



Vitamin D recommendations in clinical guidelines: A systematic review, quality evaluation and analysis of potential predictors.

Journal:	<i>International Journal of Clinical Practice</i>
Manuscript ID	Draft
Wiley - Manuscript type:	Systematic Review
Date Submitted by the Author:	n/a
Complete List of Authors:	Fraile Navarro, David; Australian Institute of Health Innovation, Center for Health Informatics López-García-Franco, Alberto; Community of Madrid Madrid Health Service Niño de Guzmán, Ena; Centro Cochrane Iberoamericano Rabassa Bonet, Montserrat; Centro Cochrane Iberoamericano Zamanillo Campos, Rocio; IdISBa Pardo, Héctor; Centro Cochrane Iberoamericano Ricci-Cabello, Ignacio; IdISBa Canelo-Aybar, Carlos; Centro Cochrane Iberoamericano Meneses-Echavez, Jose F; Norwegian Institute of Public Health Yepes-Nuñez, Juan José; Universidad de los Andes Facultad de Medicina Kuindersma, Jesse; Universitair Medisch Centrum Groningen Department of Biomedical Sciences of Cells and Systems Gich, Ignasi; Centro Cochrane Iberoamericano Alonso, Pablo ; Centro Cochrane Iberoamericano
Specialty area:	

SCHOLARONE™
Manuscripts

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Title: Vitamin D recommendations in clinical guidelines: A systematic review, quality evaluation and analysis of potential predictors.

Authors: Fraile Navarro D, López-García-Franco A, Niño de Guzmán E, Rabassa M, Zamanillo Campos R, Pardo-Hernandez H, Ricci-Cabello I, Canelo-Aybar C, Meneses-Echavez JF, Yepes-Nuñez JJ, Kuindersma J, Gich-Saladich I, Alonso-Coello P.

Affiliations:

David Fraile Navarro, MD:
Health Centre Dr Mendiguchia Carriche, Leganes, Madrid (Spain)
Primary Care, Servicio Madrileño de Salud
Australian Institute of Health Innovation, Macquarie University, Sydney (Australia)

Alberto López García-Franco, MD:
Health Centre Dr Mendiguchia Carriche, Leganes, Madrid (Spain)
Primary Care, Servicio Madrileño de Salud

Ena Niño de Guzmán, MD:
Iberoamerican Cochrane Centre, Biomedical Research Institute Sant Pau (IIB-Sant Pau), Spain

Montserrat Rabassa, PhD:
Iberoamerican Cochrane Centre, Biomedical Research Institute Sant Pau (IIB-Sant Pau), Spain

Rocío Zamanillo Campos, RD, PhD:
Health Research Institute of the Balearic Islands (IdISBa), Balearic Islands (Spain)
Department of Health, Valencian International University (VIU), Valencia (Spain)
Balearic Islands Health Services, Primary Care Research Unit of Mallorca, Balearic Islands (Spain)

Héctor Pardo-Hernández, PhD:

Sant Pau Biomedical Research Institute (IIB Sant Pau), Barcelona (Spain)

CIBER Epidemiología y Salud Pública (CIBERESP), Barcelona (Spain)

Ignacio Ricci-Cabello, BSc, PhD

Health Research Institute of the Balearic Islands (IdISBa), Balearic Islands (Spain)

CIBER Epidemiología y Salud Pública (CIBERESP) (Spain)

Balearic Islands Health Services, Primary Care Research Unit of Mallorca, Balearic Islands (Spain)

Carlos Canelo-Aybar, MD:

Iberoamerican Cochrane Centre, Biomedical Research Institute Sant Pau (IIB-Sant Pau- CIBERESP), Barcelona, Spain Centro de Estudios Económicos y Sociales en Salud, Universidad San Ignacio de Loyola, Lima, Peru.

Jose F. Meneses-Echavez

Norwegian Institute of Public Health. Oslo, Norway.

Facultad de Cultura Física, Deporte y Recreación. Universidad Santo Tomás. Bogotá, Colombia.

Juan José Yepes-Nuñez, MD, MSc, PhD

School of Medicine

Universidad de los Andes, Bogotá, Colombia

Pulmonology Service, Internal Medicine Section

Fundación Santa Fe de Bogotá University Hospital, Bogotá, Colombia

Jesse Kuindersma, BSc:

Biomedical Sciences

University of Groningen, Groningen (Netherlands)

Ignasi Gich Saladich, MD, PhD:

Iberoamerican Cochrane Centre, Biomedical Research Institute Sant Pau (IIB-Sant Pau), Spain

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Universitat Autònoma de Barcelona (UAB), Bellaterra (Spain)
CIBER Epidemiología y Salud Pública (CIBERESP) (Spain)

Pablo Alonso-Coello, MD, PhD:
Iberoamerican Cochrane Centre, Biomedical Research Institute Sant Pau (IIB-Sant Pau), Spain
CIBER Epidemiología y Salud Pública (CIBERESP) (Spain)

Corresponding author:

David Fraile Navarro. Australian Institute of Health Innovation. Level 6 75 Talavera Road, Macquarie University, Sydney NSW 2109, Australia
Email: david.frailenavarro@hdr.mq.edu.au david.frailenavarro@gmail.com
Telephone: +61 (0) 492842669

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 three databases and two guideline repositories from 2010 onwards. 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, AGREE II domains' scores and pre-specified characteristics.

Results

We included 33 guidelines, 45.5% recommended, 27.3% suggested, and 27.3% did not recommend vitamin D supplementation. Guidelines that scored higher for "editorial independence" and "overall quality score" were less likely to recommend or suggest vitamin D supplementation (median 68.8 vs. 35.4; $p=0.001$), and median 58.3 vs. 37.5; $p=0.02$). Guidance produced by government organizations and those that reported source of funding were associated with higher AGREE II scores. Unclear role of source of funding was associated with recommending or suggesting vitamin D supplementation ($p=0.034$). Editorial independence was an independent

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

predictor for recommending or suggesting vitamin D supplementation (OR 1.1; CI95% 1 to 1.2; p=0.007).

Conclusions

Policymakers, 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.

Keywords:

Vitamin D, guidelines, quality appraisal, primary care, public health,

Review: Criteria:

- In our systematic review we analyse vitamin D clinical guidelines targeted at general population for primary prevention of fractures and/or general health.
- We searched three databases and two guideline repositories from 2010 onwards.
- We performed quality appraisal using the AGREE II tool and evaluated the association between direction and strength of recommendations, AGREE II scores, and reporting of conflicts of interest.

Message for the clinic:

- Lower quality guidelines, and those with unclear reporting of conflicts of interest, are more likely to recommend vitamin D supplementation.

- End-users should remain cautious of vitamin D recommendations, especially those recommending wider population supplementation, unclear methods or reporting of conflicts of interest.
- Guideline developers should adhere to rigorous methods, including the reporting and management of COI. Stakeholders should adopt a cautionary approach when recommending interventions aimed at the general population.

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Introduction

Vitamin D plays a vital role in several physiological processes [1–4]. The best understood function is calcium regulation, counter-regulating parathyroid hormone secretion to maintain calcium serum levels [5] and calcium absorption. It is predominantly synthesized via sunlight exposure [6], as it is limited to only a few natural sources [7] in the human diet. Deficiency has been associated with low bone mineral density (BMD) [8], an increased risk of fractures [9] in adults, and severe cases may lead to rickets and osteomalacia in children [10].

The association between vitamin D supplementation and fracture risk is controversial [11]. Supplementation recommendations were initially formulated for populations with low sun exposure, particularly in northern latitudes [12]. Despite, early systematic reviews [13–15] showing a decrease in fractures among older institutionalized women, no beneficial effects have been reported in more recent reviews [16–22]. Randomized clinical trials evaluating fracture risk in the general population are lacking, with studies usually reporting surrogate outcomes, such as BMD or 25-hydroxycholecalciferol (25-OH-D) levels [23]. Moreover, vitamin D supplementation has not been shown to prevent other outcomes, such as cardiovascular outcomes or cancer [24–26], and high doses (500,000 UI of cholecalciferol) have been associated with an increased risk of falls [27–29].

Another subject of debate is what constitutes vitamin D deficiency. While some studies declared epidemic proportions of deficiency [30], others have not confirmed these claims [31]. Typically assessed by 25-OH-D levels, the threshold to maintain adequate bone health remains controversial [31]. Some authors have also expressed concerns about the rigour of clinical guideline (CG) development process [32].

Public health concerns about suboptimal vitamin D blood levels have led to the development of dietary and supplementation recommendations [31]. The Institute of Medicine (IOM) defines guidelines as “statements that include recommendations, intended to optimize patient care, that are informed by a systematic review of evidence and an assessment of the benefits and harms of alternative care options” [33]. In this context, they allow discerning of which patients or populations may require vitamin D supplementation, in case of evidence of benefit.

Despite the relevance of this public health topic, there are no evaluations of the quality of vitamin D guidelines. Our aim is to review recommendations on vitamin D supplementation, assess their quality, and explore predictive factors.

1. Methods

1.1 Protocol and registration

We previously published the protocol [34]. We have adhered to the PRISMA checklist [35]. See **Supplementary File 1**.

2.2 Eligibility criteria

We included CGs, following the definition of the Institute of Medicine (IOM): “*statements that include recommendations intended to optimize patient care that are informed by a systematic review of evidence and an assessment of the benefits and harms of alternative care options.*” [33]. We included CGs that included recommendations for vitamin D supplementation and/or screening of vitamin D. We included those targeted to the general population, defined as individuals who are healthy and have no pre-existing conditions or comorbidities. CGs for the general

1

2

3

4

5

6

7

8

9

10

11

12

13

14

15

16

17

18

19

20

21

22

23

24

25

26

27

28

29

30

31

32

33

34

35

36

37

38

39

40

41

42

43

44

45

46

47

48

49

50

51

52

53

54

55

56

57

58

59

60

population that included thresholds or definitions of vitamin D deficiency were also included.

We excluded CGs for prevention of osteomalacia and rickets in children, those targeting specific conditions only (e.g. chronic corticoid users) and CGs focused only on secondary prevention of osteoporotic fractures. We also excluded nutritional guidelines if they only formulated daily reference intakes and that did not provide specific advice on how to achieve the recommended nutrient intake.

2.3 Search methods

We searched Medline (via PubMed), EMBASE, and CINAHL from January 2010 to January 2020. We also searched the Guidelines International Network (G-I-N) and the guidelinecentral.com libraries. Search strategies are provided in **Supplementary File 2**. We also searched the references of included CGs.

2.4 Study selection and data extraction

Title and abstract, full-text screening, and data extraction were performed independently by two reviewers. We resolved disagreements through discussion or with the help of a third reviewer.

2.5 Data extraction

We extracted details on institution, region, year of publication, type of organization, target population, purpose of supplementation, vitamin D status, recommendation of vitamin D supplementation, thresholds for deficiency or insufficiency, screening advice, monitoring, sun exposure, method to obtain vitamin D, vitamin D and calcium supplementation. We used the GRADE framework to

1
2
3 classify recommendations into three categories. The first is “Recommends” (for
4 unequivocal, strong recommendations, in favour of supplementation). The next is
5 “Suggests”, which is for weak or conditional recommendations (either for or against).
6
7 Lastly, “Does not recommend”, which is for guidelines which do not recommend in
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

We also collected information concerning authors’ conflicts of interest (COI). We evaluated COI reporting process and the potential role of the source of funding [37,38]. We collected six dimensions of COI; transparency of the reporting process, reporting of authors’ affiliations, financial and intellectual COI, and the role of the source of funding of the CG. Transparency of the reporting process and role of the source of funding were classified as “clear”, “unclear” or “not reported”, depending on how explicit these were in the CG or accompanying documents. For analysis, “not reported,” or “unclear” were combined into one category, as underreporting has been previously considered a potential source of COIs or bias [39].

2.6 Quality appraisal

We assessed the quality of the CGs using the AGREE II (Appraisal of Guidelines Research and Evaluation version 2) instrument [40]. AGREE II is a well-established tool to evaluate the methodological rigour and transparency through which a guideline is developed and has been used previously in systematic reviews of CGs [41]. After initial calibration four reviewers evaluated all included CGs independently. We calculated the percentage of the maximum possible score for each domain, and its standardized range (from 0% to 100%). To ensure inter-rater reliability, we compared the item scores of each appraiser. We considered there to be a low discrepancy if there were less than 1.5 standard deviations (SD), using the

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

McMaster’s AGREE II concordance calculator [42]. If there was large discrepancy, it was resolved with the help of a fifth reviewer. The AGREE II tool does not set a threshold for defining the quality of a CG. However, we considered a CG to be acceptable if a threshold of 60% in the “Rigour of development” domain and at least two additional domains was achieved for, in line with previous AGREE II evaluations [43–45].

2.7 Analysis

We performed a descriptive analysis of the main characteristics of included CGs. For each AGREE II domain, we calculated the mean score after converting them to percentages (being 0% the minimum possible score for the domain and 100% the maximum one). We calculated the mean, median, percentile 25, percentile 75 and SD. We conducted a bivariate analysis to evaluate the potential association between vitamin D supplementation recommendations with the following factors: AGREE II scores, region, type of organization, target population, suggested method to obtain Vitamin D, advice on sun exposure, advice on food and COI reporting. We also analysed how these factors were associated with the AGREE II scores. After initial analysis and given the asymmetry on the distribution of AGREE II scores, we used non-parametric tests to explore associations (Mann-Whitney U and Kruskal-Wallis test). After performing a bivariate analysis, the statistically significant variables ($p<0.05$) were incorporated into a multivariate logistic regression model using a forward-stepwise method. Our dependent variable in the logistic regression model was vitamin D supplementation recommendation. We used IBM SPSS Statistics® version 26 for running the analysis.

3 Results

3.1 Guidelines characteristics

The initial search yielded 561 references, 60 CGs were selected for full-text review, and 33 guidelines [46,47,56–65,48,66–75,49,76–78,50–55] were included in the final analysis (**Figure 1**). These included 11 (33.3%) guidelines from Europe, 10 (30.3%) from North America, five (15%) from Asia, two (6.1%) from Oceania, two (6.1%) from South America, and three (9.1%) from international organizations. The majority (22, 67%) of guidelines were developed by scientific societies, nine (28%) by governmental organizations, and two (6%) from other types of organizations. Eighteen (54.5%) guidelines targeted elderly populations, 14 (42.4%) were the general population, and one (3%) targeted women exclusively (**Table 1, Table 2**).

3.2 Recommendations of Vitamin D supplements for general population

Almost half of the included CGs (15, 45.5%) recommended in favour of vitamin D supplementation, nine (27.3%) suggested supplementation, nine (27.3%) did not recommend or recommended against supplementation, and none of the included CGs provided weak recommendations, “suggesting” against supplementation. Most CGs (32, 97%) targeted the elderly, 21 (63%), 17 (52%) the general population, and six (18%) targeted children. Regarding vitamin D status for recommending supplementation, 13 CGs (43.3%) did not specify it, ten (33.3%) recommended supplementation when risk factors and/or established deficiency were present, and seven (23.3%) only recommended supplementation in those with established deficiency. CGs thresholds used to define vitamin D sufficiency and maintain adequate bone health, ranged from 25 nmol/L to 125 nmol/L. In thirteen CGs (39.3%) values over 75 nmol/L were suggested, over 50 nmol/L in six (18.2%),

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

over 25-30 nmol/L in four (12.1%), and in ten (30.3%) the threshold was not specified. The daily dose suggested for supplementation ranged from 400 International Units (IU) to 2000 IU (SD 559, mode=800 IU). Twelve CGs (36.4%) supplemented for general health, a further 12 (36.4%) for prevention of falls or osteoporotic fractures, and nine (27.3%) for preventing osteoporosis (**Table 1, Table 2, Table 3, Supplementary Table 1**).

Eleven CGs (33.3%) highlighted the importance of sun exposure to achieve vitamin D requirements, whereas ten CGs (30.3%) advised on dietary sources. The preferred method to achieve adequate vitamin D levels was supplementation in most CGs (24, 72.7%) and only in four (12.1%) sun exposure was favoured. Five CGs (15.2%) did not provide a specific method to obtain vitamin D. Concurrent calcium intake advice was given in 21 (63.6%) of the CGs. (**Table 1, Table 2**).

3.3 Recommendations for Vitamin D screening and monitoring

Most CGs recommended against screening for general population (20/33, 60.6%). Twelve (36.3%) CGs recommended vitamin D screening for individuals with risk factors for fractures or osteoporosis. Only two (6.1%) CGs recommended general screening for their target population. With respect to the monitoring of Vitamin D levels, it was recommended in eight (57.1%) of those recommending screening. (**Table 1, Table 2**)

3.4 Quality appraisal

In the domains of AGREE II evaluated (**Figure 2A, Supplementary Table 2**), the mean score was 60% (SD 18.2%) for “scope and purpose”, 39.7% (SD 21.3%) for “stakeholder involvement”, 32.8% (SD 20.3%) for “rigour of development”, 59.4% (SD 18.4%) for “clarity and presentation”, 27.4% (SD 19%) for “applicability”, 42.1%

(SD 23.7%) for “editorial independence”, and 44.3% (SD 17.7%) for the “overall rating”. As part of the AGREE II appraisal, the reviewers recommended four of the guidelines analysed (12.1%)(57,63,66,79), twelve (36.4%) [47,48,75,76,49–51,55,59–61,71] were recommended with modifications, and seventeen (51.5%) [46,52,69,70,72–74,77,78,53,54,56,58,62,64,67,68] were not recommended for use. Only three guidelines (9%) scored over 60% in “Rigour of development domain” and are considered high-quality. See **Supplementary Table 1** for the detailed AGREE II scores.

3.5 Conflicts of Interest reporting

Reporting of the COI management process was unclear in 18 CGs (54.5%), in ten (30.3%) it was not reported, and in 5 (7.2%) guidelines, the process was clear. Eleven (33.3%) reported panellists’ affiliations, whereas 22 (66.6%) did not. Fifteen (45.5%) reported financial ties, 9 (27.3%) did not report them clearly, and 9 (27.3%) did not report them at all. Intellectual COI were reported in seven (21.2%), with 18 (54.5%) not providing any information. The role of the source of funding was reported in just over half of the CGs (18/33; 54.5%), in nine (27.3%) was unclear, and only in six (18.2%), it was considered clear. (**Table 4**).

3.6 Associations between supplementation recommendations and predictors

Guidelines that did not recommend vitamin D supplementation (compared with those that suggested or recommended it) scored significantly higher in the “overall score” (median 58.3 vs 37.5 ($p=0.02$), and in “editorial independence” (median 68.8 vs 35.4 ($p=0.001$)) domains of the AGREE-II tool (**Figure 2B**). We did

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

not find significant differences (post-hoc analysis) between the “suggest” and “recommend” categories in both domains.

Regarding the type of organization, governmental sponsored guidelines scored significantly higher than scientific societies and other organizations in three domains and overall score (“scope and purpose”, $p=0.049$; “stakeholder involvement” $p=0.046$, “rigour of development” $p=0.02$, and “overall score” $p=0.009$).

When comparing the role of the source of funding, guidelines that reported this aspect scored significantly higher in “Scope and purpose” ($p=0.039$) and “Overall score” ($p=0.04$). Guidelines that reported COI scored significantly higher in “Rigour of development” ($p=0.012$), “Clarity and presentation” ($p=0.022$), “Editorial independence” ($p=0.002$) domains, and overall score ($p=0.029$). Guidelines that did not report financial COI scored significantly lower in the “Editorial independence” domain ($p=0.001$). Guidelines in which the role of the funding source was unclear or not reported were also associated with recommending or suggesting supplementation ($p=0.034$). Associations between COI reporting and Editorial Independence would be expected given that these measurements overlap between the AGREE-II and the additional COI evaluation we performed.

In the forward stepwise logistic regression model, “Editorial independence” remained an independent predictor for recommending vitamin D supplementation (Odds Ratio: 1.092; CI 95%, 1.02-1.16; $p=0.007$); the lower the score, the more likely supplementation was recommended. The rest of the predictors explored (AGREE Overall score, COI reporting process, Intellectual COI reporting, Funding source reporting and Screening for Vitamin D) were not included in the final model.

4 Discussion

4.1 Main findings

Our systematic review shows that, with only a few exceptions, CGs were rated as low quality. Those with lower quality scores, unclear COI reporting and management processes, or where the role of the funding source was unclear or not reported, were more likely to recommend or suggest in favour vitamin D supplementation. There was also substantial variability in the recommendations for the general population, with the majority of organizations recommending in favour but some recommending against. The majority of the guidelines recommended against screening for vitamin D deficiency.

4.2 Our results in the context of previous research

The results of our review are in line with previous AGREE II evaluations in which low scores were reported for nutritional guidelines [41,80] as well as for other topics [81–86]. Previous studies detected methodological flaws when appraising evidence to formulate recommendations in nutritional guidelines [80]. Our evaluation also shows that renowned osteoporosis organizations do not fulfil basic criteria in the guideline development process, such as rating the quality of the evidence or grading the strength of the recommendations in the guideline development process. Furthermore, they made no distinction between populations with very different baseline risks.

Our results are in agreement with previously reported ties between industry, advocacy and academia in this field [32,87]. However, we provide empirical evidence that COI are associated with more interventionist recommendations. In a systematic

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

review on COI in CGs, the authors could not identify studies informing the link between COI and recommendations [88].

Vitamin D supplementation or dietary 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 [31]. Most guidelines that we identified acknowledge these issues but do not make specific recommendations for these subgroups.

In 2011, the IOM published a landmark report that aimed to establish dietary reference intakes for vitamin D [31]. To date, it is still considered the most comprehensive and extensive study on vitamin D effects. This review recognized the low quality of available evidence about vitamin D supplementation, favouring supplementation only in specific situations where there is inadequate sun exposure [31]. Paradoxically, this report is cited in most of the guidelines evaluated to support strong recommendations in favour of supplementation. GRADE details some exceptional situations in which a strong recommendation may be warranted in the face of low-quality evidence [36]. However, none of these situations applies here. Finally, the IOM report acknowledged that the thresholds proposed by some organizations are exacerbated by an “epidemic of deficiency that does not correlate with epidemiological data” [31]. In addition to the IOM, the European Food Safety Authority (EFSA) and the UK Scientific Advisory Committee on Nutrition (SACN) produced as well updated reports on vitamin D(89,90). Although the EFSA takes a stance similar to the IOM, the SACN recommends that the government gives consideration to strategies for the UK population to achieve the RNI of 10 µg/d (400 IU/) [90].

Recommendations for vitamin D supplementation in wide population groups were based primarily on the use of surrogate markers, such as bone mineral density or serum levels of 25-OH-D [91]. This is particularly problematic given that the correlation between intake, desirable serum levels and preventive effects is unclear [31]. Despite a potential benefit of supplementation of vitamin D and calcium in specific subgroups, such as institutionalized older women [13], extrapolating this supplementation to the general population is inappropriate. Additional concerns have been raised regarding how representative of the overall population are the participants included in vitamin D trials [92]. Finally, there are economic implications for wide-spread testing [93] and supplementation, including the risk for over-medicalization. For instance, in our local context of the Madrid region (Spain), there was an increase of 1,154% (from € 535,807 to € 6,719,710) in the prescription of vitamin D, and a 2,456% increase in the laboratory testing of 25-OH-D blood levels, in the period of 2009 to 2018 [94]. However, during the same period, the incidence of hip fracture has not varied [94].

4.3 Limitations and strengths

We performed a search in three relevant medical databases and the G-I-N database; however, since the closure of guidelines.gov, there is no specific source that systematically compiles guidelines. To minimize this limitation, some of the guidelines analyzed were retrieved after snowballing. We have only included guidelines published in English or Spanish. However, we captured guidelines from all continents and not only from Spanish or English-speaking countries. We only excluded a small number of guidelines not published in these languages, and it is unlikely that these guidelines would be inconsistent with our results.

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

This review had several strengths. To our knowledge, it is the first systematic assessment of vitamin D recommendations in published CGs. We also explored for the first time the effect of COI reporting on vitamin D recommendations. We performed our analysis using rigorous and transparent methods. Evaluation of several pre-specified factors with more interventionist recommendations provides relevant information for stakeholders.

4.4 Implications for practice and research

Vitamin D is one of the most widely studied topics in medicine. However, its use in the general population remains controversial, and this is reflected in the variability of recommendations. We encourage end-users to remain cautious of vitamin D recommendations, especially those developed with unclear methods reporting, or management of COI, or those recommending wide general population screening or supplementation. Guideline developers should adhere to rigorous methods, including the reporting and management of COI. Finally, we urge scientific societies and government organizations to adopt a cautionary approach when recommending preventive or screening interventions aimed at the general population.

List of abbreviations

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

25-OH-D: 25-hydroxycholecalciferol

CGs: Clinical 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

IOM: Institute of Medicine

Declarations

Ethics approval and consent to participate

Not applicable

Consent for publication

Not applicable

Availability and data materials

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

Competing interests

RZC has received a grant been hired by the Health Research Institute of the Balearic Islands (IdISBa) thanks to the joint financing of 4 enteral nutrition companies (Nestlé, Abbot, Fresenius, and Nutricia) between September 2018 and July 2019. Also, she received a travel payment to attend a day long course by Nutricia on 2019.

ALG and PAC are authors of one of the guidelines analysed in this review(1). To maintain objectivity in the data extraction and quality appraisal process, they did not participate on this part of the study or in any other that implied analysing the guideline they authored. They do not declare any financial conflict of interest regarding this subject.

The rest of the authors declare no conflicts of interest.

Reference:

1. García-Franco AL, Fernández JAB, Muñoz EB, Piñeiro MJ, del Cura González I, Del Moral AO, et al. Actividades preventivas en la mujer. Actualización PAPPS 2018. Atención Primaria. 2018;50(Suppl 1):125.

Authors' contributions

We confirm that all listed authors meet ICMJE authorship criteria and that nobody who qualifies for authorship has been excluded.

(DFN) David Fraile Navarro: Conceptualization, Investigation, Data curation, Formal analysis, Methodology, Project administration, writing - original draft, writing review and editing, Approval of article.

(ALG) Alberto López-García-Franco: Conceptualization, Methodology, writing – review and editing, Approval of article.

(ENG) Ena Niño de Guzmán: Conceptualization, Investigation, writing – review and editing, Approval of article.

(MR) Montserrat Rabassa: Methodology, Investigation, writing – review and editing, Approval of article.

(RZC) Rocio Zamanillo Campos: Conceptualization, Investigation, writing – review and editing, Approval of article.

(HPH) Héctor Pardo-Hernandez: Investigation, writing – review and editing, Approval of article.

(IRC) Ignacio Ricci-Cabello: Investigation, writing – review and editing, Approval of article.

(CCA) Carlos Canelo-Aybar: Investigation, writing – review and editing, Approval of article.

(JFME) Jose Francisco Meneses-Echavez: Investigation, writing – review and editing, Approval of article.

(JJYN) Juan Jose Yepes-Nuñez: Investigation, writing – review and editing, Approval of article.

(JK) Jesse Kuindersma: Investigation, writing – review and editing, Approval of article.

(IGS) Ignasi Gich-Saladich: Formal analysis, writing – review and editing (equal), Approval of article.

(PAC) Pablo Alonso-Coello: Supervision, Methodology, Conceptualization, writing – review and editing, Approval of article.

Authors' information (optional)

Not applicable

Funding statement

This project was not funded.

Acknowledgements

We want to acknowledge Saskia Cheyne for English language correction and proof-reading. Pablo Alonso-Coello was supported by a Miguel Servet investigator contract from the Instituto de Salud Carlos III (CPII15/0034). Montserrat Rabassa is funded by a Sara Borrell post-doctoral contract (CD16/00157) from the Carlos III Institute of Health and the European Social Fund (ESF).

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Bibliography:

1. Rosen CJ, Adams JS, Bikle DD, Black DM, Demay MB, Manson JE, et al. The Nonskeletal Effects of Vitamin D: An Endocrine Society Scientific Statement. Endocr Rev [Internet]. 2012 Jun 17;33(3):456–92. Available from: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3365859/>
2. Theodoratou E, Tzoulaki I, Zgaga L, Ioannidis JPA. Vitamin D and multiple health outcomes: umbrella review of systematic reviews and meta-analyses of observational studies and randomised trials. BMJ [Internet]. 2014 Jan 1 [cited 2016 Jul 8];348(apr01_2):g2035. Available from: <http://www.bmj.com/content/348/bmj.g2035>
3. Martineau AR, Jolliffe DA, Hooper RL, Greenberg L, Aloia JF, Bergman P, et al. Vitamin D supplementation to prevent acute respiratory tract infections: systematic review and meta-analysis of individual participant data. BMJ [Internet]. 2017;356. Available from: <http://www.bmj.com/content/356/bmj.i6583>
4. Castro M, King TS, Kunselman SJ, Cabana MD, Denlinger L, Holguin F, et al. Effect of Vitamin D₃ on Asthma Treatment Failures in Adults With Symptomatic Asthma and Lower Vitamin D Levels. JAMA [Internet]. 2014 May 28 [cited 2017 Apr 6];311(20):2083. Available from: <http://jama.jamanetwork.com/article.aspx?doi=10.1001/jama.2014.5052>
5. Suda T, Shinki T, Kurokawa K. The mechanisms of regulation of vitamin D metabolism in the kidney. Curr Opin Nephrol Hypertens [Internet]. 1994 Jan [cited 2018 Jan 15];3(1):59–64. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/7850413>
6. Webb AR, Engelsen O. Calculated Ultraviolet Exposure Levels for a Healthy

- Vitamin D Status. Photochem Photobiol [Internet]. 2006 [cited 2017 Jun 2];82(6):1697. Available from: <http://doi.wiley.com/10.1562/2006-09-01-RA-670>
7. Bischoff-Ferrari HA, Keller U, Burckhardt P, Löttscher KQ, Gerber B, l'Allemand D, et al. Recommandations de la Commission fédérale de l'alimentation concernant l'apport de vitamine D. In: Forum Med Suisse. 2012. p. 775–8.
 8. Wacker M, Holick MF. Vitamin D—Effects on Skeletal and Extraskkeletal Health and the Need for Supplementation. Nutrients [Internet]. 2013 Jan 10;5(1):111–48. Available from: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3571641/>
 9. Cummings SR, Browner WS, Bauer D, Stone K, Ensrud K, Jamal S, et al. Endogenous hormones and the risk of hip and vertebral fractures among older women. N Engl J Med. 1998;339(11):733–8.
 10. Uday S, Höglér W. Nutritional rickets and osteomalacia in the twenty-first century: revised concepts, public health, and prevention strategies. Curr Osteoporos Rep. 2017;15(4):293–302.
 11. Bolland MJ, Grey A, Gamble GD, Reid IR. Vitamin D supplementation and falls: a trial sequential meta-analysis. lancet Diabetes Endocrinol. 2014;2(7):573–80.
 12. Webb AR, Kline L, Holick MF. Influence of Season and Latitude on the Cutaneous Synthesis of Vitamin D3: Exposure to Winter Sunlight in Boston and Edmonton Will Not Promote Vitamin D3 Synthesis in Human Skin*. J Clin Endocrinol Metab. 1988;67(2):373–8.
 13. Chapuy MC, Arlot ME, Duboeuf F, Brun J, Crouzet B, Arnaud S, et al. Vitamin D3 and calcium to prevent hip fractures in elderly women. N Engl J Med. 1992;327(23):1637–42.
 14. Tang BMP, Eslick GD, Nowson C, Smith C, Bensoussan A. Use of calcium or

calcium in combination with vitamin D supplementation to prevent fractures and bone loss in people aged 50 years and older: a meta-analysis. *Lancet*. 2007;370(9588):657–66.

15. Bischoff-Ferrari HA, Dawson-Hughes B, Staehelin HB, Orav JE, Stuck AE, Theiler R, et al. Fall prevention with supplemental and active forms of vitamin D: a meta-analysis of randomised controlled trials. *Bmj*. 2009;339:b3692.

16. Chung M, Balk EM, Brendel M, Ip S, Lau J, Lee J, et al. Vitamin D and calcium: a systematic review of health outcomes. *Evid Rep Technol Assess* (Full Rep) [Internet]. 2009 Aug [cited 2019 Aug 30];(183):1–420. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/20629479>

17. Bolland MJ, Grey A, Gamble GD, Reid IR. The effect of vitamin D supplementation on skeletal, vascular, or cancer outcomes: a trial sequential meta-analysis. *lancet Diabetes Endocrinol*. 2014;2(4):307–20.

18. Chung M, Lee J, Terasawa T, Lau J, Trikalinos TA. Vitamin D with or without calcium supplementation for prevention of cancer and fractures: an updated meta-analysis for the US Preventive Services Task Force. *Ann Intern Med*. 2011;155(12):827–38.

19. Roth DE, Leung M, Mesfin E, Qamar H, Watterworth J, Papp E. Vitamin D supplementation during pregnancy: state of the evidence from a systematic review of randomised trials. *bmj*. 2017;359:j5237.

20. Zhao J-G, Zeng X-T, Wang J, Liu L. Association Between Calcium or Vitamin D Supplementation and Fracture Incidence in Community-Dwelling Older Adults. *JAMA* [Internet]. 2017 Dec 26 [cited 2017 Dec 28];318(24):2466. Available from: <http://jama.jamanetwork.com/article.aspx?doi=10.1001/jama.2017.19344>

21. Bolland MJ, Grey A, Avenell A. Effects of vitamin D supplementation on musculoskeletal health: a systematic review, meta-analysis, and trial sequential analysis. *Lancet Diabetes Endocrinol*. 2018;6(11):847–58.
22. Yao P, Bennett D, Mafham M, Lin X, Chen Z, Armitage J, et al. Vitamin D and calcium for the prevention of fracture: a systematic review and meta-analysis. *JAMA Netw open*. 2019;2(12):e1917789–e1917789.
23. Bischoff-Ferrari HA, Dietrich T, Orav EJ, Dawson-Hughes B. Positive association between 25-hydroxy vitamin D levels and bone mineral density: a population-based study of younger and older adults. *Am J Med*. 2004;116(9):634–9.
24. Scragg R, AW S, Waayer D, al et. Effect of monthly high-dose vitamin d supplementation on cardiovascular disease in the vitamin d assessment study : A randomized clinical trial. *JAMA Cardiol [Internet]*. 2017 Apr 5; Available from: <http://dx.doi.org/10.1001/jamacardio.2017.0175>
25. Manson JE, Bassuk SS, Buring JE. Vitamin D, Calcium, and Cancer: Approaching Daylight?Vitamin D, Calcium, and CancerEditorial. *JAMA [Internet]*. 2017 Mar 28;317(12):1217–8. Available from: <https://doi.org/10.1001/jama.2017.2155>
26. Lappe J, Watson P, Travers-Gustafson D, Recker R, Garland C, Gorham E, et al. Effect of Vitamin D and Calcium Supplementation on Cancer Incidence in Older Women. *JAMA [Internet]*. 2017 Mar 28 [cited 2017 Apr 6];317(12):1234. Available from: <http://jama.jamanetwork.com/article.aspx?doi=10.1001/jama.2017.2115>
27. Sanders KM, Stuart AL, Williamson EJ, Simpson JA, Kotowicz MA, Young D, et al. Annual high-dose oral vitamin D and falls and fractures in older women: a

randomized controlled trial. *Jama*. 2010;303(18):1815–22.

28. Bischoff-Ferrari HA, Dawson-Hughes B, Orav EJ, Staehelin HB, Meyer OW, Theiler R, et al. Monthly high-dose vitamin D treatment for the prevention of functional decline: a randomized clinical trial. *JAMA Intern Med*. 2016;176(2):175–83.

29. McCullough P, Amend J. Results of daily oral dosing with up to 60,000 international units (iu) of vitamin D3 for 2 to 6 years in 3 adult males. *J Steroid Biochem Mol Biol*. 2017;173:308–12.

30. Holick MF. High prevalence of vitamin D inadequacy and implications for health. *Mayo Clin Proc [Internet]*. 2006 Mar 1 [cited 2017 Jan 5];81(3):353–73. Available from: <http://www.mayoclinicproceedings.org/article/S0025619611614651/fulltext>

31. Ross AC, Taylor CL, Yaktine AL, Del Valle HB. Dietary reference intakes for calcium and vitamin D. National Academies Press; 2011.

32. Grey A, Bolland M. Web of industry, advocacy, and academia in the management of osteoporosis. *Bmj [Internet]*. 2015;3170(July):h3170. Available from: <http://www.bmj.com/lookup/doi/10.1136/bmj.h3170>

33. Institute of Medicine (US) Committee on Standards for Developing Trustworthy Clinical Practice Guidelines, Graham R, Mancher M, Wolman DM, Greenfield S, Steinberg E. Clinical Practice Guidelines We Can Trust [Internet]. Clinical Practice Guidelines We Can Trust. National Academies Press (US); 2011 [cited 2019 Aug 30]. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/24983061>

34. Fraile Navarro D, Lopez-Garcia-Franco A, Nino de Guzman E, Pardo-Hernandez H, Canelo-Aybar C, Gich-Saladich I, et al. Vitamin D

- recommendations in nutritional guidelines: Protocol for a systematic review, quality evaluation using AGREE-2 and analysis of potential predictors. medRxiv [Internet]. 2020 Jan 1;2020.04.06.20055962. Available from: <http://medrxiv.org/content/early/2020/04/10/2020.04.06.20055962.abstract>
35. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *Ann Intern Med*. 2009;151(4):264–9.
36. Schünemann H, Brozek J, Oxman A. GRADE handbook for grading quality of evidence and strength of recommendation. GRADE Work Gr. 2009;
37. Erickson J, Sadeghirad B, Lytvyn L, Slavin J, Johnston BC. The scientific basis of guideline recommendations on sugar intake: A systematic review. *Ann Intern Med*. 2017;166(4):257–67.
38. Hakoum MB, Anouti S, Al-Gibbawi M, Abou-Jaoude EA, Hasbani DJ, Lopes LC, et al. Reporting of financial and non-financial conflicts of interest by authors of systematic reviews: a methodological survey. *BMJ Open*. 2016;6(8):e011997.
39. Bindslev JBB, Schroll J, Gøtzsche PC, Lundh A. Underreporting of conflicts of interest in clinical practice guidelines: cross sectional study. *BMC Med Ethics* [Internet]. 2013 May;14(1):19. Available from: <http://dx.doi.org/10.1186/1472-6939-14-19>
40. Brouwers MC, Kho ME, Browman GP, Burgers JS, Cluzeau F, Feder G, et al. AGREE II: advancing guideline development, reporting and evaluation in health care. *CMAJ* [Internet]. 2010 Dec 14 [cited 2017 Jan 3];182(18):E839-42. Available from: <http://www.cmaj.ca/content/182/18/E839.short>
41. Rabassa M, Ruiz SG-R, Solà I, Pardo-Hernandez H, Alonso-Coello P, García

- LM. Nutrition guidelines vary widely in methodological quality: an overview of reviews. *J Clin Epidemiol*. 2018;104:62–72.
42. McMaster University. AGREE II Rater Concordance Calculator [Internet]. Available from: <http://fhswedge.csu.mcmaster.ca/ceftp/qasite/AGREEIIRaterConcordanceCalculator.html>
43. Smith CAM, Toupin-April K, Jutai JW, Duffy CM, Rahman P, Cavallo S, et al. A systematic critical appraisal of clinical practice guidelines in juvenile idiopathic arthritis using the appraisal of guidelines for research and evaluation II (AGREE II) instrument. *PLoS One*. 2015;10(9).
44. Brosseau L, Rahman P, Toupin-April K, Poitras S, King J, De Angelis G, et al. A systematic critical appraisal for non-pharmacological management of osteoarthritis using the appraisal of guidelines research and evaluation II instrument. *PLoS One*. 2014;9(1).
45. Shallwani SM, King J, Thomas R, Thevenot O, De Angelis G, Aburub A, et al. Methodological quality of clinical practice guidelines with physical activity recommendations for people diagnosed with cancer: A systematic critical appraisal using the AGREE II tool. *PLoS One*. 2019;14(4).
46. American Geriatrics Society. American Geriatrics Society Consensus Statement: Vitamin D for Prevention of Falls and their Consequences in Older Adults. American Geriatrics Society; 2013.
47. Ebeling PR, Daly RM, Kerr DA, Kimlin MG. Building healthy bones throughout life: an evidence-informed strategy to prevent osteoporosis in Australia. *Med J Aust* [Internet]. 2013 Oct 7 [cited 2018 Aug 21];199(7 Suppl):S1. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/25370432>

- 1
2
3 48. British Columbia Medical Association. Osteoporosis: diagnosis, treatment, and
4 fracture prevention. [Internet]. Rockville MD: Agency for Healthcare Research
5 and Quality (AHRQ); 2011. Available from:
6 [http://www.guideline.gov/content.aspx?id=34286&search=%22calcium%22+an](http://www.guideline.gov/content.aspx?id=34286&search=%22calcium%22+and+%22vitamin+d%22)
7 [d+%22vitamin+d%22](http://www.guideline.gov/content.aspx?id=34286&search=%22calcium%22+and+%22vitamin+d%22)
8
9
- 10 49. Bureau of Health Promotion Taiwan. Taiwan osteoporosis practice guidelines.
11 [Internet]. Rockville MD: Agency for Healthcare Research and Quality (AHRQ);
12 Available from:
13 [http://www.guideline.gov/content.aspx?id=39382&search=%22calcium%22+an](http://www.guideline.gov/content.aspx?id=39382&search=%22calcium%22+and+%22vitamin+d%22)
14 [d+%22vitamin+d%22](http://www.guideline.gov/content.aspx?id=39382&search=%22calcium%22+and+%22vitamin+d%22)
15
16
- 17 50. Kromhout D, Spaaij CJK, De Goede J, Weggemans RM. The 2015 Dutch
18 food-based dietary guidelines. *Eur J Clin Nutr.* 2016;70(8):869.
19
20
- 21 51. Holick MF, Binkley NC, Bischoff-Ferrari HA, Gordon CM, Hanley DA, Heaney
22 RP, et al. Evaluation, treatment, and prevention of vitamin D deficiency: an
23 Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab.*
24 2011;96(7):1911–30.
25
26
- 27 52. Rizzoli R, Boonen S, Brandi M-L, Bruyère O, Cooper C, Kanis JA, et al.
28 Vitamin D supplementation in elderly or postmenopausal women: a 2013
29 update of the 2008 recommendations from the European Society for Clinical
30 and Economic Aspects of Osteoporosis and Osteoarthritis (ESCEO). *Curr Med*
31 *Res Opin* [Internet]. 2013 Apr 15 [cited 2016 Jun 17];29(4):305–13. Available
32 from:
33 <http://www.tandfonline.com/doi/abs/10.1185/03007995.2013.766162#.V2OqCt>
34 [KLTZ4](http://www.tandfonline.com/doi/abs/10.1185/03007995.2013.766162#.V2OqCt)
35
36
- 37 53. Dawson-Hughes B, Mithal A, Bonjour J-P, Boonen S, Burckhardt P, Fuleihan
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

- GE-H, et al. IOF position statement: vitamin D recommendations for older adults. *Osteoporos Int* [Internet]. 2010 Jul [cited 2016 Apr 28];21(7):1151–4. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/20422154>
54. Kaiser Permanente. Osteoporosis Screening, Diagnosis, and Treatment Guideline. 2019;
55. Kim K-I, Jung H-K, Kim CO, Kim S-K, Cho H-H, Kim DY, et al. Evidence-based guidelines for fall prevention in Korea. *Korean J Intern Med*. 2017;32(1):199–210.
56. Kim KM, Choi HS, Choi M-J, Chung HY. Calcium and Vitamin D Supplementations: 2015 Position Statement of the Korean Society for Bone and Mineral Research. *J bone Metab* [Internet]. 2015 Nov 1 [cited 2016 Apr 2];22(4):143–9. Available from: <http://e-jbm.org/DOIx.php?id=10.11005/jbm.2015.22.4.143>
57. National Institute for Healthcare Excellence (NICE). Assessment and prevention of falls in older people. 2013;(June).
58. Paper P. Clinician ' s Guide to Prevention and Treatment of Osteoporosis. 2014;2359–81.
59. Group NOG. Osteoporosis clinical guideline for prevention and treatment: Executive summary. National Osteoporosis Guideline Group; 2016.
60. Hursti U, Becker W, editors. Nordic Nutrition Recommendations 2012: Integrating nutrition and physical activity [Internet]. Kindle. Nordic Council of Ministers; 2012. 732 p. Available from: <https://www.amazon.com/Nordic-Nutrition-Recommendations-2012-Integrating-ebook/dp/B00IXNTEJY>
61. Hanley DA, Cranney A, Jones G, Whiting SJ, Leslie WD, Cole DE, et al. Vitamin D in adult health and disease: a review and guideline statement from

- Osteoporosis Canada. CMAJ [Internet]. 2010/07/14. 2010 Sep 7 [cited 2016 Jun 27];182(12):E610-8. Available from:
<http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=2934797&tool=pmc&rendertype=abstract>
62. García-Franco AL, Fernández JAB, Muñoz EB, Piñeiro MJ, del Cura González I, Del Moral AO, et al. Actividades preventivas en la mujer. Actualización PAPPS 2018. Atención Primaria. 2018;50(Supl 1):125.
63. The Royal Australian College of General Practitioners. Clinical guideline for the prevention and treatment of osteoporosis in postmenopausal women and older men. 2010;
64. Haq A, Wimalawansa SJ, Pludowski P, Anouti F Al. Clinical practice guidelines for vitamin D in the United Arab Emirates. J Steroid Biochem Mol Biol. 2018;175:4–11.
65. Force USPST, Grossman DC, Curry SJ, Owens DK, Barry MJ, Caughey AB, et al. Interventions to Prevent Falls in Community-Dwelling Older Adults: US Preventive Services Task Force Recommendation Statement. JAMA [Internet]. 2018;319(16):1696–704. Available from:
<https://www.ncbi.nlm.nih.gov/pubmed/29710141>
66. World Health Organization. Nutrition for Health and Development. Guideline. Vitamin D supplementation in pregnant women. 24 p.
67. Varsavsky M, Rozas Moreno P, Becerra Fernández A, Luque Fernández I, Quesada Gómez JM, Ávila Rubio V, et al. Recommended vitamin D levels in the general population. Endocrinol diabetes y Nutr [Internet]. 2017;64:7–14. Available from: <https://www.ncbi.nlm.nih.gov/pubmed/28440763>
68. Suominen M, Jyvakorpi S, Pitkala K, Finne-Soveri H, Hakala P, Mannisto S, et

- al. Nutritional guidelines for older people in Finland. *J Nutr Health Aging* [Internet]. 2014;18(10):861–7. Available from: <https://search.ebscohost.com/login.aspx?direct=true&db=ccm&AN=103870073&site=ehost-live>
69. Souberbielle JC, Body JJ, Lappe JM, Plebani M, Shoenfeld Y, Wang TJ, et al. Vitamin D and musculoskeletal health, cardiovascular disease, autoimmunity and cancer: Recommendations for clinical practice. *Autoimmun Rev*. 2010/07/06. 2010;9(11):709–15.
70. Schurman L, Bagur A, Claus Hermberg H, Messina OD, Negri AL, Sánchez A, et al. Guías 2012 para el diagnóstico, la prevención y el tratamiento de la osteoporosis. 2013;
71. Głuszko P, Lorenc RS, Karczmarewicz E, Misiorowski W, Jaworski M, Working Group including the representatives of the Polish Associations of Orthopedics and Traumatology Gerontology, Rheumatology, Family Medicine, Diabetology, Laboratory Diagnostics, Andropause and Menopause, Endocrinology, Radiology, and the STENKO gro R. Polish guidelines for the diagnosis and management of osteoporosis: a review of 2013 update. *Pol Arch Med Wewn* [Internet]. 2014;124(5):255–63. Available from: <https://www.ncbi.nlm.nih.gov/pubmed/24694725>
72. Moncada LVV, Mire LG. Preventing Falls in Older Persons. *Am Fam Physician* [Internet]. 2017;96(4):240–7. Available from: <https://www.ncbi.nlm.nih.gov/pubmed/28925664>
73. Maeda SS, Borba VZC, Camargo MBR, Silva DMW, Borges JLC, Bandeira F, et al. Recommendations of the {Brazilian} {Society} of {Endocrinology} and {Metabology} ({SBEM}) for the diagnosis and treatment of hypovitaminosis {D}.

- Arq Bras Endocrinol Metabol. 2014;58(5):411–33.
74. Hurley DL, Binkley N, Camacho PM, Diab DL, Kennel KA, Malabanan A, et al. THE USE OF VITAMINS AND MINERALS IN SKELETAL HEALTH: AMERICAN ASSOCIATION OF CLINICAL ENDOCRINOLOGISTS AND THE AMERICAN COLLEGE OF ENDOCRINOLOGY POSITION STATEMENT. Endocr Pract [Internet]. 2018;24(10):915–24. Available from: <https://www.ncbi.nlm.nih.gov/pubmed/30035621>
75. Dent E, Lien C, Lim WS, Wong WC, Wong CH, Ng TP, et al. The Asia-Pacific Clinical Practice Guidelines for the Management of Frailty. J Am Med Dir Assoc [Internet]. 2017;18(7):564–75. Available from: <https://www.ncbi.nlm.nih.gov/pubmed/28648901>
76. Crandall M, Duncan T, Mallat A, Greene W, Violano P, Christmas AB, et al. Prevention of fall-related injuries in the elderly: {An} {Eastern} {Association} for the {Surgery} of {Trauma} practice management guideline. J Trauma Acute Care Surg. 2016;81(1):196–206.
77. Cesareo R, Attanasio R, Caputo M, Castello R, Chiodini I, Falchetti A, et al. Italian Association of Clinical Endocrinologists (AME) and Italian Chapter of the American Association of Clinical Endocrinologists (AACE) Position Statement: Clinical Management of Vitamin D Deficiency in Adults. Nutrients [Internet]. 2018;10(5):546. Available from: <https://www.ncbi.nlm.nih.gov/pubmed/29702603>
78. Royal Osteoporosis Society. Vitamin D and Bone Health: A Practical Clinical Guideline for Patient Management. 2020;
79. Moyer VA, Force* USPST. Vitamin D and calcium supplementation to prevent fractures in adults: U.S. Preventive Services Task Force recommendation

- statement. *Ann Intern Med*. 2013/02/27. 2013;158(9):691–6.
80. Blake P, Durão S, Naude CE, Bero L. An analysis of methods used to synthesize evidence and grade recommendations in food-based dietary guidelines. *Nutr Rev*. 2018;76(4):290–300.
81. Kung J, Miller RR, Mackowiak PA. Failure of Clinical Practice Guidelines to Meet Institute of Medicine Standards. *Arch Intern Med [Internet]*. 2012 Nov 26 [cited 2017 Oct 4];172(21):1628. Available from: <http://archinte.jamanetwork.com/article.aspx?doi=10.1001/2013.jamainternmed.56>
82. Armstrong JJ, Goldfarb AM, Instrum RS, MacDermid JC. Improvement evident but still necessary in clinical practice guideline quality: a systematic review. *J Clin Epidemiol [Internet]*. 2017 Jan 1 [cited 2017 Oct 4];81:13–21. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/27565978>
83. Alonso-Coello P, Irfan A, Sola I, Gich I, Delgado-Noguera M, Rigau D, et al. The quality of clinical practice guidelines over the last two decades: a systematic review of guideline appraisal studies. *BMJ Qual Saf [Internet]*. 2010 Dec 1 [cited 2017 Oct 4];19(6):e58–e58. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/21127089>
84. Bennett WL, Odelola OA, Wilson LM, Bolen S, Selvaraj S, Robinson KA, et al. Evaluation of Guideline Recommendations on Oral Medications for Type 2 Diabetes Mellitus: A Systematic Review. *Ann Intern Med*. 2012;156(1_Part_1):27–36.
85. Nuckols TK, Anderson L, Popescu I, Diamant AL, Doyle B, Di Capua P, et al. Opioid prescribing: a systematic review and critical appraisal of guidelines for chronic pain. *Ann Intern Med*. 2014;160(1):38–47.

- 1
2
3 86. Acuña-Izcaray A, Sánchez-Angarita E, Plaza V, Rodrigo G, de Oca MM, Gich
4 I, et al. Quality assessment of asthma clinical practice guidelines: a systematic
5 appraisal. *Chest*. 2013;144(2):390–7.
6
7
8
9
- 10 87. Classen DC, Mermel LA. Specialty Society Clinical Practice Guidelines: Time
11 for Evolution or Revolution? Specialty Society Clinical Practice
12 Guidelines Specialty Society Clinical Practice Guidelines. *JAMA* [Internet].
13
14
15
16
17 2015 Sep 1;314(9):871–2. Available from:
18
19 <https://doi.org/10.1001/jama.2015.7462>
20
- 21 88. Norris SL, Holmer HK, Ogden LA, Burda BU. Conflict of Interest in clinical
22 practice guideline development: a systematic review. *PLoS One* [Internet].
23
24 2011;6. Available from: <http://dx.doi.org/10.1371/journal.pone.0025153>
25
26
27
- 28 89. EFSA Panel on Dietetic Products N and A (NDA). Dietary reference values for
29 vitamin D. *EFSA J*. 2016;14(10):e04547.
30
31
32
- 33 90. SACN VD. Health report. *Sci Advis Comm Nutr*. 2016;
34
- 35 91. Bolland MJ, Avenell A, Grey A. Assessment of research waste part 1: an
36 exemplar from examining study design, surrogate and clinical endpoints in
37
38 studies of calcium intake and vitamin D supplementation. *BMC Med Res*
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60
92. Bolland MJ, Grey A, Avenell A. Assessment of research waste part 2: wrong
study populations-an exemplar of baseline vitamin D status of participants in
trials of vitamin D supplementation. *BMC Med Res Methodol*. 2018;18(1):101.
101.
93. LeFevre ML, LeFevre NM. Vitamin D Screening and Supplementation in
Community-Dwelling Adults: Common Questions and Answers. *Am Fam*
Physician [Internet]. 2018 Feb 15 [cited 2019 Aug 30];97(4):254–60. Available
from: <http://www.ncbi.nlm.nih.gov/pubmed/29671532>

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

94. García-Franco AL, Navarro DF, Corrochano EC. Vitamina D: el traje nuevo del
Rey Sol. Atención Primaria [Internet]. 2019 Feb 1 [cited 2019 Feb
15];51(2):57–8. Available from:
<https://www.sciencedirect.com/science/article/pii/S021265671930040X>

Table 1: Characteristics of the included guidelines.

Region	Frequency	%
International	3	9.1
Europe	11	33.3
North America	10	30.3
South America	2	6.1
Asia	5	15.2
Oceania	2	6.1
Type of Organization		
Scientific Society	22	66.7
Government Organization	9	27.3
Other	2	6.1
Target population		
General Population	14	42.4
Older population	18	54.5
Women	1	3
Vitamin D supplementation		
Does not recommend	9	27.3
Suggests	9	27.3
Recommends	15	45.5
Vitamin D status for recommendation		
Any	13	39.4
With risk factors and/or deficiency	10	30.3
Deficiency	7	21.2
Total	30	90.9
Non-Applicable	3	9.1
Vitamin D screening advice		
No	20	60.6
Yes, with risk factors	11	33.3
Yes	2	6.1
Favoured method for Vitamin D obtention		
No method favoured	5	15.2
Supplementation	24	72.7
Sun exposure	4	12.1
Food advice		
No	21	63.6
Yes	10	30.3
Unclear	2	6.1
Sun exposure advice		
No	22	66.7
Yes	11	33.3

Table 2: Guideline characteristics

Guideline Name	Institution	Region	Year	Type of organization	Target population	Purpose of supplementation	Vitamin D status for Supplementation	25-OH-D threshold for deficiency or insufficiency *
Vitamin D for Prevention of Falls and their Consequences in Older Adults	American Geriatrics Society	North America	2014	Scientific Society	Population older than 65	Prevention of falls and fractures	Not specified	75 nmol/L
Building healthy bones throughout life an evidence-informed strategy to prevent osteoporosis in Australia	Australia and New Zealand bone and mineral society & osteoporosis Australia	Oceania	2013	Scientific Society	General population with risk factors of deficiency	Overall Health	N/A	50 nmol/L to 75nmol/L
Osteoporosis: diagnosis, treatment, and fracture prevention	British Columbia Medical Association	North America	2011	Governmental Organization	General population	Prevention of osteoporosis	Not specified	30 to 50 nmol/L
Taiwan Osteoporosis Practice Guidelines	Bureau of Health Promotion Taiwan	Asia	2011	Governmental Organization	General population with risk factors of deficiency	Prevention of osteoporosis	With risk factors or deficiency	75 nmol/L
Dutch Dietary Guidelines 2015 / Evaluation of dietary reference values for vitamin D	Health Council of the Netherlands	Europe	2015	Governmental Organization	General population with risk factors of deficiency	Prevention of fractures	With risk factors or deficiency	30 to 50 nmol/L
Evaluation, Treatment, and Prevention of Vitamin D Deficiency: An Endocrine Society Clinical Practice Guideline	Endocrine Society	North America	2011	Scientific Society	General population with risk factors of deficiency	Prevention of falls and fractures	With risk factors or deficiency	50 nmol/L
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 (ESCEO)	Europe	2013	Scientific Society	Population older than 50	Prevention of osteoporosis	Not specified	75 nmol/L
IOF position statement: vitamin D recommendations for older adults	International Osteoporosis Foundation	International	2013	Scientific Society	Population older than 60	Prevention of falls and fractures	Deficiency / Insufficiency	75 nmol/L
Osteoporosis Screening, Diagnosis, and Treatment Guideline	Kaiser Permanente	North America	2019	Other	Population older than 50 and women	Prevention of osteoporosis	Cloudy months	Not specified
Evidence-based guidelines for fall prevention in Korea	Korean Association of Internal Medicine	Asia	2017	Scientific Society	Older population	Prevention of falls and fractures	With risk factors or deficiency	Not specified
Calcium and Vitamin D Supplementations: 2015 Position Statement of the Korean Society for Bone and Mineral Research	Korean Bone Society	Asia	2015	Scientific Society	Population older than 50	Prevention of fractures	Not specified	75 nmol/L
Assessment and prevention of falls in older people	National Institute for Health and Care Excellence (NICE)	Europe	2013	Governmental Organization	Population older than 65	Prevention of fractures	N/A	Not specified
Clinician's Guide to Prevention and Treatment of Osteoporosis	National Osteoporosis Foundation	North America	2016	Scientific Society	Recommendations apply to postmenopausal	Prevention of osteoporosis	Not specified	75 nmol/L

					women and men age 50 and older.			
Osteoporosis Clinical guideline for prevention and treatment Executive Summary	National Osteoporosis Guideline Group	Europe	2016	Scientific Society	Older population	Prevention of osteoporosis	N/A	Not specified
Nordic Nutrition Recommendations 2012: Integrating nutrition and physical activity	Nordic nutrition recommendations	Europe	2012	Governmental Organization	General population	Overall Health	Not specified	50 nmol/L
Vitamin D in adult health and disease: a review and guideline statement from Osteoporosis Canada	Osteoporosis Canada	North America	2010	Scientific Society	General population	Prevention of osteoporosis	Not specified	75 nmol/L
Preventive Activities in women PAPPS (preventive and promotional ACTIVITIES PROGRAM health)	Spanish Society of Family Medicine (SEMFyC)	Europe	2018	Scientific Society	Women older than 65	Prevention of osteoporosis	Deficiency	Not specified
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	Oceania	2010	Scientific Society	Postmenopausal women and older men	Prevention of osteoporosis	Deficiency	60 nmol/L
Clinical practice guidelines for vitamin D in the United Arab Emirates	United Arab Emirates*	Asia	2016	Governmental Organization	General population	Overall Health	Not specified	30 to 50 nmol/L
Vitamin D and calcium supplementation to prevent fractures in adults: U.S. Preventive Services Task Force recommendation statement	United States Preventive Services Task Force	North America	2018	Governmental Organization	Population older than 65	Prevention of falls and fractures	Deficiency	Not specified
Vitamin D supplementation in pregnant women	World Health Organization	International	2012	Governmental Organization	Pregnant women	maternal and infant health outcomes	Deficiency	50 nmol/L to 75nmol/L
Vitamin D recommendations in general population (<i>Recomendaciones de vitamina D para la población general</i>)	Spanish Society of Endocrinology and Nutrition (SEEN)	International	2017	Scientific Society	General population	bone and non-skeletal health outcomes	With risk factors or deficiency	75 to 125 nmol/L
NUTRITIONAL GUIDELINES FOR OLDER PEOPLE IN FINLAND	Finnish National Nutrition Council	Europe	2014	Governmental Organization	Population older than 65	Overall Health	Not specified	Not specified
Vitamin D and musculoskeletal health, cardiovascular disease, autoimmunity and cancer: Recommendations for clinical practice.	Vitamin D Summit Meeting	Europe	2010	Other	General population	musculoskeletal health, cardiovascular disease, autoimmunity and cancer	With risk factors or deficiency	75 to 100 nmol/L
2012 Guidelines for diagnosis, prevention and treatment of osteoporosis	Argentinian society of osteoporosis and Argentinian society of osteology and mineral metabolism. Sociedad Argentina de Osteoporosis y la Asociación Argentina de Osteología y Metabolismo Mineral	South America	2013	Scientific Society	Population older than 65	Prevention of fractures	insufficiency	75 nmol/L

Polish guidelines for the diagnosis and management of osteoporosis: a review of 2013 update	Polish Associations of Orthopaedics and Traumatology, Rehabilitation, Gerontology, Rheumatology, Family Medicine, Diabetology, Laboratory Diagnostics, Andropause and Menopause, Endocrinology, Radiology, and the STENKO group	Europe	2014	Scientific Society	General population	Prevention of osteoporosis	Not specified	75 nmol/L
Preventing Falls in Older Persons	American Association of Family Physicians	North America	2017	Scientific Society	Older population	preventing falls in older people	Not specified	Not specified
Recommendations of the Brazilian Society of Endocrinology and Metabology (SBEM) for the diagnosis and treatment of hypovitaminosis D	Brazilian Society of Endocrinology and Metabology (SBEM)	South America	2014	Scientific Society	General population	treatment of deficiency	High risk for deficiency	75 nmol/L
THE USE OF VITAMINS AND MINERALS IN SKELETAL HEALTH: AMERICAN ASSOCIATION OF CLINICAL ENDOCRINOLOGISTS AND THE AMERICAN COLLEGE OF ENDOCRINOLOGY (AACE/ACE) POSITION STATEMENT	American association of clinical endocrinologists and the american college of endocrinology (aace/ace)	North America	2018	Scientific Society	General population	Skeletal Health	Deficiency	50 nmol/L
The Asia-Pacific Clinical Practice Guidelines for the Management of Frailty	Society for Post-Acute and Long-Term Care Medicine	Asia	2017	Scientific Society	Older Population	Frailty prevention	Deficiency	Not specified
Prevention of fall-related injuries in the elderly: An eastern association for the surgery of trauma practice management guideline	Eastern Association for the Surgery of Trauma Injury Control and Violence Prevention	North America	2016	Scientific Society	Population older than 65	prevention of falls	Not specified	Not specified
Position Statement: Clinical Management of Vitamin D Deficiency in Adults	Italian Association of Clinical Endocrinologists (AME) and Italian Chapter of the American Association of Clinical Endocrinologists (AACE)	Europe	2018	Scientific Society	General Population	treatment of deficiency	Deficiency or with risk factors	75 nmol/L
Vitamin D and Bone Health: A Practical Clinical Guideline for Patient Management	Royal Osteoporosis Society (ROS), previously National Osteoporosis Society (NOS)	Europe	2020	Scientific Society	Population older than 65	Overall Health	At risk for deficiency or insufficient sun	25 to 50 nmol/L

*As defined by guideline authors as either, target status to maintain adequate general or bone health, threshold for starting supplementation, or to define deficiency or insufficiency.

Table 3 Vitamin D and related recommendations in guidelines

GUIDELINE NAME	VITAMIN D SUPPLEMENTATION	VITAMIN D SCREENING ADVICE	VITAMIN D MONITORING ADVICE	FOOD ADVICE	SUN EXPOSURE ADVICE	FAVOURED METHOD FOR OBTENTION	SUGGESTED VITAMIN D DOSE (UI)	CALCIUM ADVICE
VITAMIN D FOR PREVENTION OF FALLS AND THEIR CONSEQUENCES IN OLDER ADULTS	Recommends	No	No	Yes	Yes	Supplementation	1000	No
BUILDING HEALTHY BONES THROUGHOUT LIFE AN EVIDENCE-INFORMED STRATEGY TO PREVENT OSTEOPOROSIS IN AUSTRALIA	Does not recommend	With risk factors	No	No	Yes	Sun exposure	N/A	Yes
OSTEOPOROSIS: DIAGNOSIS, TREATMENT, AND FRACTURE PREVENTION	Recommends	No	No	Yes	No	Supplementation	Different doses	No
TAIWAN OSTEOPOROSIS PRACTICE GUIDELINES	Recommends	Yes	Yes	No	No	Supplementation	800-1000	Yes
DUTCH DIETARY GUIDELINES 2015 / EVALUATION OF DIETARY REFERENCE VALUES FOR VITAMIN D	Suggests	No	No	Yes	Yes	No method favoured	400-800	Yes
EVALUATION, TREATMENT, AND PREVENTION OF VITAMIN D DEFICIENCY: AN ENDOCRINE SOCIETY CLINICAL PRACTICE GUIDELINE	Suggests	With risk factors	Not reported	Yes	No	Supplementation	2000-6000	No
VITAMIN D SUPPLEMENTATION IN ELDERLY OR POSTMENOPAUSAL WOMEN: A 2013 UPDATE OF THE 2008 RECOMMENDATIONS	Recommends	With risk factors	Not reported	Unclear	No	Supplementation	800-1000	Yes
IOF POSITION STATEMENT: VITAMIN D RECOMMENDATIONS FOR OLDER ADULTS	Recommends	With risk factors	Yes	Not clear	No	No method favoured	2000	Yes
OSTEOPOROSIS/FRACTURE PREVENTION NATIONAL GUIDELINE SUMMARY	Suggests	No	No	yes	No	Supplementation	1000-2000	Yes
EVIDENCE-BASED GUIDELINES FOR FALL PREVENTION IN KOREA	Suggests	No	No	No	No	Supplementation	Not reported	Yes
CALCIUM AND VITAMIN D SUPPLEMENTATIONS: 2015 POSITION STATEMENT OF THE KOREAN SOCIETY FOR BONE AND MINERAL RESEARCH	Recommends	No	Yes	No	No	Supplementation	800	Yes

FALLS: ASSESSMENT AND PREVENTION OF FALLS IN OLDER PEOPLE	Does not recommend	No	No	No	No	Supplements	N/A	Yes
CLINICIAN'S GUIDE TO PREVENTION AND TREATMENT OF OSTEOPOROSIS	Suggests	With risk factors	Yes	Yes	No	Supplementation	800 to 1000	No
OSTEOPOROSIS CLINICAL GUIDELINE FOR PREVENTION AND TREATMENT EXECUTIVE SUMMARY	Does not Recommend	No	Not reported	No	No	Supplementation	N/A	Yes
NORDIC NUTRITION RECOMMENDATIONS 2012: INTEGRATING NUTRITION AND PHYSICAL ACTIVITY	Recommends	No	Not reported	yes	Yes	Supplementation	800	Yes
VITAMIN D IN ADULT HEALTH AND DISEASE: A REVIEW AND GUIDELINE STATEMENT FROM OSTEOPOROSIS CANADA	Recommends	With risk factors	Not reported	yes	Yes	Supplementation	Different doses	Yes
PREVENTIVE ACTIVITIES IN WOMEN PAPPS (PREVENTIVE AND PROMOTIONAL ACTIVITIES PROGRAM HEALTH)	Does not recommend	No	Not reported	yes	Yes	Sun exposure/diet	800	Yes
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	Does not recommend	No	No	no	Yes	Sun exposure	800	Yes
CLINICAL PRACTICE GUIDELINES FOR VITAMIN D IN THE UNITED ARAB EMIRATES	Recommends	With risk factors	yes	no	No	Supplementation	400 - 2000	No
VITAMIN D AND CALCIUM SUPPLEMENTATION TO PREVENT FRACTURES IN ADULTS: U.S. PREVENTIVE SERVICES TASK FORCE RECOMMENDATION STATEMENT	Recommends against	No	No	No	No	Supplementation	N/A	Yes
VITAMIN D SUPPLEMENTATION IN PREGNANT WOMEN	Recommends against	No	No	No	No	No method favoured	200	No
VITAMIN D RECOMMENDATIONS IN GENERAL POPULATION (RECOMENDACIONES DE VITAMINA D PARA LA POBLACIÓN GENERAL)	Suggests	With risk factors	yes	No	No	Supplementation	600-1000	No

NUTRITIONAL GUIDELINES FOR OLDER PEOPLE IN FINLAND	Recommends	No	No	No	NO	Supplementation	800	No
VITAMIN D AND MUSCULOSKELETAL HEALTH, CARDIOVASCULAR DISEASE, AUTOIMMUNITY AND CANCER: RECOMMENDATIONS FOR CLINICAL PRACTICE.	Recommends	Yes	yes	No	No	Supplementation	800	No
2012 GUIDELINES FOR DIAGNOSIS, PREVENTION AND TREATMENT OF OSTEOPOROSIS	Suggests	No	yes	No	Yes	Sun exposure	800 -2000	Yes
POLISH GUIDELINES FOR THE DIAGNOSIS AND MANAGEMENT OF OSTEOPOROSIS: A REVIEW OF 2013 UPDATE	Recommends	No	yes	No	No	Supplementation	800 -2000	Yes
PREVENTING FALLS IN OLDER PERSONS	Recommends	No	No	No	No	Supplementation	>800	Yes
RECOMMENDATIONS OF THE BRAZILIAN SOCIETY OF ENDOCRINOLOGY AND METABOLOGY (SBEM) FOR THE DIAGNOSIS AND TREATMENT OF HYPOVITAMINOSIS D	Does not recommend	No	yes	Yes	Yes	No method favoured	1000-2000	No
THE USE OF VITAMINS AND MINERALS IN SKELETAL HEALTH: AMERICAN ASSOCIATION OF CLINICAL ENDOCRINOLOGISTS AND THE AMERICAN COLLEGE OF ENDOCRINOLOGY (AACE/ACE) POSITION STATEMENT	Does not recommend	With risk factors	No	No	No	No method favoured	1000	Yes
THE ASIA-PACIFIC CLINICAL PRACTICE GUIDELINES FOR THE MANAGEMENT OF FRAILTY	Suggests	No	No	No	Yes	Supplementation	800-1000	No
PREVENTION OF FALL-RELATED INJURIES IN THE ELDERLY: AN EASTERN ASSOCIATION FOR THE SURGERY OF TRAUMA PRACTICE MANAGEMENT GUIDELINE	Suggests	No	no	No	No	Supplementation	400-800	Yes
POSITION STATEMENT: CLINICAL MANAGEMENT OF VITAMIN D DEFICIENCY IN ADULTS	Recommends	With risk factors	No	No	Yes	Supplementation	2000	No
VITAMIN D AND BONE HEALTH: A PRACTICAL CLINICAL GUIDELINE FOR PATIENT MANAGEMENT	Recommends	With risk factors	Yes	No	No	Supplementation	400	Yes

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46

Table 4 Conflicts of Interest Reporting in Guidelines

GUIDELINE NAME	INSTITUTION	COI PROCESS REPORTING	COI AFFILIATION REPORTING	COI FINANCIAL REPORTING	COI INTELECTUAL REPORTING	ROLE OF FUNDING SOURCE REPORTING
VITAMIN D FOR PREVENTION OF FALLS AND THEIR CONSEQUENCES IN OLDER ADULTS	American Geriatrics Society	Unclear	Clear	Clear	Unclear	Unclear
BUILDING HEALTHY BONES THROUGHOUT LIFE AN EVIDENCE-INFORMED STRATEGY TO PREVENT OSTEOPOROSIS IN AUSTRALIA	Australia and New Zealand bone and mineral society & osteoporosis Australia	Clear	Unclear	Clear	Unclear	Unclear
OSTEOPOROSIS: DIAGNOSIS, TREATMENT, AND FRACTURE PREVENTION	British Columbia Medical Association	Not reported	Unclear	Unclear	Unclear	Not reported
TAIWAN OSTEOPOROSIS PRACTICE GUIDELINES	Bureau of Health Promotion Taiwan	Unclear	Unclear	Clear	Unclear	Unclear
DUTCH DIETARY GUIDELINES 2015 / EVALUATION OF DIETARY REFERENCE VALUES FOR VITAMIN D	Health Council of the Netherlands	Not reported	Not reported	Not reported	Not reported	Not reported
EVALUATION, TREATMENT, AND PREVENTION OF VITAMIN D DEFICIENCY: AN ENDOCRINE SOCIETY CLINICAL PRACTICE GUIDELINE	Endocrine Society	Unclear	Clear	Clear	Clear	Not reported
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 (ESCEO)	Unclear	Clear	Clear	Unclear	Unclear
IOF POSITION STATEMENT: VITAMIN D RECOMMENDATIONS FOR OLDER ADULTS	International Osteoporosis Foundation	Unclear	Unclear	Unclear	Unclear	Not reported
OSTEOPOROSIS/FRACTURE PREVENTION NATIONAL GUIDELINE SUMMARY	Kaiser Permanente	Not reported	Not reported	Not reported	Not reported	Not reported
EVIDENCE-BASED GUIDELINES FOR FALL PREVENTION IN KOREA	Korean Association of Internal Medicine	Unclear	Unclear	Unclear	Unclear	Not reported
CALCIUM AND VITAMIN D SUPPLEMENTATIONS: 2015 POSITION STATEMENT OF THE KOREAN SOCIETY FOR BONE AND MINERAL RESEARCH	Korean Bone Society	Unclear	Unclear	Unclear	Unclear	Not reported
FALLS: ASSESSMENT AND PREVENTION OF FALLS IN OLDER PEOPLE	National Institute for Health and Care Excellence (NICE)	Unclear	Unclear	Unclear	Unclear	Clear
CLINICIAN'S GUIDE TO PREVENTION AND TREATMENT OF OSTEOPOROSIS	National Osteoporosis Foundation	Unclear	Clear	Clear	Unclear	Unclear
OSTEOPOROSIS CLINICAL GUIDELINE FOR PREVENTION AND TREATMENT EXECUTIVE SUMMARY	National Osteoporosis Guideline Group	Not reported	Unclear	Unclear	Unclear	Clear
NORDIC NUTRITION RECOMMENDATIONS 2012: INTEGRATING NUTRITION AND PHYSICAL ACTIVITY	Nordic nutrition recommendations	Not reported	Not reported	Not reported	Not reported	Not reported
VITAMIN D IN ADULT HEALTH AND DISEASE: A REVIEW AND GUIDELINE STATEMENT FROM OSTEOPOROSIS CANADA	Osteoporosis Canada	Clear	Clear	Clear	Clear	Unclear
PREVENTIVE ACTIVITIES IN WOMEN PAPPS (PREVENTIVE AND PROMOTIONAL ACTIVITIES PROGRAM HEALTH)	Spanish Society of Family Medicine (SEMFyC)	Unclear	Unclear	Unclear	Unclear	Not reported
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	Clear	Clear	Clear	Clear	Clear

CLINICAL PRACTICE GUIDELINES FOR VITAMIN D IN THE UNITED ARAB EMIRATES	United Arab Emirates*	Not reported	Not reported	Not reported	Not reported	Not reported
VITAMIN D AND CALCIUM SUPPLEMENTATION TO PREVENT FRACTURES IN ADULTS: U.S. PREVENTIVE SERVICES TASK FORCE RECOMMENDATION STATEMENT	United States Preventive Services Task Force	Unclear	Clear	Clear	Clear	Clear
VITAMIN D SUPPLEMENTATION IN PREGNANT WOMEN	World Health Organization	Unclear	Clear	Clear	Clear	Unclear
VITAMIN D RECOMMENDATIONS IN GENERAL POPULATION (RECOMENDACIONES DE VITAMINA D PARA LA POBLACIÓN GENERAL)	Spanish Society of Endocrinology and Nutrition (SEEN)	Clear	Unclear	Unclear	Unclear	Clear
NUTRITIONAL GUIDELINES FOR OLDER PEOPLE IN FINLAND	Finnish National Nutrition Council	Not reported	Not reported	Not reported	Not reported	Not reported
VITAMIN D AND MUSCULOSKELETAL HEALTH, CARDIOVASCULAR DISEASE, AUTOIMMUNITY AND CANCER: RECOMMENDATIONS FOR CLINICAL PRACTICE.	Vitamin D Summit Meeting	Unclear	Unclear	Clear	Unclear	Unclear
2012 GUIDELINES FOR DIAGNOSIS, PREVENTION AND TREATMENT OF OSTEOPOROSIS	Argentinian society of osteoporosis and Argentinian society of osteology and mineral metabolism. Sociedad Argentina de Osteoporosis y la Asociación Argentina de Osteología y Metabolismo Mineral	Unclear	Clear	Clear	Unclear	Not reported
POLISH GUIDELINES FOR THE DIAGNOSIS AND MANAGEMENT OF OSTEOPOROSIS: A REVIEW OF 2013 UPDATE	Polish Associations of Orthopedics and Traumatology, Rehabilitation, Gerontology, Rheumatology, Family Medicine, Diabetology, Laboratory Diagnostics, Andropause and Menopause, Endocrinology, Radiology, and the STENKO group	Unclear	Unclear	Unclear	Unclear	Unclear
PREVENTING FALLS IN OLDER PERSONS	American Association of Family Physicians	Unclear	Unclear	Clear	Unclear	Not reported
RECOMMENDATIONS OF THE BRAZILIAN SOCIETY OF ENDOCRINOLOGY AND METABOLOGY (SBEM) FOR THE DIAGNOSIS AND TREATMENT OF HYPOVITAMINOSIS D	Brazilian Society of Endocrinology and Metabolism (SBEM)	Unclear	Clear	Clear	Unclear	Not reported
THE USE OF VITAMINS AND MINERALS IN SKELETAL HEALTH: AMERICAN ASSOCIATION OF CLINICAL ENDOCRINOLOGISTS AND THE AMERICAN COLLEGE OF ENDOCRINOLOGY (AACE/ACE) POSITION STATEMENT	American association of clinical endocrinologists and the american college of endocrinology (aace/ace)	Clear	Clear	Clear	Unclear	Not reported
THE ASIA-PACIFIC CLINICAL PRACTICE GUIDELINES FOR THE MANAGEMENT OF FRAILTY	Society for Post-Acute and Long-Term Care Medicine	Not reported	Not reported	Not reported	Not reported	Not reported
PREVENTION OF FALL-RELATED INJURIES IN THE ELDERLY: AN EASTERN ASSOCIATION FOR THE SURGERY OF TRAUMA PRACTICE MANAGEMENT GUIDELINE	Eastern Association for the Surgery of Trauma Injury Control and Violence Prevention	Not reported	Not reported	Not reported	Not reported	Not reported
POSITION STATEMENT: CLINICAL MANAGEMENT OF VITAMIN D DEFICIENCY IN ADULTS	Italian Association of Clinical Endocrinologists (AME) and Italian Chapter of the American Association of Clinical Endocrinologists (AACE)	Unclear	Not reported	Not reported	Not reported	Not reported
VITAMIN D AND BONE HEALTH: A PRACTICAL CLINICAL GUIDELINE FOR PATIENT MANAGEMENT	Royal Osteoporosis Society (ROS), previously National Osteoporosis Society (NOS)	Not reported	Not reported	Not reported	Not reported	Clear

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46

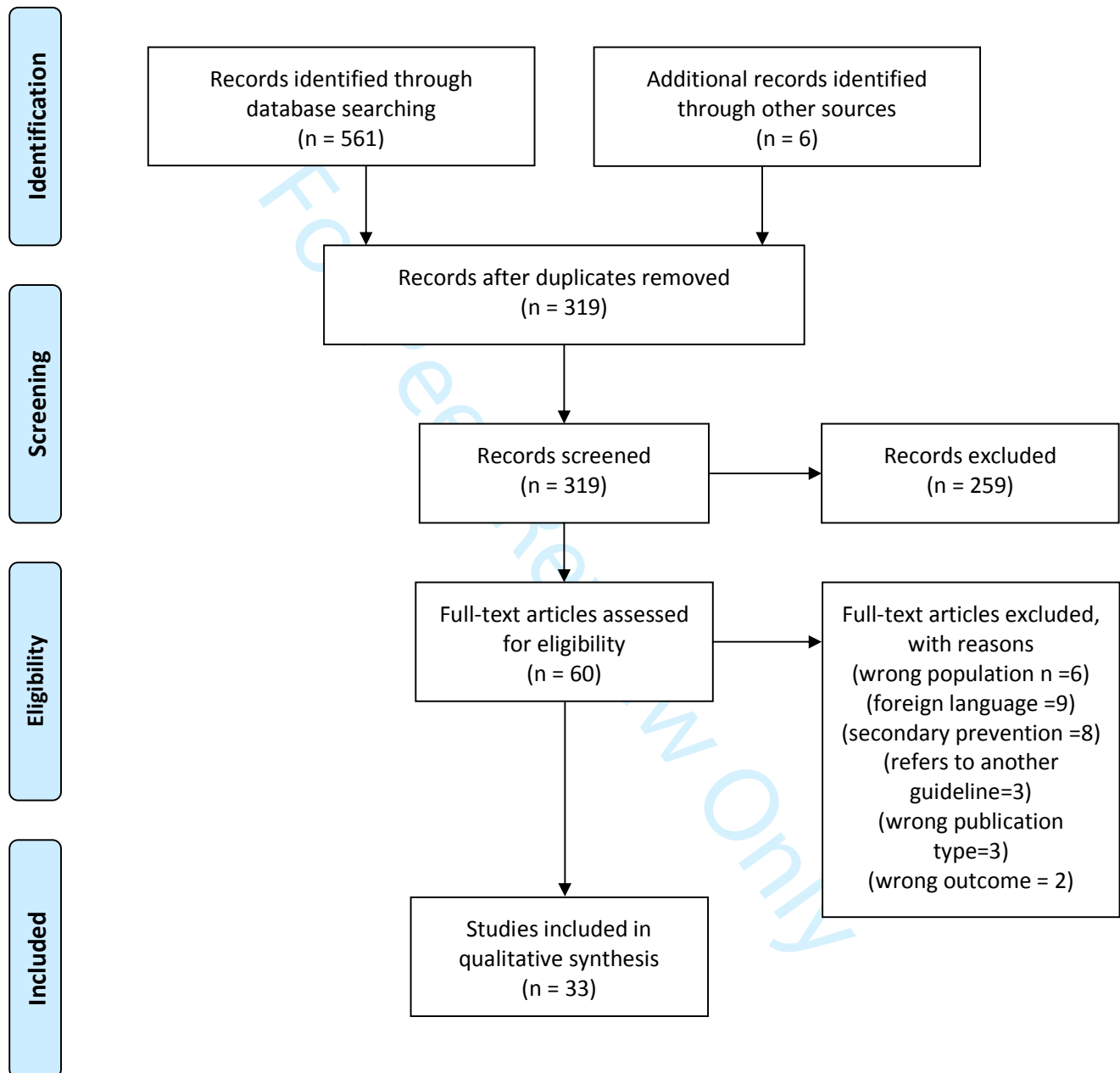
Footnotes:

* Referred as a guideline for the country in the paper, but no specific institution mentioned.

For Peer Review Only



PRISMA 2009 Flow Diagram

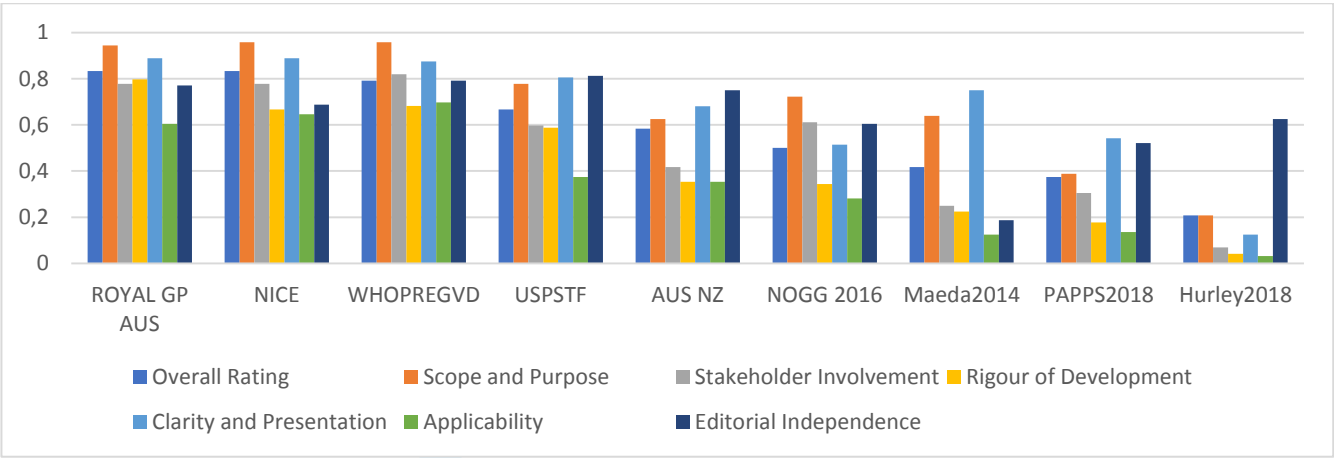


From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

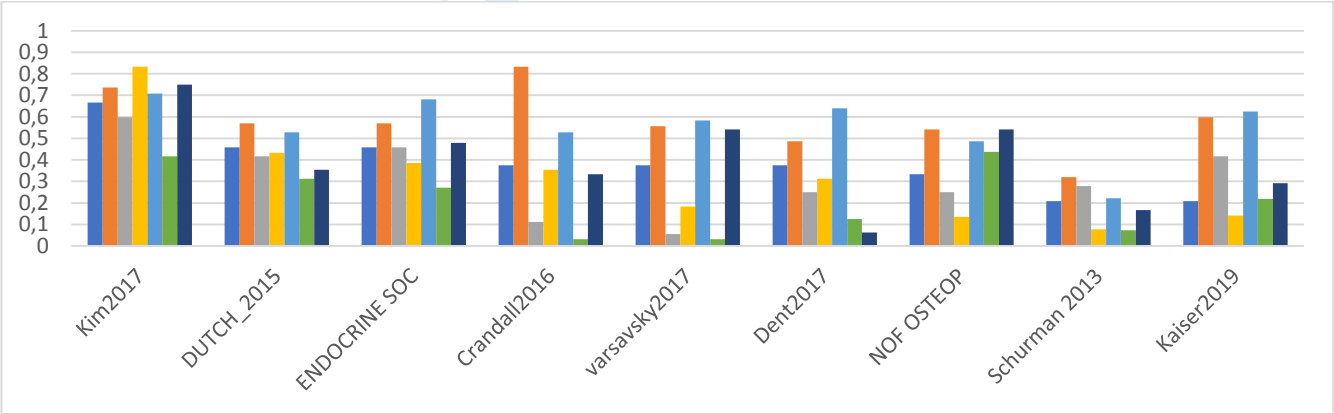
For more information, visit www.prisma-statement.org.

Figure 2A AGREE II Mean Domain Scores by type of Vitamin D supplementation recommendation

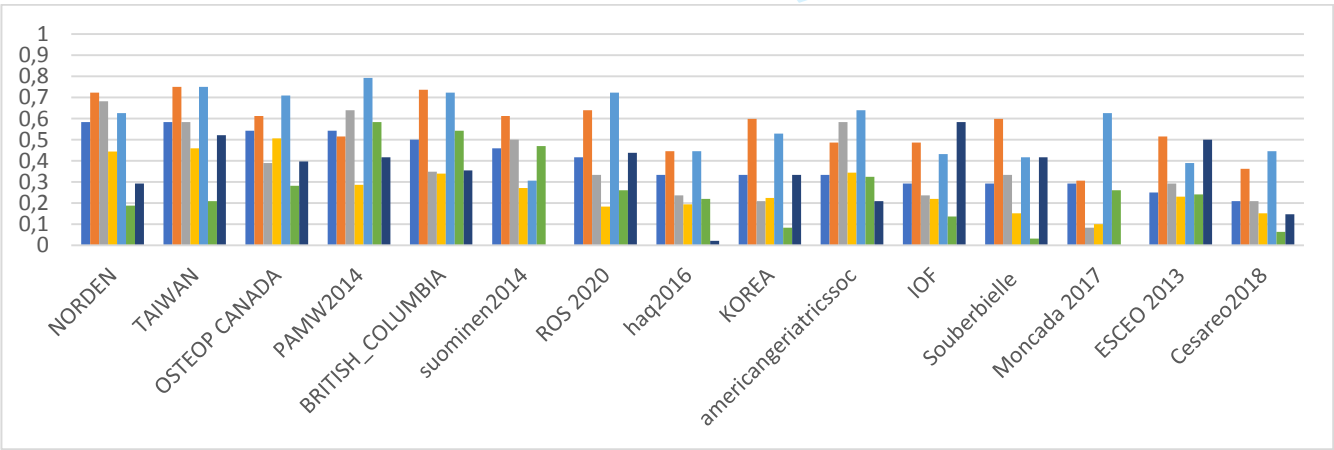
Does not recommend



Suggests



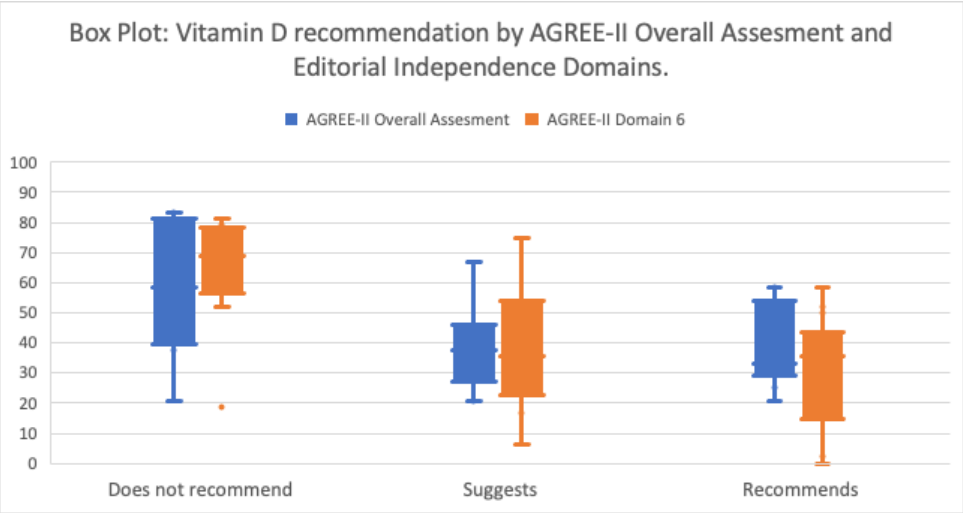
Recommends



Guideline name/institution abbreviations:
americangeriatricssoc Vitamin D for Prevention of Falls and their Consequences in Older Adults1 , American Geriatrics Society. AUS NZ Building healthy bones throughout life an evidence-informed strategy to prevent osteoporosis in Australia2, Australia and New Zealand bone and mineral society & osteoporosis Australia. BRITISH_COLUMBIA Osteoporosis: diagnosis, treatment, and fracture prevention3, British Columbia Medical Association. TAIWAN Taiwan Osteoporosis Practice Guidelines4, Bureau of Health Promotion Taiwan. DUTCH_2015 Dutch Dietary Guidelines 2015 / Evaluation of dietary reference values for vitamin D5,6, Health Council of the Netherlands. ENDOCRINE SOC Evaluation, Treatment, and Prevention of Vitamin D Deficiency: An Endocrine Society Clinical Practice

Guideline⁷, Endocrine Society. **ESCEO 2013** Vitamin D supplementation in elderly or postmenopausal women: a 2013 update of the 2008 recommendations⁸, European society for clinical and economic aspects of osteoporosis and osteoarthritis (ESCEO). **IOF** IOF position statement: vitamin D recommendations for older adults¹⁰, International Osteoporosis Foundation. **Kaiser2019** Osteoporosis/Fracture Prevention National Guideline Summary¹¹, Kaiser Permanente. **Kim2017** Evidence-based guidelines for fall prevention in Korea¹², Korean Association of Internal Medicine. **KOREA** Calcium and Vitamin D Supplementations: 2015 Position Statement of the Korean Society for Bone and Mineral Research¹³, Korean Bone Society. **NICE** Falls: Assessment and prevention of falls in older people¹⁴, National Institute for Health and Care Excellence (NICE). **NOF OSTEOP** Clinician's Guide to Prevention and Treatment of Osteoporosis¹⁵, National Osteoporosis Foundation. **NOGG 2016** Osteoporosis Clinical guideline for prevention and treatment Executive Summary¹⁷, National Osteoporosis Guideline Group. **NORDEN** Nordic Nutrition Recommendations 2012: Integrating nutrition and physical activity¹⁸, Nordic nutrition recommendations. **OSTEOP CANADA** Vitamin D in adult health and disease: a review and guideline statement from Osteoporosis Canada¹⁹, Osteoporosis Canada. **PAPPS2018** Preventive Activities in women²⁰, Program of Preventive activities in Primary Care (PAPPS), Spanish Society of Family Medicine. **ROYAL GP AUS** 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. **haq2016** Clinical practice guidelines for vitamin D in the United Arab Emirates²³, United Arab Emirates. **USPSTF** Vitamin D and calcium supplementation to prevent fractures in adults: U.S. Preventive Services Task Force recommendation statement²⁴, United States Preventive Services Task Force. **WHOPREGVD** Guideline: Vitamin D supplementation in pregnant women²⁵, Vitamin D supplementation in pregnant women, World Health Organization. **varsavsky2017** Vitamin D recommendations in general population (Recomendaciones de vitamina D para la población general). **suominen2014** nutritional guidelines for older people in finland. **Souberbielle** Vitamin D and musculoskeletal health, cardiovascular disease, autoimmunity and cancer: Recommendations for clinical practice. **Schurman 2013** 2012 Guidelines for diagnosis, prevention and treatment of osteoporosis. **PAMW2014** Polish guidelines for the diagnosis and management of osteoporosis: a review of 2013 update. **Moncada 2017** Preventing Falls in Older Persons. **Maeda2014** Recommendations of the Brazilian Society of Endocrinology and Metabology (SBEM) for the diagnosis and treatment of hypovitaminosis D. **Hurley2018** THE USE OF VITAMINS AND MINERALS IN SKELETAL HEALTH: AMERICAN ASSOCIATION OF CLINICAL ENDOCRINOLOGISTS AND THE AMERICAN COLLEGE OF ENDOCRINOLOGY (AACE/ACE) POSITION STATEMENT. **Dent2017** The Asia-Pacific Clinical Practice Guidelines for the Management of Frailty. **Crandall2016** Prevention of fall-related injuries in the elderly: An eastern association for the surgery of trauma practice management guideline, Eastern Association for the Surgery of Trauma Injury Control and Violence Prevention. **Cesareo2018** Italian Association of Clinical Endocrinologists (AME) and Italian Chapter of the American Association of Clinical Endocrinologists (AACE) Position Statement: Clinical Management of Vitamin D Deficiency in Adults, Italian Association of Clinical Endocrinologists. **ROS 2020** Vitamin D and Bone Health: A Practical Clinical Guideline for Patient Management.

Figure 2B



* Maeda SS, Borba VZC, Camargo MBR, Silva DMW, Borges JLC, Bandeira F, et al. Recommendations of the Brazilian Society of Endocrinology and Metabology (SBEM) for the diagnosis and treatment of hypovitaminosis D. Arq Bras Endocrinol Metabol. 2014;58(5):411–33.

Note: This Box Plot depicts mean, 1st Quartile (Q1) and 3rd Quartile (Q3), Interquartile Ranges (IQR), Maximum (Q3 + 1.5*IQR), Minimum (Q1 -1.5*IQR) and outliers “*”.