Systematic Review

Vitamin D deficiency in nursing home residents: a systematic review

Orlagh Feehan, Pamela J. Magee, L. Kirsty Pourshahidi, David J. Armstrong, and Emeir M. McSorley

Context: *Vitamin D deficiency is a global public health issue, particularly in nursing home residents.* ***Objective:*** *This review critically summarizes the prevalence of vitamin D deficiency in nursing home residents worldwide. In addition, it outlines the effect of vitamin D intervention, alone or in combination with other nutrients or therapies, on improving vitamin D status and associated health outcomes in nursing home residents.* ***Data Sources, Extraction, and Analysis:*** *Searches were conducted of electronic databases for articles published from 2010 to May 2021. After screening of the 366 papers initially identified, 58 articles were included.* ***Conclusions:*** *A paucity of observational studies in nursing homes suggests a high prevalence of vitamin D deficiency ranging from 8% [25(OH)D <25 nmol/L], up to 94% [25(OH)D <50 nmol/L] in some cohorts where supplement use was low. Reported factors associated with deficiency and suboptimal vitamin D status include lack of sunlight exposure, poor dietary intake of vitamin D, limited vitamin D food fortification, frailty, poor renal function, and low use of vitamin D supplements. Residents who are severely deficient, deficient, or insufficient in vitamin D require remedial vitamin D supplementation prior to maintenance supplementation at doses >800 IU/day. High-dose vitamin D supplementation may reduce respiratory illness; however, supportive data are limited. Oral nutritional supplements, in combination with exercise, may benefit physical function and performance, whereas supplementation with vitamin D– and calcium-fortified foods has been associated with improved quality of life and reduced bone resorption. Globally, vitamin D deficiency is highly prevalent in nursing home residents. There is an urgent need for standardized dietary and supplementation guidelines to prevent deficiency in this vulnerable group.*

INTRODUCTION

Vitamin D deficiency is a global public health issue frequently observed in older adults. The National Institute for Health and Care Excellence guidelines within the United Kingdom define deficiency as a circulating 25-hydroxyvitamin D [25(OH)D] concentration <25 nmol/L resulting in an increased risk of poor

Affiliation: *O. Feehan, P. J. Magee, L. K. Pourshahidi, D. J. Armstrong*, and *E. M. McSorley* are with the Nutrition Innovation Centre for Food and Health, Ulster University, Coleraine, Northern Ireland, United Kingdom. *L. K. Pourshahidi* and *D. J. Armstrong* are with the Department of Rheumatology, Altnagelvin Hospital, Western Health and Social Care Trust, Londonderry, United Kingdom.

Correspondence: *E. M. McSorley*, Nutrition Innovation Centre for Food and Health, Ulster University, Coleraine, Northern Ireland BT52 1SA, UK. E-mail: Em.mcsorley@ulster.ac.uk.

Key words: Aged, aged ≥80 years, musculoskeletal health, nursing home, older adults, status, supplementation, vitamin D, 25(OH)D.

https://doi.org/10.1093/nutrit/nuac091

musculoskeletal health.[1] This deficiency cutoff is consistent with <30 nmol/L recommended by the US Institute of Medicine.[2] Traditionally, research has focused on the role of vitamin D for the maintenance of musculoskeletal health, whereas more recently, it is evident that poor vitamin D status can negatively affect other health outcomes, including physical and mental well-being. Nonclassical roles of vitamin D in health include protection from bacterial and viral infections, better lung function, benefits to the cardiovascular and nervous systems, as well as the prevention of some cancers.[3]

Ergocalciferol (vitamin D_2) is sourced from the ultraviolet (UV) irradiation of ergosterol, which is a steroid found in some plants but largely in fungi.[4] Vitamin D_3 (cholecalciferol) is the natural form of vitamin D and is not biologically active. Its activation depends on the solar UV irradiation of 7-dehydrocholesterol (present in the skin), which leads to the formation of pre-vitamin D_3. Vitamin D can also be sourced through the diet (eg, eggs, fish, fortified foods); however, few foods contain sufficient amounts, making it challenging to achieve requirements through diet alone.[5] Vitamin D binding proteins transport vitamin D within the blood to the liver, where hydroxylation of the C25 carbon occurs, catalyzed by the vitamin D hydroxylase enzyme, leading to the production of 25-hydroxyvitamin D_3. Vitamin D binding protein transports 25-hydroxyvitamin D_3 to the kidney, where additional hydroxylation at the C1 carbon occurs, catalyzed by the 1α-hydroxylase enzyme to form the active form of vitamin D: 1,25-dihydroxyvitamin D_3.[6,7] Nevertheless, assessment of 25(OH)D concentration is routinely used in practice to measure vitamin D status because of the short half-life and low circulating levels of 1,25-dihydroxyvitamin D_3.[8] Active 1,25-dihydroxyvitamin D_3 interacts with ligand-dependent transcription factors known as vitamin D receptors (VDRs). VDRs form a heterodimer with the retinoid receptor to regulate gene transcription by binding to vitamin D responsive elements in the promoter region of target genes. VDRs are located in a variety of tissues and organs, not just those directly implicated in calcium homeostasis, such as bone, kidneys, and parathyroid gland, suggesting that vitamin D may have a broad range of functions, such as control of immune responses, embryogenesis, and carcinogenesis.[9,10]

Several factors can affect the metabolism of vitamin D, including parathyroid hormone, which stimulates 1α-hydroxylase activity, potentially through acting on the promoter region of the enzyme. With advancing age, metabolism of vitamin D and calcium becomes compromised, resulting in diminished calcium absorption, compromised renal production of 1,25-dihydroxyvitamin D_3, decreased VDRs, and intestinal resistance of calcium absorption to circulating 1,25-dihydroxyvitamin D3.[7,10] This, in addition to other factors associated with ageing, such as poor dietary intake, medication use, increasing adiposity, and lack of time spent outdoors (owing to frailty and/or compromised mobility) (Figure 1), significantly places older adults and, in particular, nursing home residents at risk of vitamin D deficiency.[11] Given the most recent SARS-Cov-2 (the virus causing COVID-19) global pandemic, the vulnerability of nursing home residents has been highlighted, with the role of vitamin D in the prevention and treatment of acute respiratory tract infections receiving great attention.[12] Numerous systematic reviews and meta-analyses have demonstrated that low vitamin D status is significantly associated with a higher risk of COVID-19 infection[13–15] along with increased mortality and severity of disease.[14] The COVID-19 pandemic resulted in high death rates of nursing home residents who are already at increased risk of viral infections, owing to compromised immunity associated with ageing. With the proven benefit of vitamin D for immune function, it is more important than ever to improve vitamin D status in this group.

Little is known about the vitamin D status or dietary intakes of nursing home residents across the globe and, consequently, there are currently no specific recommendations for dietary intake or supplementation in this vulnerable group most at risk of deficiency. A limited number of observational studies have assessed the vitamin D status of older adults in nursing homes, with the available evidence, which is summarized in this review, suggesting a high prevalence of vitamin D deficiency. Older adults are recommended to consume between 600 and 800 IU vitamin D/day depending on the target vitamin D status [ranging from a 25(OH)D concentration ≥25 to 75nmol/L] and/or the functional outcome being investigated[2,16–18]; however, it is unclear if nursing home residents are actually meeting these recommendations. In the present review, we summarize the available evidence on the vitamin D status of nursing home residents and critically discuss the effect of vitamin D supplementation, alone and in combination with other nutrients or therapies, on improving vitamin D status and health outcomes.

METHODS

Search methods for identification of studies

Searches were conducted of the Medline (Ovid) and CINAHL databases in May 2021. The search strategy

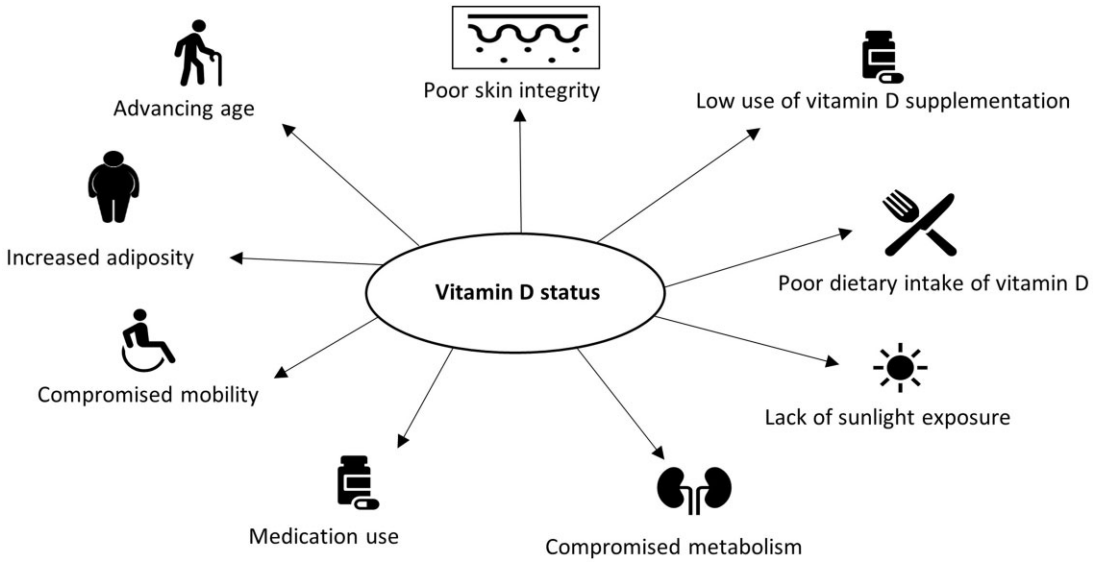

Figure 1 **Factors affecting vitamin D status in older adults.**

consisted of combinations of the terms "nursing homes," "residential facilities," "homes for the aged," "aged," "aged, 80 and over," "vitamin D," "cholecalciferol," and "ergocalciferols." Key words were chosen on the basis of what was suggested by each database (see Appendix 1 in the Supporting Information online). The term "care home" was not included as a search term, because its description was "care at home," which does not meet the inclusion criteria for this review. The search was limited by publication year (from 2010 to May 2021), English language, and human-only studies before screening.

Eligibility criteria

Articles were deemed eligible for inclusion if they were completed in older adults, at least 1 group in the study comprised nursing home residents, and they reported either blood concentrations of vitamin D or percentage vitamin D deficiency or sufficiency. Observation studies were included if they reported vitamin D status or percentage vitamin D deficiency or sufficiency of nursing home residents. Intervention studies were included if they examined the effect of vitamin D supplementation on vitamin D status or any health outcome such as falls, fractures, acute respiratory infections, or muscle strength. Intervention studies were also included if they examined the effect of vitamin D supplementation in combination with other nutrients or therapy on any health outcome, as previously described. Only human-focused research articles published in the English language and published after 2010 were eligible to be included in this review. Systematic reviews, literature reviews, meta-analyses, case reports, letters, animal and in vitro studies, studies not published in English, retracted articles, articles not reporting vitamin D status or providing data on deficiency or sufficiency, and articles published before 2010 were excluded from the analysis. For the purpose of this review, if a research paper reported more than 1 study within the research article or reported findings on more than 1 group of participants other than nursing home residents (eg, diabetic cohort, children, and community-dwelling older adults), the data were not presented for that group. A PICO (Participants, Intervention, Comparison, Outcomes) strategy was developed to define inclusion and exclusion criteria for intervention studies (Table 1). PRISMA guidelines for systematic reviews were followed. All vitamin D status values were reported in units of nanomoles per liter for consistency.

Study selection and data extraction

Article results from the database searches were exported to Refworks and duplicates were removed. Paper titles and abstracts were screened for eligibility using the criteria outlined above. Relevant information including age, sex, country, vitamin D status, percentage of deficiency or sufficiency, intervention type, and relevant results and conclusions was extracted from the articles.

Quality assessment

To best assess the quality of eligible studies, the Newcastle-Ottawa scale[19] and the adapted Newcastle-Ottawa scale for observation studies were used to assess cohort, case-control, and observational studies. The studies were scored using a predefined star system, in

Table1 **PICOS criteria for inclusion and exclusion of intervention studies**

	Inclusion criteria	Exclusion criteria
Population	Older adults in nursing homes	Studies without at least 1 group of nursing home residents studied Humans only
Intervention	Vitamin D alone or in combination with other nutrients or therapy	Studies that do not have at least 1 vitamin D intervention group
Comparison	Vitamin D status	Studies without reported vitamin D status or figures on deficiency or sufficiency
Outcomes	Vitamin D status, adult health outcomes, such as bone turnover markers, physical function	Studies that did not measure vitamin D status or adult health outcomes
Study design	Observation studies, randomized controlled trials, nonrandomized controlled trials	Animal studies, in vitro studies, letters, literature reviews, systematic reviews, meta-analysis, retracted, non-English language, reports, no vitamin D status or figures on deficiency or sufficiency, published before 2010

which more stars corresponded to better quality. For intervention studies, the Cochrane Collaboration's tool for assessing risk of bias[20] was used as a method of quality assessment. This tool assesses areas at risk of bias within studies, such as random sequence allocation, allocation concealment, performance, detection, attrition, and reporting bias. The studies were then rated as of "low," "unclear," or "high" risk of bias in each of these areas.

RESULTS

A total of 366 papers were identified from the database searches, 308 of which were removed for the following reasons: 90 papers were duplicates; 51 were systematic reviews, literature reviews, or meta-analyses; and 167 were excluded after title, abstract, and full-text screening (Figure 2). The final number of articles included in the review was 58. Of the 58 studies, we identified 26 observation studies (Table 2),[21–46] 18 vitamin D–intervention studies to improve vitamin D status (Table 3),[47–64] and 14 studies that intervened with vitamin D alone or in combination with other nutrients or therapies and assessed health outcomes (Table 4).[65–78] For cohort, case-control, and cross-sectional studies, 2 of 32 studies scored 13 of 13 stars and 10 studies scored ≥10 stars. For intervention studies, 25 studies scored low risk of bias in the categories of reporting bias, 17 studies in attribution bias, and 19 studies in random-sequencing-allocation selection bias. Allocation concealment bias and performance bias varied across the studies, with nearly half reporting either high or low risk of bias. The greatest number of studies with unclear risk of bias were categorized as such because of detection bias.

DISCUSSION

Vitamin D status of older adults in nursing homes

Vitamin D deficiency can have a significant impact on the health and welfare of older adults in nursing homes[79]; to date, 26 studies have reported on the vitamin D status of this population (Table 2) (n = 1 study reported prevalence of vitamin D deficiency only).[30] Vitamin D concentrations ranged from 17 nmol/L to 115 nmol/L, and reported incidence of vitamin D deficiency ranged from 8% up to 94% in some cohorts in which supplementation use was low.[31] Higher concentrations of vitamin D were associated with vitamin D supplement use[37] as well as year-round sunlight exposure.[25] Deficiency and suboptimal vitamin D status were frequently reported in studies where residents had limited sunlight exposure and dietary intake of vitamin D was poor.[21,22] Furthermore, a lack of vitamin D food fortification, frailty, low use of vitamin D supplements,[31] and poor renal function[28] were associated with a lower vitamin D status.

Thirteen studies did not report the proportions of deficiency or sufficiency or any form of cutoff data (Table 1), making it difficult to draw conclusions on the exact prevalence of vitamin D deficiency in nursing home residents. Although <50 nmol/L was the cutoff used in most studies to define deficiency, some studies used the cutoff of <25 nmol/L, possibly owing to the guidance given by national agencies.[1,2] If the cutoff of <50 nmol/L was applied to all studies, an even greater degree of deficiency would have been reported. Prevalence of 25(OH)D concentration >75 nmol/L, deemed optimal for effects on vitamin D on calcium, bone, and muscle metabolism and nonskeletal outcomes (eg, immune function),[15,17] ranged from as low as 0%[21] to 28.8%[44] and as high as 87.1% in 1 cohort in

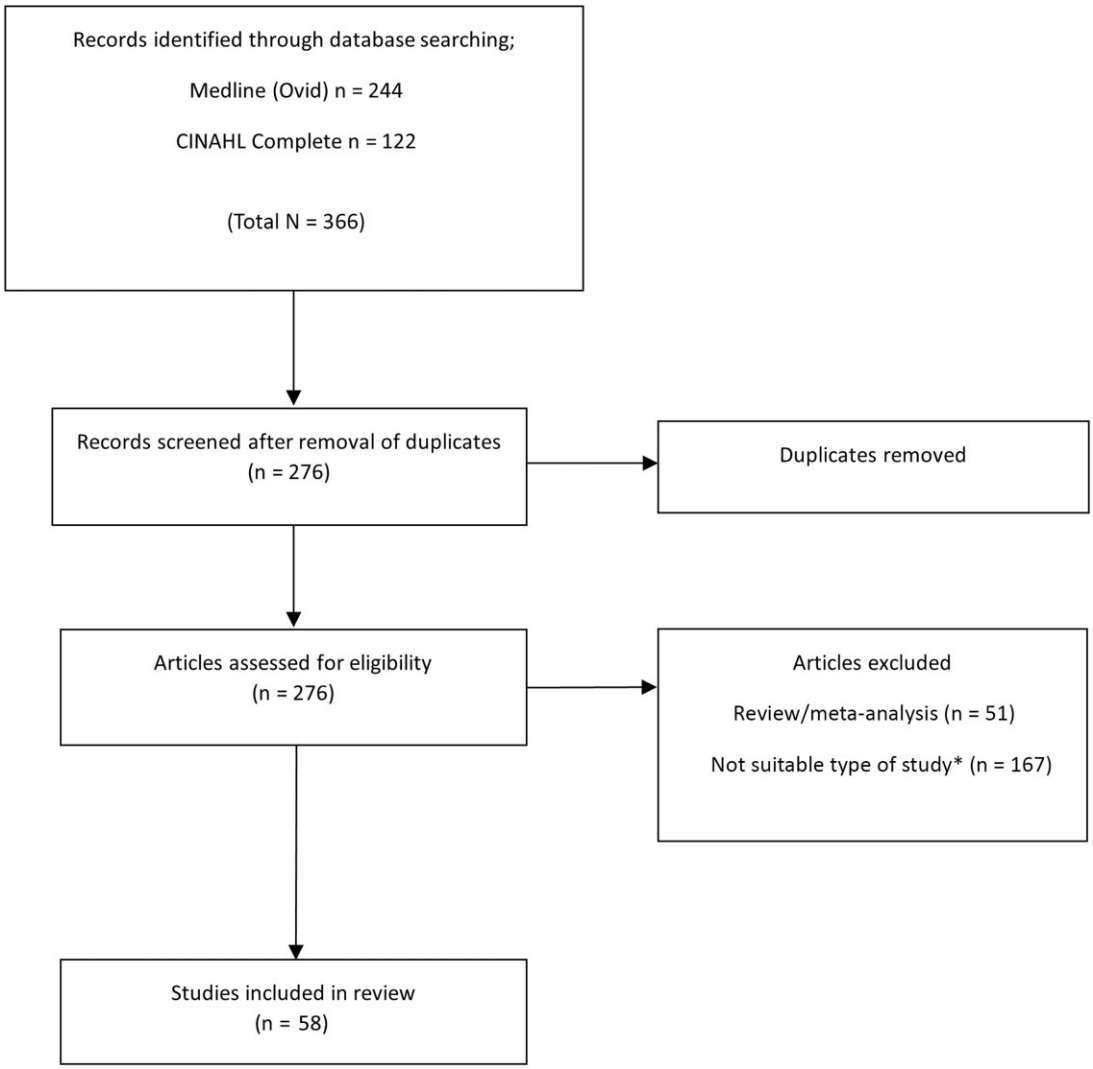

Figure 2 **PRISMA flow diagram.** Search was limited by English-language only and humans-only articles and publication year 2010 in advance of search. *Studies considered not suitable included literature reviews, systematic reviews, meta-analyses, letters, reports, animal and in vitro studies, retracted papers and no vitamin D status or figures on deficiency and sufficiency.

which supplement use was frequent.[37] With a high prevalence of vitamin D deficiency and suboptimal status, there is a clear need for specific guidelines to improve the vitamin D status of nursing home residents across the globe.

Supplement use was not reported in 10 studies, and another 6 studies excluded participants if they were taking vitamin D supplementation. Supplementation has been shown to be effective in improving vitamin D status in New Zealand, where a government funded universal supplementation program in nursing home residents contributed to the prevention of vitamin D insufficiency, with only 1.5% of supplement users having a vitamin D status <50 nmol/L, compared with 65.3% in nonsupplement users.[37] It is noteworthy that multivitamin supplement use was not reported by any of the studies and could be a potential additional source of supplemental vitamin D. This should be quantified by future studies where possible. Despite its importance for vitamin D synthesis, time spent outdoors exposed to sunlight was reported by 3 of the 26 studies, with 1 study highlighting that residents had only a few minutes of sun exposure on an active day.[21] In addition, to our knowledge, no studies have been conducted in countries of northern latitudes such as Sweden or Denmark where the ability to synthesize vitamin D from sunlight exposure is limited to the spring and summer months.[80] Older adults who are immobile, have dementia, or are unable to go outdoors could be at an even greater risk of lower vitamin D status due to negligible sunlight exposure.[81] With sunlight exposure low throughout the year and reported dietary intake of vitamin D as little as

Table 2 **Vitamin D status of older adults in nursing homes**

Reference type of study recruitment locations	Country	No. of participants	Age, mean (SD), y	Sex (no.)	25(OH)D status, mean (SD), nmol/L	25(OH)D cutoff for deficiency, nmol/L	Deficiency, %	Additional % 25(OH)D cutoff data	BMI, kg/m^2 sunlight exposure, mean (SD)	Dementia/cognitive impairment, % vitamin D supp use, %	Dietary vitamin D, IU/d Dietary calcium, mg/d mean (SD)
Portela et al (2010)[21] NR Social-status institutions	Spain and Argentina	97 C	Spain: 82 (7.1) Argentina: 81.3 (7.9)	97 F; 0 M	Spain: 29.25 (5.8) Argentina: 34 (6.1)	<50	Spain: 90 Argentina: 86	Spain: 47% severely deficient (<25 nmol/L) Argentina: 32% severely deficient 0% >75 nmol/L	NR Active day: few minutes between 10 AM and 4 PM	NR Excluded if taking vit D supp	Spain: 50.8 (NR) Argentina: 160 (NR) 800 (NR)
Kuwabara et al (2010)[22] Cross-sectional 1 NH	Japan	50 C	87.6 (8.0)	35 F; 15 M	27.75 (3.1)	NR	NR	Hypovitaminosis: <50 nmol/L 40% <25 nmol/L 58% 25–50 nmol/L n = 1 ≥ 50 nmol/L	21 (3.8) NR	NR NR	160 (1.4) 494 (53)
McWilliams et al (2011)[23] Prospective cohort NH residents admitted to hospital	USA	71C	81.5 (10.9)	49 F, 29 M	22.7 ± 11.0	47.5	NR	72% had low status (<75 nmol/L)	NR NR	53.5% Dementia NR	NR NR
Sitter et al (2011)[24] NR Two personal NHs	Canada	14 P 13 C	83 (9.8)	9 F; 5 M	Time A (2–3 mo after admission): 55 (25) Time B (4 mo after time A): 58.5 (24.9)	<25	Time A: 8 time B: 0	Time A 75% insufficient (25–75 nmol/L); 17% optimal (75–250 nmol/L) Time B 83% insufficient; 17% optimal	NR NR	Excluded if had either NR	NR NR
Kruavit et al (2012)[25] Cross-sectional 2 Elderly care institutions	Thailand	93 C	75.2 (6.0)	93 F; 0 M	69.3 (15.4)	NR	NR	61.3% Insufficiency (≤70 nmol/L) 38.7% >70 nmol/L 21.5% <50 nmol/L 77.4% <75 nmol/L	24.1 (3.6) 16% >2 h/d	NR Ca + vit D supp: 6.5%	NR 322.3 (158.4)
Oudshoorn et al (2012)[26] Cross-sectional Residential homes	The Netherlands	426 C	81 (7.2)	315 F; 111 M	39.1 (21.4) [25(OH)D3]	NR	NR	67% <50 nmol/L 27% <25 nmol/L	NR NR	Mean (SD) MMSE score: 26.5 (2.6) excluded if had dementia prescribed Ca + vit D: 12% not prescribed Ca + vit D: 7%	NR 826 (242)
Pilz et al (2012)[27] Prospective cohort 95 NHs	Austria	961 C	83.7 (6.1)	961 F; 0 M	17.5 (13.7–25.5)[a]	NR	NR	7% >50 nmol/L 93% <50 nmol/L	Q1: 25.2 (4.6) Q2: 26 (5.3) Q3: 26 (4.4) Q4: 26.3 (4.5) NR	NR Q1–Q4 vit D supplementation: 0.4%, 0%, 2.1%, 14.3%, respectively Ca supplementation: 1.2%, 0.8%, 4.6%, 18.5%, respectively	NR NR
Terabe et al (2012)[28] Cross-sectional 48 NHs	Japan	403 C	86.5 (NR)	403 F; 0 M	41.75 (NR) [25(OH)D3]	<50	78.1		<85 y: 20.7 (4.4) ≥85 y: 20 (3.3) NR	NR NR	NR NR
Trummer et al (2012)[29] Prospective cohort 95 NHs	Austria	1093 C	84 (6)	926 F; 167 M	F: 22 (8) M: 24.25 (5.9)	<50	94	98% <75 nmol/L	NR NR	NR excluded if taking vit D supp	NR NR
Verhoeven et al (2012)[30] Cross-sectional 53 NHs	Belgium	589 C	83.8 (7.2)	448 F; 141 M	NR	<50	75.6	93.9% <75 nmol/L	NR NR	Excluded if had either NR	NR NR
Diekmann et al (2013)[31] Observational longitudinal 2 Municipal NHs	Germany	189 P 115 C	86.3 (7.8)	84 F; 31 M	T1 (baseline): 20.8 (16.5–17)[a] T2 (1 y follow-up): 21.3 (14.9–58.6)[a]	<50	T1: 93.9 T2: 71.3	T1 and T2, respectively: 6.1% and 28.7% >50 nmol/L 70.4% and 57.3% <25 nmol/L 0 vs 4.3% severely deficient (<10 nmol/L)	26.6 ± 5.3 NR	71.8% Cognitive impairment MMSE score, mean (SD): 16.5 (10.3) 28.7%	NR NR

(continued)

Table 2 **Continued**

Reference type of study recruitment locations	Country	No. of participants	Age, mean (SD), y	Sex (no.)	25(OH)D status, mean (SD), nmol/L	25(OH)D cutoff for deficiency, nmol/L	Deficiency, %	Additional % 25(OH)D cutoff data	BMI, kg/m^2 sunlight exposure, mean (SD)	Dementia/cognitive impairment, % vitamin D supp use, %	Dietary vitamin D, IU/d Dietary calcium, mg/d mean (SD)
Kojima et al (2013)[32] Retrospective chart review/cross-sectional 1 Veterans Affairs community NH	USA	104 C	70.6 (12.6)	0 F; 10 4M	Total group: 52.5 (3.9) deficient: 32.5 (4.4) not deficient: 72.5 (6.9)	<50	49		26.7 (6.9) NR	33.7% Dementia excluded if taking vit D supp	NR NR
Maeda et al (2013)[33] Cross-sectional 2 NHs	Brazil	177 C	76.2 (9)	128 F; 49 M	37.6 (29.9)	NR	NR	NR	26.3 (5.6) NR	NR 6.2%	NR NR
Samefors et al (2014)[34] Prospective cohort 11 NHs	Sweden	333 C	F: 86 (NR) M: 83 (NR)	226 F; 107 M	Total group [25(OH)D3]: 40.2 (16) Q1: 24.1 (4.1) Q2: 33.4 (2.2) Q3: 42.1 (2.8) Q4: 62.3 (14.7)	<50	80	14.4% Severely deficient (<25 nmol/L) 65.8% insufficient (26–50 nmol/L) 15.3% 51–75 nmol/L 4.5% >76 nmol/L	Q1: 24.6 (4.5) Q2: 24.7 (4.6) Q3: 25.9 (5.1) Q4: 24.9 (3.9) NR	NR excluded if taking vit D supp	NR NR
Peláez et al (2015)[35] Prospective, observational, noninterventional cohort 1 NH	Spain	72 C	84.7 (NR)	56 F; 16 M	ABI >1.4: 19.95 (6.82) ABI 1.4–0.9: 19.07 (8.23) ABI <0.9: 17.01 (6.56)	NR	NR	NR	29 (5) NR	NR NR	NR NR
Törmä et al (2015)[36] Controlled 4 NHs	Sweden	172P 101 C	EF: 83.8 (7.4) EOV: 86.5 (6.9)	73 F; 28 M	EF: 34.9 (47.2)[a] EOV: 35.8 (39.7)[a]	<50	66.66		EF: 24.1 (5.9) EOV: 23.8 (4.1) NR	Dementia EF: 42% EOV: 37% NR	NR NR
MacDonell et al (2016)[37] Cross-sectional 16 Residential aged-care facilities	New Zealand	309 C	85 (8)	209 F; 100 M	Mean (95%CI) 89.9 (85.2–94.5)	NR	NR	17.8% of total group insufficient (<50 nmol/L) 65.3% non-supp users vs 1.5% supp users <50 nmol/L supp users: 87.1% >75 nmol/L, 27.1% >125 nmol/L	Mean (95%CI) 25.8 (25.1–26.4) NR	NR 75% 50 000 IU vit D_3/mo 18.4% not taking any form of vit D supp	NR NR
Navarro-Martínez et al (2016)[38] Cross-sectional 4 NHs	Spain	104 C	84 (75–99)[b]	104 F; 0 M	Robust: 115 (6) Pre-frail: 71.5 (4) Frail: 70 (3)	NR	NR	NR	NR NR	Excluded if severe cognitive impairment (MMSE score <21) MMSE score: 24 (21–30)[b] Excluded if on vit D supp	NR NR
Shinkov et al (2016)[39] Cross-sectional screening 4 NHs	Bulgaria	66 C	74.5 (69.8–78)[a]	26 F; 40 M	17.8 (9.4–28.6)[a]	25–50	65.2	4.5% Sufficient (>50 nmol/L)	26 (4.5) NR	NR 0%	Average between 100 and 400 800 (NR)
Arnljots et al (2017)[40] Cross-sectional 22 NHs	Sweden	545 C	86 (6.9)	370 F; 175 M	34 (21)	<25	Total group: N = 41 supp user: 44 non-supp users: 6.4	Total group: 3.7% <12.5 nmol/L 82% <50 nmol/L 94% <75 nmol/L 6.4% >75 nmol/L supp user vs non-supp user 4.4% vs 0% 45% vs 22 4.9% vs 43% 1.8% vs 29%	NR April to August: 6.6 (7.1) h/wk 20% ≤1 h/wk	55% Dementia 17%	NR NR
Kucukler et al (2017)[41] Cross-sectional 2 NHs	Turkey	71 C	76 (0.8)	0 F; 71 M	38.25 (0.8)	NR	NR	NR	25.6 (0.5) NR	24.3% Dementia NR	NR NR
Kojima et al (2017)[42] Cross-sectional 1 Veterans Affairs NH	USA	238 C	73.4 (13.1)	0 F; 238 M	Total group: 58.5 (9.8) supp users: 66.4 (9.3) non-supp users with status <45: 29.25 (3.8)	NR	NR	37.4% <50 nmol/L	26.5 (6.7) NR	NR 36.1%	NR NR

(continued)

Table 2 **Continued**

Reference type of study recruitment locations	Country	No. of participants	Age, mean (SD), y	Sex (no.)	25(OH)D status, mean (SD), nmol/L	25(OH)D cutoff for deficiency, nmol/L	Deficiency, %	Additional % 25(OH)D cutoff data	BMI, kg/m^2 sunlight exposure, mean (SD)	Dementia/cognitive impairment, % vitamin D supp use, %	Dietary vitamin D, IU/d Dietary calcium, mg/d mean (SD)
					non-supp users with status >45: 59.62 (7.0)						
Schwartz et al (2018)[43] Cross-sectional analysis 1 NH	USA	79 C	87.4 (8)	51 F; 28 M	87.25 (12.8)	NR	NR	NR	27.3 (5.8) NR	NR NR	NR NR
Sousa et al (2019)[44] Cross-sectional 9 NHs	Brazil	153 C	81.7 (9.2)	120 F; 33 M	59.75 (16.6–31)[a]	NR	NR	28.8% Sufficient (75–150 nmol/L)	Categories thin: 46.4%; normal: 31.1%; excess weight: 22.7% NR	Cognitive impairment mild: 6.3%; moderate: 18.1%; severe: 66.7% 5.9%	112 (3.2) 997.9 (291.8)
Griffin et al (2020)[45] Cross-sectional NHs	Ireland	273C	81.5 (11.7)[a]	176 F; 97 M	29.7 (13–147.8)[a]	<25	42	25% Insufficient (25–50 nmol/L) 33% sufficient (>50 nmol/L)	NR NR	NR NR	NR NR
Okan et al (2020)[46] Cross-sectional 1NH	Turkey	36C	74 (8)	13 F; 23 M	35.8 (8)	25–47.5	64%	100% Insufficient (50–72.5 nmol/L)	F: 29.4 (5.4); M: 27.3±(4.7) Positive association of 25(OH)D with sunlight exposure 11 AM to 3 PM	NR Excluded if taking vit D supp	NR NR

Data are presented as mean (standard deviation) unless otherwise indicated.

[a]Median (interquartile range).

[b]Range.

Abbreviations: 25(OH)D, 25-hydroxyvitamin D; 25(OH)D3, 25-hydroxyvitamin D_3; ABI, ankle-brachial index; BMI, body mass index; C, completed; Ca, calcium; EF, external facilitation; EOV, education outreach visits; F, female; M, male; MMSE, Mini-Mental State Examination; NH, nursing home; NR, not reported; P, participated; Q, quartile; Signif, significant; Supp, supplement; T, time; USA, United States of America; vit, vitamin.

50.8 IU/d,[21] vitamin D supplementation and/or food fortification may be more relevant strategies to prevent vitamin D deficiency in this group.

Medication use was considered in 5 studies and, in all cases, was not significantly associated with vitamin D status.[23,30,31,37,44] Chronic diseases associated with ageing often require the frequent use of medications, and several drugs such as antiepileptic drugs, statins, antiinflammatory agents, and antihypertensives can interfere with vitamin D and bone metabolism.[82] Regular monitoring of vitamin D status would be beneficial, taking into consideration potential contraindications of medication to better understand and limit adverse drug reactions and/or improve the efficacy of various drugs.[82] A large proportion of studies either did not report data on the incidence of dementia or cognitive impairments, conditions that are highly prevalent in nursing home residents,[83,84] or they excluded residents on the basis of these criteria. Inclusion of such participants in future studies would make for a more representative cohort and may help determine the true prevalence of vitamin D deficiency in all nursing home residents. Another potentially important covariate for vitamin D status is body mass index (BMI). Research has shown that a higher BMI is associated with a lower 25(OH)D concentration,[33] a lower 25(OH)D response to supplementation in older adults, and is a risk factor for vitamin D deficiency in nursing home residents.[32] Therefore, consideration should be given to the individuals' BMI when deciding on the dose of vitamin D supplementation required to restore status to sufficiency.

Supplementation of vitamin D and its effect on raising vitamin D status

A variety of routes of vitamin D administration have been explored in interventions, including capsules, liquid drops, intramuscular injection, and sunlight/UV exposure (Table 3). Oral supplementation (capsules or liquid) of vitamin D_3 was the most frequently reported method of administration albeit there is controversy regarding the best form or type of vitamin D supplementation for use in intervention studies in older adults. Some studies suggest that vitamin D_3 (cholecalciferol) is more effective in increasing 25(OH)D concentration in comparison with vitamin D_2.[85] It has been proposed that both of these calciferols have different binding affinities for VDRs; in addition, vitamin D_3 is the favored substrate for liver 25-hydroxylase and should be the preferred choice for supplementation.[3] The studies in the present review intervened with both vitamin D_3 and D_2, the majority with D_3. Duration of supplementation ranged from 4 weeks to 1 year, and the dose regimen ranged from 0 to 4000 IU/d, 5600 to 100 000 IU/wk, or 400 000 IU every 2 weeks. Method of administration included loading doses (100 000 IU 3–4 times every 2 wk)[59] followed by a maintenance dose (monthly dose of 25 000 IU or 50 000 IU, or 100 000 IU every 13 wk),[57,61] a single "megadose" (600 000 IU),[53] a daily dose (0 to 2000 IU),[47,49–51] and a daily dose (800 IU) vs weekly supplementation (8000–50 000 IU).[55,58,60]

Vitamin D supplementation regimens to normalize vitamin D status in nursing home residents with severe deficiency, deficiency, or insufficiency were investigated in 4 studies.[50,53,57,62] Regardless of the description of deficiency, all studies applied a vitamin D status cutoff of <50 nmol/L for inclusion in their study and aimed to increase 25(OH)D concentration to >75 nmol/L after supplementation. Given the favorable nature of vitamin D_3, supplementation with vitamin D_3 instead of vitamin D_2 should be encouraged and could potentially lead to sufficiency being reached quicker.[86] As expected, the 2 interventions which used the highest dose of vitamin D (a single "megadose intramuscular injection of 600 000 IU vitamin D_3 or 100 000 IU vitamin D_2 per week for 12 wk) were shown to significantly increase 25(OH)D concentrations by the greatest amount and achieve optimal vitamin D status [25(OH)D >75 nmol/L]. These findings are comparable to the National Institute for Health and Care Excellence guidance on the most appropriate treatment regimen for those with vitamin D deficiency, recommending 300 000 IU administered weekly or split over daily doses for 6–10 weeks followed by a maintenance dose of ~800 to 2000 IU daily or intermittently at a higher equivalent dose. It is important to note, however, that very-high-dose vitamin D supplementation has been shown to result in some adverse effects in older people, including increased risk of falls and fractures; therefore, standard clinical practice is to give more modest doses daily or weekly. In terms of applying a cutoff of >75 nmol/L as optimal vitamin D status, The European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis and the Endocrine Society recommend achieving a 25(OH)D concentration of 75 nmol/L for optimal effects on skeleton and mobility; therefore, >75 nmol/L may be a useful target before maintenance supplementation is commenced. Nonresponders to supplementation had a significantly higher BMI than responders, as well as a higher incidence of renal insufficiency.[50] A higher dose of supplementation, such as a single loading dose or loading dose followed by a maintenance dose may be needed for those with a higher BMI. Those with renal insufficiency may need a lower dose of supplementation for a longer time, such as 2000 IU/d.[59]

Table 3 **Supplementation of vitamin D and its effect on raising vitamin D status**

Reference type of study recruitment locations	Country	No. of participants	Age, mean (SD), y	Sex	Type of vit D intervention; route of administration	Duration	25(OH)D status: baseline, mean (SD), nmol/L	25(OH)D status: after intervention, mean (SD), nmol/L	**Main conclusions**[a]
Schwalfenberg et al (2010)[47] Retrospective chart review 1 NH facility	Canada	68 P 68 C	80.7 (9.8)	49 F; 19 M	Vit D_3; Oral supp: ND; 2000 IU/d	Minimum 5 mo (5–10 mo)	NR	5 mo 119.4 (28.1) 25(OH)D3	*Daily supplementation with 2000 IU of vitamin D_3 can achieve 25(OH)D levels of >80 nmol/L in most residents living in a nursing home setting, with no levels reaching a toxic range—thus confirming the utility of oral vitamin D supplementation to improve vitamin D status.*
Chel et al (2011)[48] Pilot intervention Low and medium care wards of 1 psychogeriatric NH	The Netherlands	8 C	79 (8)	5F; 3M	Half-body UVB: 2-min half-body irradiation with UVB at 1.0 standard erythema dose (0.5 MED) once/wk	8 wk	28.5 (NR)	46.5 (NR)	*An 8-week course of weekly, frontal half-body irradiation with UVB, at 0.5 MED, leads to an significant increase in 25(OH)D serum levels, but this period is too short to reach vitamin D sufficiency.*
Dinizulu et al (2011)[49] Observational Long-term care institutions	Ireland	63 P	Vit D: 82.1 (7.4) Ca + vit D: 79.5 (7.2)	63 F; 0 M	Vit D_3: supp: ND; 800 IU/d, n = 19 100 mg Ca + 800 IU/d, n = 41	3 mo	Vit D: 25.3 (16) Ca + vit D: 34.7 ± 23.7	Vit D: 78.5 (NR) Ca + vit D: 69.2 (NR)	*Vitamin D alone appears as effective as combined calcium/vitamin D treatment in restoring serum vitamin D levels in older community dwelling and institutionalized patients. a prospective randomized trial would help confirm these findings.*
Shin et al (2011)[50] Retrospective chart review n = 1 long-term care facility	USA	24 P 24 C	Resp 80 (NR) non-resp: 81 (NR)	NR	Vit D_3; Oral supp: ND; 2000 IU/d	At least 12 wk	Mean (range) resp (n = 14): 47 (34.5–67.5) non-resp (n = 10): 96.75 (75–134.25)	Resp: 47.5 (28.5–63) non-resp: 66 (44.5-73)	*Some long-term care elderly patients respond to three months of vitamin D supplementation. The reason why some patients did not respond cannot be determined from this study.*
Ioannidis et al (2012)[51] Cross-sectional 4 Long-term care facilities	Canada	102 P	83.2 (8.7)	70 F; 32 M	Vit D_3: NR 0 IU/d, n = 50 1–400 IU/d, n = 18 401–800 IU/d, n = 9 >800 IU/d, n = 21	N/A	0 IU: 62.2 (27.5) 1–400 IU: 72.8 (22.2) 401–800 IU: 98.9 (26.3) >800 IU: 96 (26.2)	N/A	*Most residents taking more than 400 IU/d of vitamin D_3 achieve optimal levels of 25(OH)D. Nevertheless, although vitamin D supplementation appears to clinically increase serum 25(OH)D levels, some residents in LTC homes are not taking adequate vitamin D supplementation and are not reaching the therapeutic target.*
Sambrook et al (2012)[52] Clustered RCT 51 Aged-care facilities	Australia	602 P 524 C	86.4	427 F; 175 M	Sunlight vs sunlight + oral Ca supp vs control; UV, n = 190 UV+, n = 207 usual care (control), n = 205 sunlight exposure was 30–40 min, 5 d/wk + Ca supplement: 600 mg/d	12 mo	Baseline total group: 32.9[b] control: 33.2 UV: 36.2 UV+: 31.1	NR	*Increased sunlight exposure did not reduce vitamin D deficiency or falls risk in frail older people. This public health strategy was not effective most likely due to poor adherence to the intervention.*
Tellioglu et al (2012)[53] Randomized prospective 1 NH	Turkey	66 P 62 C	IM: 75.5 (6.1) oral: 75.3 (7.5)	33F; 33M	Vit D_3; IM injection vs oral liquid poured on bread: IM (n = 34): 600 000 IU;	12 wk	IM: 29.4 (7.6) Oral: 37.17 (6.9)	IM: 125.85 (14.2) Oral: 107.35 (13.4)	*In vitamin D deficient/insufficient elderly, a single megadose of cholecalciferol increased vitamin D levels significantly and the majority of the patients reached optimal levels. Although both administration routes are effective and appear to be safe, IM application is more*

(continued)

Table 3 **Continued**

Reference type of study recruitment locations	Country	No. of participants	Age, mean (SD), y	Sex	Type of vit D intervention; route of administration	Duration	25(OH)D status: baseline, mean (SD), nmol/L	25(OH)D status: after intervention, mean (SD), nmol/L	**Main conclusions**[a]
					Oral (n = 32): 600 000 IU a single "megadose"				*effective in increasing 25(OH)D levels and balance performance.*
Durvasula et al (2014)[54] Secondary analysis of Sambrook et al[52] 34 Residential aged-care facilities	Australia	397 P 248 C	86.4 (6.6)	179 F; 69 M	Sunlight vs sunlight+oral Ca supplement; sunlight only and sunlight+Ca supplement participants from the previous RCT were included in analysis	6 mo	32.4 (22.9–50.6)[b]	34.6 (23.8–48.4)[b]	*Natural UVR exposure can increase 25OHD levels in older people in residential care, but depends on the season of exposure. However, due to inadequate sun exposure, 25OHD did not reach optimal levels.*
Feldman et al (2014)[55] Cross-sectional 5 Residential care facilities	Canada	236 P 236 C	85 (7.7)	176F; 60M	vit D NR 20 000 IU/wk	1 y	NR	Mean (95%CI) 102 (98–106)	*Twelve months after implementation of a 20 000-IU/wk vitamin D protocol for older adults in residential care, mean 25OHD concentrations were high, and there was no evidence of poor vitamin D status. Given the absence of demonstrated benefit of high 25OHD concentrations to the residential care population, dosages less than 20 000 IU/wk of vitamin D are recommended.*
Veleva et al (2014)[56] Cross-sectional patient file Dementia care units in 1 NH	The Netherlands	71 P 71 C	83 (7)	46 F; 25 M	Vit D_3 capsule vs drops: capsule (n = 52): 5600 IU/wk Drops (n = 19): 7500 IU/wk	At least 3 mo	NR	Total group: 77 (30) capsules: 90 (22) drops: 41 (8)	*In most of these residents, vitamin D supplementation once a week with cholecalciferol capsules containing 5600 IU (equivalent to 800 IU daily) resulted in vitamin D sufficiency (serum 25(OH)D $\geq$ 50 nmol/L).*
Wijnen et al (2015)[57] Open-label, single-center, randomized NH residents recruited at outpatient clinic visit	The Netherlands	30 P 22 C	84 (76–87)[b]	17 F; 13 M	Vit D_3: Oral liquid supp LD (n = 16): 2 × 50 000 IU/wk + monthly dose of 25 000 IU or 50 000 IU DD (n = 14): 800 IU/d	6 mo	LD: 27.1 (16.4–32.8)[b] DD: 20.9 (15.9–29.6)	LD: 61 (54–72)[b] DD: 44 (26–50)	*In NH patients with severe 25OHD deficiency, an individualized calculated cholecalciferol LD is likely to be superior to a DD of cholecalciferol 800 IU in terms of the ability to rapidly normalize vitamin D levels.*
Schwartz et al (2016)[58] Double-blinded RCT 1 NH	USA	81 P 72 C	87.4 (8)	51 F; 30 M	Vit D_3: capsules (n = 20): 800 IU/d n = 19 2000 IU/d n = 20 4000 IU/d n = 13 50 000 IU/wk	16 wk	Baseline (total group): 72.5 (9)	Postintervention (each group): 800 IU: 82.5 (9) 2000 IU: 85 (10) 4000 IU: 107.5 (10) 50 000 IU: 153.5 (6)	*25(OH) D increased linearly with 800-4000 IU/d and 50 000 IU/wk D_3 without a ceiling effect. Data suggest some elderly will require over 800 IU/d D_3 to ensure adequate vitamin D status.*
Delomas et al (2017)[59] Open- label, randomized single-blind controlled 1 NH	France	111 P 111 C	85.1 (6.7)	77 F; 34 M	Vit D_3: Oral supp: vial of liquid (n = 53) Treatment: 4 × 100 000 IU every 2 wk control (n = 58): if deficient (<25 nmol/L): 4 ×	6 wk	NR	Treatment: 110.44 (15.4) control: 89.5 (6.5)	*A single loading protocol is at least as effective and safe as tailored regimen in terms of the ability to rapidly normalize 25(OH)VitD values. The often required dosage of 25(OH)VitD is reasonably not necessary to initiate VitD supplementation protocol in this vulnerable population.*

(continued)

Table 3 **Continued**

Reference type of study recruitment locations	Country	No. of participants	Age, mean (SD), y	Sex	Type of vit D intervention; route of administration	Duration	25(OH)D status: baseline, mean (SD), nmol/L	25(OH)D status: after intervention, mean (SD), nmol/L	**Main conclusions**[a]
					100 000 IU every 2 wk if insufficient (25–50 nmol/L): 3 × 100 000 IU every 2 wk if suboptimal (50–72.5 nmol/L): 2 × 100 000 IU every 2 wk				
Mol et al (2018)[60] Descriptive 1 NH	Turkey	36 P 29 C	NR	22 F; 14 M	Vit D_3 + butylhydroxyanisole in star anise oil; oral drops: DDG (n = 12): 800 IU/d WDG-moderate (n = 12): 5600 IU/wk WDG-high (n = 12): 8000 IU/wk	26 wk	Baseline DDG: 47.41 (8.28) WDG-moderate: 58.18 (12.67) WDG-high: 66.83 (9.6)	DDG: 69.25 (9.72) WDG-moderate: 70.25 (14.42) WDG-high: 72.5 (7)	*Weekly (5600 IU/wk) moderate supplementation of Vitamin D could be more beneficial than weekly (8000/wk) high supplementation among nursing home residents.*
Toren-Wielema et al (2018)[61] Cross-sectional observation 12 Somatic and psychogeriatric NHs	The Netherlands	204 P 156 C	Median (range): 85 (56–99)[b]	110F; 46M	Vit D_3: oral liquid ampoule, 1 × 200 000 IU LD + MD of 100 000 IU every 13 wk	November 2015 to August 2016 (10 mo)	<4 MDs: 73 (29) ≥4 MDs: 85 (27)	N/A	*This standardized VDDR was not efficacious in obtaining and maintaining an adequate VDTL in this nursing home resident population.*
Mueangpaisarn et al (2020)[62] Double-blinded placebo-controlled trial 2 Institutionalized NHs	Thailand	94 P 85 C	STD: 77.9 (9.5) HD: 81.5 (8.8)	94 F; 0 M	Vit D_2 capsules: STD (n = 48): 40 000 IU/wk HD (n = 46): 100 000 IU/wk	12 wk	STD: 48.25 (6.2) HD: 47.75 (6.5)	STD: 86.25 (8.1) HD: 128.5 (19.5)	*Subjects who received high dose ergocalciferol achieved more optimal 25(OH)D levels than those who received standard dose. High dose ergocalciferol is preferred to optimize 25(OH)D levels in subjects with severe vitamin D deficiency.*
Samefors et al (2020)[63] Clustered RCT NHs	Sweden	42P 38C	I: 85.5 (12)[b] CO: 87 (10)[b]	23 F; 19 M	Sunlight exposure; I: 20–30 min sunlight exposure, daily CO: Usual living	2 mo	Total group: 45 (28)[b] I: 42.5 (23)[b] CO: 52 (36)[b]	Total group: 64 (34)[b] I: 53.5 (33)[b] CO: 65 (35)[b]	*Active encouragement to spend time outdoors during summertime improved the levels of serum 25(OH)D and self-perceived mental health significantly in older people in nursing homes and could complement or replace oral vitamin D supplementation in the summer.*
Okan et al (2022)[64] RCT 1 NH	Turkey	40C	76 (6)	18 F; 22 M	Sunlight exposure: I (n = 20): sunlight exposure 5 d/wk CO (n = 20): no sunbathing offered	4 wk	I: 60 (130 CO: 52.5 (10)	I: 80 (16) CO: 55 (10)	*Sunlight exposure was a sufficient source to increase 25(OH)D in most elderly people living in the nursing home. Organizing sunbathing sessions as an independent nursing intervention is recommended for the elderly people living in nursing homes in order to prevent vitamin D deficiency and related consequences.*

Data are presented as mean (standard deviation) unless otherwise indicated.

[a]Quoted directly from the cited articles.

[b]Median.

Abbreviations: 25(OH)D, 25-hydroxyvitamin D; C, completed; Ca, calcium; CO, control group; DD, daily dose; DDG, daily-dose group; F, female; HD, high dose; I; intervention group; IM, intramuscular; LD, loading dose; M, male; MD, maintenance dose; MED, minimal erythema dose; N/A, not applicable; ND, not defined; NH, nursing home; NR, not reported; P, participated; RCT, randomized control trial; Resp, responder; SD, standard deviation; signif, significant; STD, standard dose; Supp, supplement; USA, United States of America; UV, increased sunlight exposure; UV+, sunlight exposure + 600 mg Ca carbonate; UVB, ultraviolet B light; UVR, ultraviolet radiation; VDTL, vitamin D trough level; VDDR, vitamin D dosing regimen; vit, vitamin; WBV, whole-body vibration; WDG-high, weekly dose group–high; WDG-moderate, weekly dose group–moderate.

In terms of daily supplementation with vitamin D, there appears to be a need for a higher dose than 800 IU/d. A higher maintenance dose such as 2000–4000 IU/d may be considered for certain groups, such as those with malabsorption disorders or those with compromised metabolism of vitamin D. Daily supplementation of vitamin D_3 in combination with calcium was not any more effective at achieving sufficiency than vitamin D alone.[49] Supplementation with 5600 IU/wk vitamin D_3 also was effective for maintenance supplementation,[56,60] with 8000 IU/wk resulting in diarrhea effects in some participants, potentially owing to vitamin D not being fully absorbed. Therefore, a lower dose of 5600 IU/wk was recommended.[60] The effect of UVB and UV exposure on increasing vitamin D status through direct sunlight exposure and half-body UVB irradiation has also been investigated in nursing home residents.[48,52,54,63,64] Overall, it was concluded that supplementation could be a more practical and effective intervention to improve vitamin D status. Adherence to sunlight exposure of 30 min/d 5 d/wk was a study limitation, with participants losing interest as time went on.[52]

In summary, the effect of a variety of intervention doses and durations on vitamin D status has been investigated; however, owing to the limited data available and heterogeneity in study design, it is difficult to draw definitive conclusions. Supplementation should be initiated at the earliest point,[31] targeting individuals who are deficient or severely deficient at baseline so that higher-dose remedial supplementation is received prior to maintenance supplementation at a relatively lower dose. Monitoring vitamin D status to determine the most effective dose and duration of supplementation for the maintenance of vitamin D status at a desirable concentration post intervention should also be encouraged. This has not been investigated to date, to our knowledge; however, it would provide useful information on whether individuals need to take continuous supplementation for long periods to restore vitamin D status to a sufficient level and maintain it.

Supplementation of vitamin D alone and in combination with other nutrients or therapies and its effect on health outcomes

Several studies have investigated the effect of vitamin D supplementation both alone and in combination with other nutrients or therapies on health outcomes in nursing home residents (Table 4). The primary outcomes investigated include physical function and quality of life, acute respiratory infections, and biological markers.

Physical function

Physical outcome measures and functionality were the most investigated outcomes. Two studies assessed the effect of the same vitamin D intervention on different outcomes.[65,67] Both studies showed that the higher vitamin D_3 dose (1600 IU/d) resulted in a greater vitamin D status although it was not anymore superior to the lower dose (880 IU/d) in resultant physical benefits. Whole-body vibration did not add any additional benefit to musculoskeletal health when compared with no training.

Three studies assessed the effect of similar oral nutritional supplements in combination with exercise training on physical function and performance.[72,74,77] Oral nutritional supplements in addition to exercise improved function, nutritional status, and quality of life, with a greater improvement seen in frailer residents with lower vitamin D status and lower functionality.[72] In comparison, others have shown that exercise training alone or in combination with oral nutritional supplements resulted in no additional physical benefits.[74,77] This finding may be attributed to the complex nature of introducing exercise to nursing home residents as well as a gradual decline in health in this group over the 6-month study period. In 1 study, a vitamin D_3– and calcium-fortified bread improved overall score in quality of life[71]; nevertheless, owing to the small sample size and short study duration, this pilot study should be seen as a model for a larger, more robust vitamin D supplementation study designed to assess physical and psychological effects in nursing home residents.

Acute respiratory infections

Only 1 study investigated the effect of vitamin D supplementation on acute respiratory infections as the main health outcome.[75] Vitamin D deficiency has been associated with a negative effect on immunity, leading to greater vulnerability to infection.[87] Vitamin D has immunomodulatory effects on both the innate and adaptive immune systems, modulates the expression of antimicrobial peptides, for instance cathelicidin, and affects the inflammatory cascade via nuclear factor κ-light-chain-enhancer of activated B cells.[88] In a cohort of nursing home residents, high-dose vitamin D_3 supplementation resulted in significantly fewer acute respiratory infections per person-year and a greater incidence of falls than the standard dose,[75] which was proposed to be related to the greater mobility of these patients, in turn, leading to a greater risk of falling. This U-shaped curve for vitamin D and falls has been reported by others and should be taken into

Table 4 **Supplementation with vitamin D alone and in combination with other nutrients or therapies and its effect on health outcomes**

Reference Type of study Recruitment locations	Country	No. of participants	Age, mean±SD, y	Sex	Type of intervention	Duration	Primary outcome measures	**Main conclusions**[a]
Bogaerts et al (2011)[65] RCT NHs	Belgium	113 P 111 C	WBV+CD: 80.3 (5.3) WBV+HD: 79.8 (5.3) CD group: 78.7 (5.6) HD group: 79.6 (5.2)	111 F; 0 M	Type ND: WBV+CD (n = 28) 880 IU/d vit D_3 WBV+HD (n = 26) 1600 IU/d vit D_3 CD group (n = 28) HD group (n = 29) All received 1000 mg Ca WBV (exercise 3 times/wk on a vibration platform)	6 mo	Balance: computerized posturography Functionality: 10-m walk test, TUG, shuttle walk Fall risk	*HD vitamin D supplementation is not more efficient than conventional dosing in improving functionality in institutionalized elderly. WBV training on top of vitamin D supplementation provided an added benefit with regard to walking, TUG performance, and endurance capacity.*
Bonjour et al (2011)[66] Crossover RCT 6 NHs/institutions for elderly	France	29 P 21 C	86.9 (6.3)	29 F; 0 M	Fortified vs standard cheese; Intervention: 2 × 100g/d fortified cheese (total: 100 IU vit D + 302 mg Ca) Control: 2 × 100g/d standard cheese (total: 0 IU vit D + 236 mg Ca)	12 wk total: 6 wk on control; 6 wk on intervention	CTX TRAP-5b 25(OH)D PTH	*Consumption of soft plain cheese increasing the supply of vitamin D, calcium and proteins, could reduce bone resorption and thereby reduce the risk of incidental fragility fractures in the long term.*
Verschueren et al (2011)[67] RCT NHs/service apartments/cloistered communities	Belgium	113 P 111 C	WBV+CD: 80.3 (5.3) WBV+HD: 79.8 (5.3) CD group: 78.7 (5.6) HD group: 79.6 (5.2)	111 F; 0 M	Type ND: WBV+CD (n = 28) 880 IU/d vit D_3 WBV+HD (n = 26) 1600 IU/d vit D3 CD group (n = 28) HD group (n = 29) All received 1000 mg Ca WBV (exercise 3 times/wk on a vibration platform)	6 mo	Isometric and dynamic strength; leg-mass muscle; hip BMD	*In institutionalized older women over 70 y old, the WBV training program described herein does not provide additional musculoskeletal benefit over vitamin D supplementation. Compared with conventional doses of vitamin D (880 IU), a higher dose of 1600 IU induced significantly higher levels of circulating vitamin D but was not more efficient in enhancing either muscle mass or strength or increasing hip BMD in this population.*
Kaviani et al (2012)[68] Interventional prospective 1 NH	Iran	76 P	78.7 (8)	52 F; 24 M	Oral pill; 50 000 IU vit D_3/wk	8 wk	Insulin resistance Fasting plasma glucose 25(OH)D	*Before and after the intervention, vitamin D deficiency had no relationship with FPG level and insulin resistance. Vitamin D intake had no significant effect on FPG level, but it increased the prevalence of insulin resistance significantly.*
Bonjour et al (2013)[69] Double-blinded RCT 10 NHs	France	59 P 56 C	CY: 85.1 (1.3)[b] FY: 85.8 (1.2)	58 F; 0 M	FY vs CY: FY group (n = 32): 2 × 125 g/d (total: 400 IU vit D_3 + 800 mg Ca) CY group (n = 27): 2 × 125 g/d (total: 400 IU vit D_3 + 280 mg Ca)	8 wk	25(OH)D PTH Bone resorption markers: TRAP5b and CTX	*This study in institutionalized elderly at high risk for osteoporotic fracture suggests that fortification of dairy products with vitamin D_3 and calcium provides a greater prevention of accelerated bone resorption as compared with nonfortified equivalent foods.*
Mocanu et al (2013)[70] Single-arm clinical trial 1 NH	Romania	45 P 23 C	68.3	28 F; 17 M	Fortified bread: Follow up after 1 y and 3 y after discontinuation of 100 g bread bun/d for 12 mo containing 5000 IU vit D_3 + 320g Ca	3 y	25(OH)D PTH BMD	*Vitamin D nutritional status exhibits a long half-life in the body, and a true steady-state plateau may not even be reached 1 year after a discontinuation in dose. Furthermore, once the need for vitamin D has been established, based on a low baseline serum 25(OH)D concentrations, the appropriate action is to maintain corrective vitamin D supplementation over the long term.*

(continued)

Table 4 **Continued**

Reference Type of study Recruitment locations	Country	No. of participants	Age, mean±SD, y	Sex	Type of intervention	Duration	Primary outcome measures	**Main conclusions**[a]
Costan et al (2014)[71] Longitudinal prospective 1 NH	Romania	45 P 40 C	VFX: 71.6 (7.2) VF: 69.9 (5.2)	28 F; 17 M	Fortified bread: 1 × 100 g bread roll/d containing 5000 IU vit D_3 + 320 g Ca	12 mo	Health-related quality of life (pain, physical function, social function, general health perception, and mental function)	*Daily consumption of bread fortified with 125 g vitamin D3 was efficient and safe to raise serum 25(OH)D concentrations to > 75 nmol/L and to induce significant improvement of the total score of QUALEFFO-41. Vitamin D supplementation also significantly diminished pain perception and ameliorated physical functions.*
Abizanda et al (2015)[72] Multicentric prospective observation 4 NHs	Spain	91 P 69 C	85.6 (5.6)	27 M; 64 F	Oral drink: 2 × 200 mL ONS daily + exercise 5 × d/wk Each ONS contains: 300 kcal, 20 g protein, 3 g fiber, 500 IU vit D, 480 mg Ca	12 wk	SPPB SF-LLFDI Handgrip strength EQ5DVAS BMI Mini-nutrition assessment	*A 12-wk intervention with oral nutritional supplementation plus physical exercise improves function, nutritional status, and quality of life in frail institutionalized older adults.*
Heijboer et al (2015)[73] Intervention NH residents	The Netherlands	49 P	Median (range): 82 (71–97)	0 F; 49 M	Oral tablet: 600 IU vit D/d vs placebo All participants received 500 mg Ca carbonate	16 wk	25(OH)D status Testosterone concentration	*In this post hoc analysis of three small clinical trials, vitamin D treatment (600–2000 IU daily) for 6 wk to 4 months does not affect the, at baseline normal, testosterone concentrations in male patients with heart failure, male nursing home residents or male non-Western immigrants living in the Netherlands.*
Corcoran et al (2017)[74] Cluster RCT 20 senior living facilities	USA	121 P 93 C	82.3 (8)	101 F; 20 M	Oral drink: ENP (n = 47): drink + exercise 3 d/wk SAP (n = 46): 3 d/wk Each drink contains 300 kcal, 13 g fat, 24 g carbohydrate, 20 g milk protein, 500 IU vit D, 480 mg Ca	6 mo	SPPB Handgrip strength Mini-nutrition assessment	*This facility-led exercise-nutritional supplement program was not effective at improving physical function or blood levels of 25-hydroxyvitamin D and IGF-1, possibly due to a decline in nutritional status observed in the intervention group coupled with challenges related to program implementation and fidelity.*
Ginde et al (2017)[75] RCT 25 skilled nursing and assisted living facilities	USA	107 P 77 C	HD: 80 (10) STD: 82 (10)	HD: 33 F; 22 M STD: 29 F; 23 M	Capsule: HD (n = 55): 100 000 IU/L × monthly dose vit D_3 STD (n = 52): placebo (if currently taking 400–1000 IU vit D3/d) or 12 000 IU/mo (if currently taking <400 IU vit D_3/d)	12 mo	Incidence of ARIs Falls/fractures 25(OH)D Hypercalcemia Kidney stones	*Monthly high dose vitamin D_3 supplementation reduced the incidence of ARI in older long-term care residents but was associated with a higher rate of falls without an increase in fractures.*
Kotlarczyk et al (2017)[76] Secondary analysis Long-term care facilities	USA	137 P 137 C	Def: 85.8 (1) Insuff: 85.6 (0.8) Suff: 84.9 (0.6)	137 F; 0 M	Oral supplement: ND Deficient (n = 26): 50 000 IU/wk for 8 wk initially Then Def, Insuff (n = 40) and Suff (n = 71) participants received 800 IU vitamin D_3/d	24 mo	Physical function: ADL, PPT, gait speed cognitive function: cognition, mental health Falls	*Even after correction of vitamin D deficiency and maintenance of adequate levels (above 20 ng/ml) for two years, women who were deficient at baseline had the greatest functional declines and risk of falling.*
Franzke et al (2019)[77] RCT, observer-blinded 5 senior residences	Austria	96 P 80 C	83.1 (6.1)	84 F; 12 M	Oral liquid drink; CT (n = 40): cognitive training twice/wk	6 mo	Micronutrient assessment physical fitness: 6-min walking, chair-rise test, isokinetic dynamometry, handgrip strength	*Six months of elastic band resistance training with or without protein-vitamin supplementation improved physical function, but had no biological impact*

(continued)

Table 4 **Continued**

Reference Type of study Recruitment locations	Country	No. of participants	Age, mean±SD, y	Sex	Type of intervention	Duration	Primary outcome measures	**Main conclusions**[a]
					RT (n = 41): resistance training twice/wk RTS (n = 36): RT + supplement twice/wk= 2× liquid drinks with each containing 150 kcal, 20.7 g protein, 9.3 g carbohydrate, 3.0 g fat, 1.2 g roughage, 800 IU vit D, 250 g of Ca, vit C, E, B_6, B_{12}, folic acid, magnesium			*on the status on fat soluble micronutrients.*
Veleva et al (2020)[78] RCT 3 NHs	The Netherlands	78 P 52 C	UVB: 84.2 (79.5–87.5) vit D: 83.6 (77.5–88.5)	54 F; 24 M	UVB light vs vit D capsule; half-body UVB irradiation twice/wk Vit D: 5600 IU vit D_3 once/wk	6 mo	Well-being: CMAI and the Cornell scale	*The exposure of nursing home residents with dementia to UVB light showed no positive benefits in terms of wellbeing. UVB treatment may have a positive effect on the restless/tense behavior characteristic of advanced dementia, but more research is needed to confirm this finding.*

Data are presented as mean (standard deviation).

[a]Quoted directly from the cited articles.

[b]Standard error of the mean.

Abbreviations: 25(OH)D, 25-hydroxyvitamin D; ADL, activities of daily living; ARI, acute respiratory infection; BMD, bone mineral density; BMI, body mass index; C, completed; Ca, calcium; CMAI, Cohen Mansfield Agitation Inventory; CT, cognitive training; CTX, carboxyl-terminal cross-linked telopeptide of type 1 collagen; CY, nonfortified control yogurt; DD, daily dose; DDG, daily-dose group; DEF, deficient; ENP, exercise program + nutritional supplement; EQ5DVAS; EuroQoL-5 Dimensions visual analogic scale; F, female; FY, calcium-fortified yogurt; GDS-SF, geriatric depression scale-short form; IG-1, insulin-like growth factor 1; IM, intramuscular; Insuff, insufficient; IQR, interquartile range; LD, loading dose; M, male; MD, maintenance dose; MED, minimal erythema dose; MNA-SF, Short-Form Mini Nutritional Assessment; N/A, not applicable; ND, not defined; NH, nursing home; NR, not reported; ONS, oral nutritional supplement; P, participated; PPT, physical performance test; PTH, parathyroid hormone; RCT, randomized control trial; Resp, responder; RT, resistance training; RTS, resistance training combined with calcium and protein supplementation; SAP, health education program; SF-LLFDI, Short-Form Late-Life Function and Disability Instrument; signif, significant; SPPB, Short Physical Performance Battery; STD, standard dose; SUFF, sufficient; TRAP-5b, tartrate-resistant phosphate isoform-5b; TUG, timed up and go; USA, United States of America; UV, ultraviolet light; UVB, ultraviolet B light; VF, vertebral fracture; VFX, without vertebral fracture; vit, vitamin; WDG, weekly dose group; FPG, fasting plasma glucose.

consideration when deciding a supplementation regimen for someone with a history of falling.[89]

It is noteworthy that given the COVID-19 global pandemic, nursing home residents have been among the worst affected by high death rates. Several systematic reviews and meta-analyses have been conducted recently showing that a low serum 25(OH)D concentration is significantly associated with a higher risk of COVID-19 infection,[12–14] mortality, and severity of COVID-19.[13] More robust randomized controlled trials are needed to substantiate these findings and to investigate the potential beneficial role of vitamin D supplementation in the prevention and treatment of COVID-19 in nursing home residents.

Biological markers

Two studies investigated vitamin D_3 and calcium-fortified dairy-product intervention, both resulting in a significant increase in vitamin D status and a decrease in parathyroid hormone concentrations and the bone resorption markers carboxy-terminal collagen cross-links and tartrate-resistant acid phosphatase-5b,[66,69] albeit a higher dose of vitamin D_3 than used in the study (400 IU/d) would be required to reach a vitamin D status >50 nmol/L.[69] Both studies were conducted in a small sample of women and over a short period; additional research is needed.

Overall, oral nutritional supplements in combination with exercise may benefit physical function and performance, whereas supplementation with vitamin D and calcium-fortified foods has been associated with improved quality of life and reduced bone resorption. Most studies had small sample sizes, were short in duration, and used low doses of vitamin D or a low degree of fortification. In addition, several studies had strict inclusion criteria that limited inclusion of frailer participants and did not have a control or placebo group.

CONCLUSION

Globally, vitamin D deficiency is highly prevalent in nursing home residents, with reported rates ranging from 8% up to 94%. Nevertheless, nursing home residents are still regularly underrepresented in observation and intervention studies,[90] and there are currently no specific dietary or supplementation guidelines for this vulnerable group. Future studies should take into consideration the variety of factors affecting a resident's vitamin D status, and residents with low 25(OH)D concentration require remedial supplementation with much higher doses of vitamin D prior to maintenance supplementation. The recommended maintenance supplementation dose is >800 IU/d or weekly supplementation with 5600 IU/wk. Oral nutritional supplements in combination with exercise has shown some benefit to physical function and performance in nursing home residents. Vitamin D_3 and calcium-fortified foods resulted in benefits in quality of life and reduction in bone resorption. High-dose vitamin D_3 supplementation may reduce incidence of acute respiratory infections; however, there are a lack of sufficient studies on this to date. There is an urgent need for standardized dietary and supplementation guidelines to prevent vitamin D deficiency in this vulnerable group.

Acknowledgements

We acknowledge Hannah Benson and James McMullan, research interns, for their help with data extraction.

Author contributions. E.M.M., D.J.A., PJ.M., and K.P. supervised this study. All authors contributed to study conceptualization; methodology; writing, reviewing, and editing the manuscript; approval of the final version; and are accountable for all aspects of work. O.F. conducted the formal analysis, data curation, analysis, and interpretation.

Funding. This project was supported by doctoral degree funding received from the Department for the Economy. The authors thank the Rank Prize for the COVID-19 Response grant.

Declaration of interest. E.M.M., P.J.M., and K.P. report receiving a grant from BetterYou Ltd, outside the work submitted. K.P. reports receiving a grant from Devenish Nutrition Ltd, outside the work submitted. D.J.A. reports being on the advisory boards of the Royal Osteoporosis Society, National Osteoporosis Guideline Group and UCB Pharma; receiving personal fees from Internis Pharma for being a speaker; and owning GlaxoSmithKline stock, all outside of the work submitted.

Supporting Information

The following Supporting Information is available through the online version of this article at the publisher's website.

Appendix S1.

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