGE OF GENERAL PRACTITIONERS</p> <p>SWISS FEDERAL COMMISSION RECOMMENDATIONS REGARDING VITAMIN D UPTAKE²², SWISS FEDERAL COMMISSION</p> <p>CLINICAL PRACTICE GUIDELINES FOR VITAMIN D IN THE UNITED ARAB EMIRATES²³, UNITED ARAB EMIRATES</p> <p>VITAMIN D AND CALCIUM SUPPLEMENTATION TO PREVENT FRACTURES IN ADULTS: U.S. PREVENTIVE SERVICES TASK FORCE RECOMMENDATION STATEMENT²⁴, UNITED STATES PREVENTIVE SERVICES TASK FORCE</p> <p>GUIDELINE: VITAMIN D SUPPLEMENTATION IN PREGNANT WOMEN²⁵, VITAMIN D SUPPLEMENTATION IN PREGNANT WOMEN, WORLD HEALTH ORGANISATION</p>	North America	2014	General population	Suggests	With risk factors	No	Supplementation	No	No
	North America	2016	General population	Suggests	No	Yes	Supplementation	No	No
	Europe	2016	Older population	Suggests	No	Yes	Supplementation	No	Yes
	Europe	2012	General population	Recommends	No	Yes	Supplementation	Yes	No
	North America	2010	General population	Recommends	With risk factors	Yes	Supplementation	Yes	No
	Europe	2014	Population older than 65	Does not recommend	No	Yes	Supplementation	Yes	No
	Oceania	2010	Postmenopausal women and older men	Does not recommend	No	Yes	Sun exposure	Yes	No
	Europe	2012	General population	Recommends	With risk factors	No	Supplementation	No	Yes
	Asia	2016	General population	Recommends	With risk factors	No	Supplementation	No	No
	North America	2013	Population older than 65	Does not recommend †	No	Yes	Supplementation	No	Yes
	International	2012	Pregnant women	Does not recommend	No	No	No method favoured	No	No

*Only consider the use of supplements if there is limited sun exposure. ** Establish dietary recommended intakes, specifies that it's assuming no sun exposure. No specific recommendation of supplements. ***Specifies that there is no conclusive evidence of fall prevention with vitamin D supplements. † It does not recommend supplements for preventing fractures but does it to prevent falls in older adults with high risk.

Table 2: Vitamin D supplementation per population.

NAME OF ORGANIZATION	TARGET POPULATION	PAEDIATRIC	ADULT	ELDER	WOMEN
AMERICAN GERIATRICS SOCIETY	Population older than 65			☐	
AUSTRALIA AND NEW ZEALAND BONE AND MINERAL SOCIETY & OSTEOPOROSIS AUSTRALIA	General population	☐	☐	☐	☐
BRITISH COLUMBIA MEDICAL ASSOCIATION	General population	☐	☐	☐	
BUREAU OF HEALTH PROMOTION TAIWAN	General and older population		☐	☐	
DUTCH HEALTH COUNCIL	General population	☐	☐	☐	
ENDOCRINE SOCIETY	General population	☐	☐	☐	☐
EUROPEAN SOCIETY FOR CLINICAL AND ECONOMIC ASPECTS OF OSTEOPOROSIS AND OSTEOARTHRITIS	General population	☐	☐	☐	☐
INSTITUTE OF MEDICINE	General population	☐	☐	☐	
INTERNATIONAL OSTEOPOROSIS FOUNDATION	Population older than 60			☐	
KAISER PERMANENTE	Population older than 50 and women			☐	☐
KOREAN ASSOCIATION OF INTERNAL MEDICINE	Population older than 65			☐	
KOREAN BONE SOCIETY	Population older than 50			☐	☐
NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE	Population older than 65			☐	
NATIONAL OSTEOPOROSIS FOUNDATION OSTEOPOROSIS PREVENTION GUIDELINE	General population		☐	☐	☐
NATIONAL OSTEOPOROSIS FOUNDATION PEAK BONE MASS RECOMMENDATIONS	General population		☐	☐	
NATIONAL OSTEOPOROSIS GUIDELINE GROUP	Older population			☐	
NORDIC NUTRITION RECOMMENDATIONS	General population		☐	☐	☐
OSTEOPOROSIS CANADA	General population		☐	☐	
SPANISH FAMILY MEDICINE SOCIETY	Population older than 65			☐	☐
ROYAL AUSTRALIAN COLLEGE OF GENERAL PRACTITIONERS	Postmenopausal women and older men			☐	☐
SWISS FEDERAL COMMISSION	General population	☐	☐	☐	
UNITED ARAB EMIRATES	General population	☐	☐	☐	☐
UNITED STATES PREVENTIVE SERVICES TASK FORCE	Population older than 65			☐	
WORLD HEALTH ORGANIZATION: VITAMIN D SUPPLEMENTATION IN PREGNANT WOMEN	Pregnant women		☐		☐

Table 3: Conflicts of interest reporting in guidelines.

GUIDELINE (INSTITUTION)	COI PROCESS REPORTING	COI REPORTING AFFILIATION	COI REPORTING FINANCIAL	COI REPORTING INTELLECTUAL	INSTITUTIONAL FINANCIAL	INSTITUTIONAL ADVOCATORY	OVERALL EVALUATION
THE NATIONAL OSTEOPOROSIS FOUNDATION'S POSITION STATEMENT ON PEAK BONE MASS DEVELOPMENT AND LIFESTYLE FACTORS: A SYSTEMATIC REVIEW AND IMPLEMENTATION RECOMMENDATIONS, NATIONAL OSTEOPOROSIS FOUNDATION VITAMIN D FOR PREVENTION OF FALLS AND THEIR CONSEQUENCES IN OLDER ADULTS, AMERICAN GERIATRICS SOCIETY OSTEOPOROSIS CLINICAL GUIDELINE FOR PREVENTION AND TREATMENT EXECUTIVE SUMMARY, NATIONAL OSTEOPOROSIS GUIDELINE GROUP EVALUATION, TREATMENT, AND PREVENTION OF VITAMIN D DEFICIENCY: AN ENDOCRINE SOCIETY CLINICAL PRACTICE GUIDELINE, ENDOCRINE SOCIETY IOF POSITION STATEMENT: VITAMIN D RECOMMENDATIONS FOR OLDER ADULTS, INTERNATIONAL OSTEOPOROSIS FOUNDATION VITAMIN D AND CALCIUM SUPPLEMENTATION TO PREVENT FRACTURES IN ADULTS: U.S. PREVENTIVE SERVICES TASK FORCE RECOMMENDATION STATEMENT, UNITED STATES PREVENTIVE SERVICES TASK FORCE PREVENTIVE ACTIVITIES IN WOMEN, PROGRAM OF PREVENTIVE ACTIVITIES IN PRIMARY CARE (PAPPS), SPANISH SOCIETY OF FAMILY MEDICINE NORDIC NUTRITION RECOMMENDATIONS 2012: INTEGRATING NUTRITION AND PHYSICAL ACTIVITY, NORDIC NUTRITION RECOMMENDATIONS DUTCH DIETARY GUIDELINES 2015 / EVALUATION OF DIETARY REFERENCE VALUES FOR VITAMIN D, HEALTH COUNCIL OF THE NETHERLANDS DIETARY REFERENCE INTAKES FOR CALCIUM AND VITAMIN D, INSTITUTE OF MEDICINE SWISS FEDERAL COMMISSION RECOMMENDATIONS REGARDING VITAMIN D UPTAKE, SWISS FEDERAL COMMISSION VITAMIN D SUPPLEMENTATION IN ELDERLY OR POSTMENOPAUSAL WOMEN: A 2013 UPDATE OF THE 2008 RECOMMENDATIONS, EUROPEAN SOCIETY FOR CLINICAL AND ECONOMIC ASPECTS OF OSTEOPOROSIS AND OSTEOARTHRITIS. BUILDING HEALTHY BONES THROUGHOUT LIFE AN EVIDENCE-INFORMED STRATEGY TO PREVENT OSTEOPOROSIS IN AUSTRALIA, AUSTRALIA AND NEW ZEALAND BONE AND MINERAL SOCIETY & OSTEOPOROSIS AUSTRALIA CALCIUM AND VITAMIN D SUPPLEMENTATIONS: 2015 POSITION STATEMENT OF THE KOREAN SOCIETY FOR BONE AND MINERAL RESEARCH, KOREAN BONE SOCIETY OSTEOPOROSIS: DIAGNOSIS, TREATMENT, AND FRACTURE PREVENTION, BRITISH COLUMBIA MEDICAL ASSOCIATION CLINICAL GUIDELINE FOR THE PREVENTION AND TREATMENT OF OSTEOPOROSIS IN POSTMENOPAUSAL WOMEN AND OLDER MEN AND TREATMENT OF OSTEOPOROSIS IN POSTMENOPAUSAL WOMEN AND OLDER MEN, ROYAL AUSTRALIAN COLLEGE OF GENERAL PRACTITIONERS TAIWAN OSTEOPOROSIS PRACTICE GUIDELINES, BUREAU OF HEALTH PROMOTION TAIWAN FALLS: ASSESSMENT AND PREVENTION OF FALLS IN OLDER PEOPLE, NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE (NICE) OSTEOPOROSIS/FRACTURE PREVENTION NATIONAL GUIDELINE SUMMARY, KAISER PERMANENTE GUIDELINE: VITAMIN D	Clear	No	Yes	No	Unclear	Yes	Detected
	Clear	Yes	Yes	No	Unclear		Detected
	Clear	No	Yes	No	Yes	Yes	Detected
	Clear	Yes	Yes	Yes	Yes		Detected
	Clear	No	Yes	No	Unclear	Yes	Detected
	Clear	Yes	Yes	Yes	No	No	Undetected
	Clear	No	Yes	No	Unclear	No	Undetected
	Not Reported	Not Reported	Not Reported	Not Reported	Not Reported	Not Reported	Not Reported
	Not Reported	Not Reported	Not Reported	Not Reported	Not Reported	Not Reported	Not Reported
	Unclear	Yes	No	No	No	No	Undetected
	Clear	No	Yes	No	No	Unclear	Detected
	Clear	Yes	Yes	No	Unclear	Yes	Detected
	Clear	No	Yes	No	Yes	Unclear	Detected
	Clear	No	Yes	No	Unclear	Unclear	Undetected
	Clear	No	Yes	No	Unclear	Unclear	Undetected
	Clear	Yes	Yes	Yes	No	No	Undetected
	Clear	No	Yes	Yes	No		Undetected
	Not Reported	Not Reported	Not Reported	Not Reported	Not Reported	Not Reported	Not Reported
	Clear	No	Yes	Yes	No	Unclear	Undetected

Clear	No	Yes	No	Yes	Unclear	Detected
Unclear	Yes	No	No	No	Unclear	Detected
Not Reported	Not Reported	Not Reported	Not Reported	Not Reported	Not Reported	Not Reported
Clear	Yes	Yes	No	Yes	Yes	Detected

Figures

Figure 1

PRISMA Flow chart

*Acronym / abbreviation correspondence with society and/or guidelines:

National Osteoporosis Foundation peak bone mass recommendations : **NOF (peak bone)**, National Osteoporosis Foundation Osteoporosis prevention Guideline: **NOF Osteoporosis**, International Osteoporosis Foundation: **IOF**, National Osteoporosis Guideline Group: **NOGG**, Endocrine Society: **Endocrine Soc**, United States Preventive Services Task Force: **USPSTF**, Program of Preventive activities in Primary Care (PAPPS): **PAPPS**, Dutch Health Council: **Dutch Health**, Institute of Medicine: **IOM**, Swiss Federal Commission: **Swiss Federal**, Nordic Nutrition Recommendations: **Nordic**, European society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis: **ESCEO**, Osteoporosis Australia: **Aus NZ**, Korean Bone Society: **Korean Bone**, Osteoporosis Canada: **Osteop Canada**, British Columbia Medical Association: **British Columbia**, Royal Australian College of General Practitioners: **Royal GPs Aus**, Bureau of health promotion Taiwan: **Taiwan**, National Institute for Health and Care Excellence: **NICE**, Kaiser permanente: **Kaiser**, World Health Organization: Vitamin D supplementation in pregnant women: **WHO**, Korean Association of Internal Medicine: **KAIM**, United Arab Emirates: **UAE**.

Figure 2

AGREE II domains in guidelines score by type of recommendation given

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