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Vitamin D inadequacy among post-menopausal women: a systematic review

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Summary

Background: Vitamin D inadequacy has been studied extensively, due to concerns about ageing populations, associations with osteoporosis and other disorders (including non-musculoskeletal), and high prevalence.
Aim: To review recent reports on the prevalence of vitamin D inadequacy among post-menopausal women with and without osteoporosis and/or other musculoskeletal diseases.
Design: Systematic review.
Methods: We reviewed publications in the past 10 years reporting prevalence estimates for vitamin D inadequacy, reported as serum 25(OH)D values below various levels. Thirty published studies in the English language were identified, from January 1994 through April 2004.
Results: In osteoporotic populations, the prevalence of 25(OH) vitamin D concentration <12 ng/ml ranged from 12.5% to 76%, while prevalence rates reached 50% to 70% of patients with a history of fracture(s) using a cut-off of 15 ng/ml. In post-menopausal women, the prevalence of 25(OH) vitamin D concentrations $\leqslant$20 ng/ml ranged from 1.6% to 86% for community-living and institutionalized women, respectively. The most common factors associated with inadequate vitamin D levels included limited sun exposure, lack of dietary vitamin D intake, nursing home environment, wintertime, and increasing age (over 70 years).
Discussion: The prevalence of inadequate vitamin D levels appears to be high in post-menopausal women, especially in those with osteoporosis and history of fracture. Vitamin D supplementation in this group might offer scope for prevention of falls and fracture, especially in elderly and osteoporotic populations.

Introduction

Several factors have recently thrust the concern over inadequate vitamin D levels into the forefront of medicine: the significant increase in ageing populations and life expectancies worldwide; the association between low vitamin D levels and poor musculoskeletal health; the recent resurgence of the health problems associated with vitamin D inadequacy including rickets; and the role that vitamin D inadequacy might play in other chronic diseases.[1–3] Vitamin D plays an important role in bone growth and maintenance by enhancing intestinal absorption of calcium and influencing

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bone metabolism in other ways. Its importance in bone development has been recognized since the late 19th/early 20th centuries, when rickets (osteomalacia) was widespread and was found to be controllable by vitamin D supplementation, either by sun exposure or diet.[4] In the mid-to-late 20th century, it became evident that vitamin D inadequacy was very common among the elderly, and was implicated in the development of osteopenia and osteoporosis.[5–7] Vitamin D inadequacy has also been implicated as a contributing factor to muscle weakness and falls, and is now well documented in the literature.[1,8–12] Consequently, osteoporosis prevention and treatment guidelines developed by respected authorities, including the International Osteoporosis Foundation, contain recommendations for maintaining adequate vitamin D levels, measured by serum 25(OH)D.[13]

We aimed to identify and systematically summarize published reports regarding the prevalence of inadequate vitamin D level, focusing on post-menopausal women with and without osteoporosis and/or musculoskeletal diseases.

Methods

Relevant articles in the English language from January 1994 to April 2004 were identified by Medline and EMBASE search engines. Primary subject headings (vitamin D deficiency, vitamin D insufficiency, hypovitaminosis D, vitamin D status, serum vitamin D level) were combined using 'and' with secondary terms (osteoporosis, prevalence, incidence, outcomes, cost, 50 years of age, 60 years of age, post-menopausal women, and the elderly) resulting in numerous Boolean searches. As serum 25(OH)D is the accepted functional indicator of vitamin D status,[14] all studies that reported the prevalence of vitamin D inadequacy, expressed as a percentage of a particular population with clearly defined low 25(OH)D levels (defined in many articles as 'vitamin D deficiency' or 'vitamin D insufficiency'), were included, regardless of the primary objective of the study. To minimize the impact of confounding factors such as illness and medications, which may affect vitamin D serum levels, this study was limited to the following populations: post-menopausal women, including elderly women and women with musculoskeletal health issues, since they are the most commonly associated with complications of vitamin D deficiency. This last category includes osteoporotic and osteopenic women, women referred to rheumatology and bone clinics, women with osteoarthritis, women with chronic musculoskeletal pain, history of fractures and those with primary hyperparathyroidism.

In total, approximately 100 articles were obtained using the search terms defined above. Thirty met the inclusion criteria of post-menopausal women, and are summarized here. Prevalence data are summarized separately for post-menopausal women with and without musculoskeletal health issues. They are sorted first by vitamin D status, and then by age. If a study reported two prevalence figures for seasonal variation or different 25(OH)D thresholds, both values were reported in the tables. We also reported mean serum 25(OH)D levels for the populations studied, where available and the assay method to determine serum 25(OH)D concentrations.

Results

The majority of studies reported a fairly high prevalence of serum 25(OH)D values below specified cut-off points among post-menopausal women. There were 22 studies reporting prevalence of at least 1:4 people (25%) with inadequate 25(OH) vitamin D concentrations, using a 25(OH)D cut-off of 20 ng/ml or lower. Overall, the prevalence of 25(OH) vitamin D concentrations $\leqslant$12 ng/ml ranged from 1.6%[15] to 86%.[16]

Table 1 summarizes data for post-menopausal women with osteoporosis and/or other musculoskeletal disorders. Among the studies that reported cut-offs of 12 ng/ml or lower, the prevalence of vitamin D inadequacy ranged from 12.5% to 76%.[17–24] Among the studies that reported cut-offs between 15 ng/ml and 25 ng/ml, the prevalence of inadequate vitamin D concentrations ranged from 11.3% to 64%.[23–28] More than half of individuals with a history of fracture had mean serum 25(OH)D concentrations <15 ng/ml, ranging from 50% to 70%, independent of season.[21,22] These groups were older, each having an average age of >75 years. A concentration of vitamin D <12 ng/ml was present in 12.5% to 76% of the osteoporotic populations, including referrals.[17,19,21,24] The only large global study of osteoporosis and vitamin D status in post-menopausal women ($n=7564$) reported that 28.4% of individuals had vitamin D <20 ng/ml, with the highest levels of inadequacy seen in Latin America (39.7%), Southern Europe (39.3%), Central Europe (39.0%), and Pacific Rim (24.1%).[24] The impact of the season and of age on the prevalence of vitamin D inadequacy is highlighted in an Italian study conducted by Bettica *et al.*[17] In wintertime, the prevalence of

Table 1 Vitamin D status in post-menopausal women with osteoporosis and/or other musculoskeletal diseases[a]

Study/authors	*n*	Average age (years)[b]	Mean serum 25(OH)D (ng/ml) (SD)	Serum 25(OH)D cut-off concentration (ng/ml)[c]	Population below concentration (%)	Season[d]	Study location	Other population-specific characteristics	Assay method[e]
Isaia *et al.*[19]	700	67.8 ± 5.7	10.9 (10)	5	27.00%	B	Italy	Elderly women referred to an osteoporosis centre	RIA. Commercial kit (detection limit 1.5 ng/ml; Dia Sorin). Inter-assay CV 10.1%
Aguado *et al.*[23]	171	56 ± 5	13.89 (7.75)	10	36.00%	N/A	Spain	Women referred to a rheumatology clinic	RIA (Incstar). Inter- and intra-assay CV <15%
Lips *et al.*[24]	7564	66.5 ± 7.1	27.87 (12.17)	10	24.30%	B	Global	Osteoporotic women	RIA (Incstar). Inter-assay CV 9.8–12.2%
Bettica *et al.*[17]	570	59.2 ± 7.7	18.3 (8.3)	12	38.50%	L	Italy	Women with osteoporosis referrals	RIA (Nichols Institute Diagnostics). Inter- and intra-assay CVs were 13.1% and 9.2%, respectively
Bettica *et al.*[17]	570	59.2 ± 7.7	18.3 (8.3)	12	12.50%	H	Italy	Women with osteoporosis referrals	
Carnevale *et al.*[18]	62	59.6 ± 1.59	18.62 (9.29)	12	27.40%	B	Italy	Primary hyperparathyroidism patients	RIA (Dia Sorin). Inter- and intra-assay CV were 10.2% and 8.2%
Isaia *et al.*[19]	700	67.8 ± 5.7	10.9 (10)	12	76.00%	B	Italy	Elderly women referred to an osteoporosis centre	RIA. Commercial kit (detection limit 1.5 ng/ml; DiaSorin). Inter-assay CV 10.1%
Bettica *et al.*[17]	68	70+	18.3 (8.3)[f]	12	51.20%	L	Italy	Women with osteoporosis referrals	RIA (Nichols Institute Diagnostics). Inter- and intra-assay CVs were 13.1% and 9.2%, respectively
Bettica *et al.*[17]	68	70+	18.3 (8.3)[f]	12	16.70%	H	Italy	Women with osteoporosis referrals	
Sahota *et al.*[20]	119	71.4 ± 4.9	N/A	12	26.90%	B	UK	Healthy community-dwelling elderly women referred to a clinic for a vertebral fracture	RIA. (Dia Sorin)

(continued...)

Table 1 Continued

Study/authors	*n*	Average age (years)[b]	Mean serum 25(OH)D (ng/ml) (SD)	Serum 25(OH)D cut-off concentration (ng/ml)[c]	Population below concentration (%)	Season[d]	Study location	Other population-specific characteristics	Assay method[e]
LeBoff *et al.*[21]	30	77.93 ± 9.17	12.76 (N/A)	12	50.00%	B	Boston, USA	Osteoporotic women with hip fractures	RIA (Incstar). Inter- and intra-assay CVs ranged between 2.3% and 12.1%
Harwood *et al.*[22]	150	81.2	11.42	12	70.00%	N/A	UK	Hip fracture population	RIA (Incstar). NR 25–115 nmol/l. Inter- and intra-assay CVs ranged between 4–8% and 2.5–11%
Aguado *et al.*[23]	171	56 ± 5	13.89 (7.75)	15	64.00%	N/A	Spain	Women referred to a rheumatology clinic	RIA (Incstar). Inter- and intra-assay CVs <15%
Glowacki *et al.*[25]	68	66 (46–89)	20.15 (N/A)	15	22.00%	B	Boston, USA	Post-menopausal osteoarthritic White women	RIA (Incstar). Inter- and intra-assay were 12.1% and 8.7% respectively
Mezquita-Raya *et al.*[26]	161	61 ± 7	18.8 (8.4)	15	39.10%	L	Spain	Post-menopausal women, 51.6% with osteoporosis, referred to a clinic	RIA (Incstar). Reference value 27.8 ± 9.45 ng/ml. Inter-assay CV 8.6–12.5%
Jesudason *et al.*[27]	486	63 ± 9.5	24.72 (9.84)	16	20.00%	N/A	Australia	Women with osteoporosis referrals	RIA (Immuno Diagnostic Systems). Reference range 40–160 nmol/l
Lips *et al.*[24]	7564	66.5 ± 7.1	27.87 (12.17)	20	28.40%	B	Global	Osteoporotic women	RIA (Incstar). Inter-assay CV 9.8–12.2%
Jesudason *et al.*[27]	486	63 ± 9.5	24.72 (9.84)	24	54.00%	N/A	Australia	Ambulatory women referred for osteoporosis	RIA (Immuno Diagnostic Systems). Reference range 40–160 nmol/l
Soontrapa *et al.*[28]	106	69.42 ± 6.77	33.32 (7.14)	25	11.30%	N/A	Thailand	Normal, osteopenic and osteoporotic populations combined	RIA (Dia Sori). Inter-assay CV 9.4–11.0%

[a]Other musculoskeletal disease populations include patients referred to rheumatology and bone clinics and patients with chronic musculoskeletal pain, history of fractures and falls, or those with primary hyperparathyroidism. [b]Mean ± SD, range, or approximate average. Mean age was not always reported for the population for which the prevalence estimates were given, but rather smaller sub-populations. In those cases, an approximate value is given. [c]If data were presented in nmol, they were divided by 2.54 to obtain ng/ml. [d]L, low sun/winter and spring, H, high sun/autumn and summer; B, both; N/A, not available. [e]RIA, radio-immuno assay. [f]Mean listed is for entire study population of 570.

vitamin D inadequacy rose by 51.2% in the subgroup of women aged 70 years and older vs. 38.5% for the whole study population, aged 41–80 years. In summertime, vitamin D inadequacy was less frequent and similar in age groups, occurring in 16.7% of women aged 70 and older and in 12.5% of the whole study population.

Among the studies of post-menopausal women without osteoporosis and/or musculoskeletal diseases that reported cut-offs of 20 ng/ml or lower, the prevalence of vitamin D inadequacy ranged from 1.6% to 86% (Table 2).[15,16,29–40] The study reporting the lowest prevalence (1.6%) was conducted among 64 community-living women during the low season in the US.[15] The highest prevalence (86%) was found in an Australian study of 252 elderly women living in a residential (nursing home) environment.[16] Among the studies that reported cut-offs of 10 ng/ml or lower, the prevalence of vitamin D inadequacy ranged from 3% to 49%.[29–32] Prevalence of vitamin D inadequacy varied by region. Most of the lower prevalence estimates were observed in the US, which has more vitamin-D-fortified foods and supplements than the rest of the world. For example, only 8% of a US nursing home population had 25(OH)D <12 ng/ml.[15] The highest prevalence was reported for community-living elderly/post-menopausal women in southern European countries: 32% in Italy[33] had 25(OH)D <12 ng/ml and 39%[37] to 59.6%[34] in France had 25(OH)D $\leqslant 12$ ng/ml. A few years earlier, Van der Wielen had also reported the highest prevalence of vitamin D concentrations <12 ng/ml: 47% for women living in southern European countries (Italy, Spain and Greece).[35] In Denmark, middle-aged post-menopausal women (45–48 years) not taking vitamin D supplement and avoiding sun exposure had a high prevalence of vitamin D inadequacy (32.8%, using a cut-off of 10 ng/ml),[29] whereas elderly women (>70 years) living in north-east of the US had a low prevalence of vitamin D inadequacy: estimates ranging from 4% to 8% were reported by Kinyamu[15,36] using a cut-off of 12 ng/ml; an estimate of 12% using a cut-off of 15 ng/ml was reported by Rapuri *et al.*[39] Two studies, both of small sample size, assessed the variation of the prevalence of vitamin D inadequacy according to the season.[31,33] In the Italian study of Romagnoli *et al.*, the prevalence of vitamin D inadequacy was 4.5% during the high season ($n=22$), but 32% during the low season ($n=25$).[33] In the Australian study of Ley *et al.*, one third of the 36 elderly women living in an age care facility had 25(OH)D concentrations <10 ng/ml during midsummer. This prevalence rose to 49% among the 39 women tested during midwinter.[31]

As would be expected, studies demonstrating lower prevalence of vitamin D inadequacy reported higher mean serum 25(OH)D levels: using a cut-off of 12 ng/ml, Bettica *et al.* estimated a prevalence of vitamin D inadequacy of 12.5%, and mean serum 25(OH)D of 18.3 ng/ml,[17] whereas Isaia *et al.* estimated a prevalence of vitamin D inadequacy of 76%, with mean serum 25(OH)D 10.9 ng/ml.[19] Furthermore, studies examining populations with higher mean serum 25(OH)D levels tended to use higher thresholds for the levels used to define vitamin D inadequacy. For example, in Soontrapa *et al.*, the mean serum 25(OH)D concentration was 33.3 ng/ml, and vitamin D inadequacy was defined as $\leqslant 25$ ng/ml,[28] while in Bettica *et al.*, the mean serum 25(OH)D concentration was 18.3 ng/ml and vitamin D inadequacy was defined as <12 ng/ml.[17]

Based on this literature review, the risk factors for vitamin D inadequacy most often found in post-menopausal women include limited sun exposure and time spent outdoors, inadequate dietary vitamin D intake, winter season and increased age (>70 years).

Discussion

We found a high prevalence of vitamin D inadequacy in post-menopausal women with osteoporosis and/or other musculoskeletal disorders, particularly among those with fracture and osteoporosis. More than half of individuals with a history of fracture had vitamin D concentrations <15 ng/ml, ranging from 50% to 70%. Among osteoporotic women (including referrals), the prevalence of vitamin D inadequacy was 12.5% to 76%, using a cut-off of 12 ng/ml. Even some post-menopausal women without osteoporosis and/or musculoskeletal disorders have high levels of vitamin D inadequacy. This is especially true of women living in nursing homes outside the US. In institutionalized elderly women, vitamin D inadequacy is due to insufficient vitamin D intake and lack of sunlight exposure. Although one would expect lower concentrations of vitamin D in a nursing home population not exposed to sunlight, in comparison to a free-living population, in a US study these two populations had similar serum 25(OH)D concentrations, probably because of the nursing home's policy of providing a high milk intake enriched in both vitamin D and calcium.[15] Inadequate levels of vitamin D are also reported among women not taking vitamin D

Table 2 Vitamin D status in post-menopausal women without osteoporosis and/or other musculoskeletal diseases[a]

Study/authors	*n*	Average age (years)[b]	Mean serum 25(OH)D concentration (ng/ml) (SD)	Serum 25(OH)D cut-off concentration, (ng/ml)[c]	Population below concentration (%)	Season[d]	Study location	Other population-specific characteristics	Assay method[e]
Brot *et al.*[29]	2016	45–48	N/A	10	7.0%	L	Denmark	Healthy women	CPBA. (Lund & Sorensen, 1979) Inter- and intra-assay CVs were 10.2% and 8.3%, respectively
Brot *et al.*[29]	2016	45–48	N/A	10	3.0%	H	Denmark	Healthy women	
Brot *et al.*[29]	<2016	45–48	N/A	10	32.8%	L	Denmark	Healthy women who avoid sun and do not supplement with vitamin D	
Semba *et al.*[30]	371	65+	20.82 (N/A)	10	12.6%	B	Baltimore, USA	WHAS I, more disabled women	Radioreceptor assay (Nichols Institute Diagnostics). Inter- and intra-assay CVs were 9.6% and 7.5%, respectively
Semba *et al.*[30]	682	70–80	22 (N/A)	10	6.2%	B	Baltimore, USA	WHAS II, less disabled women	
Ley *et al.*[31]	39	74–98	10.44 (5.58)	10	49.0%	L	New Zealand	Elderly subjects living in a care facility, 82% independently mobile	RIA (Incstar kit)
Ley *et al.*[31]	36	74–98	15.61 (9.27)	10	33.0%	H	New Zealand	Elderly subjects living in a care facility, 82% independently mobile	
Flicker *et al.*[32]	667	83.7 ± 8.7	15.63 (8)	10	22.0%	B	Australia	Residential population, low level of care	RIA (Incstar,). Inter-assay CV was 9.2% for the low control (24 nmol/l) and 11.8% for the medium control (58 nmol/l)
Flicker *et al.*[32]	952	83.7 ± 9.1	12.36 (7.76)	10	45.0%	B	Australia	Residential population, high level of care	
Sambrook *et al.*[16]	252	86.7 ± .6	6.69 (4.72)[f]	11	86.0%	B	Australia	Women in residential facilities and hostels	CPBA
Romagnoli *et al.*[33]	25	62.28 ± 6.59	18.07 (11.22)	12	32.0%	L	Italy		RIA (Incstar). Inter- and intra-assay CVs were 10.2% and 8.1%, respectively
Romagnoli *et al.*[33]	22	62.36 ± 10.41	35.47 (19.53)	12	4.5%	H	Italy		
Souberbielle *et al.*[34]	280	70*	N/A	12	59.6%	H	France	Healthy elderly people	CPBA (Amersham Pharmacia Biotech)

Van der Wielen, *et al.*[35]	410	71–76	13.90 (N/A)	12	47.0%	L	Europe	Free-living elderly women	CPBA (TNO Nutrition and Food Research Institute). Inter-assay CV 7–10%, intra-assay CV 4–7%
Kinyamu *et al.*[36]	245	71 ± 3	34.60 (11.10)	12	4.0%	B	NE, USA	Free-living elderly women not taking vitamin D supplement	Non-equilibrium radio-receptor assay (Incstar). Intra-assay CV 10%
Kinyamu *et al.*[36]	131	71 ± 4	28.97 (9.06)	12	<1.0%	B	NE, USA	Free-living elderly women taking vitamin D supplement	
Kinyamu *et al.*[15]	64	71 ± 4	29 (8)	12	1.6%	L	NE, USA	Free-living elderly women exposed to sunlight	Competitive binding assay. Purification of serum on Sep-Pak cartridges (Waters Associates). Inter-assay variation 5%
Chapuy *et al.*[37]	440	80 ± 3	16.73 (9.84)	12	39.00%	L	France	Elderly healthy women living at home	RIA (Incstar). Inter- and intra-assay variances were 11% and 5%
Kinyamu *et al.*[15]	60	84 ± 9	27 (11)	12	8.00%	L	NE, USA	Nursing home population not exposed to sunlight	Competitive binding assay. Purification of serum on Sep-Pak cartridges (Waters Associates). Inter-assay variation 5%
Jacques *et al.*[38]	469	65–95	27.95 (11.42)	15	14.50%	B	MA, USA	Framingham heart study	CPBA. Inter- and intra-assay CVs were 10% and 7%, respectively
Rapuri *et al.*[39]	307	71 ± 0.20	27.3 (0.072)	15	12.00%	L	NE, USA	Elderly women not taking vitamin D supplements	CPBA. Purification of serum on Sek-Pak cartridges (Waters Associates). Inter-assay CV 5%
Rapuri *et al.*[39]	101	72 ± 0.045	31.97 (N/A)	15	3.60%	L	NE, USA	Elderly women supplemented with vitamin D	
Elliot *et al.*[40]	49	89 (68–100)	N/A	20	60.00%	L	WI, USA	Women from a long-term care facility, 70% residents, all ambulatory	RIA (Nichols Laboratories). Inter- and intra-assay CVs were 10.9% and 10.2%, respectively

[a]Other musculoskeletal disease populations include patients referred to rheumatology and bone clinics and patients with chronic musculoskeletal pain, history of fractures and falls, or those with primary hyperparathyroidism. [b]Mean ± SD, range, or approximate average. Mean age was not always reported for the population for which the prevalence estimates were given, but rather smaller subpopulations. In those cases, an approximate value is given. [c]If data were presented in nmol, they were divided by 2.54 to obtain ng/ml. [d]L, low sun/winter and spring, H, high sun/autumn and summer; B, both; N/A, not available. [e]RIA, radio-immuno assay; CPBA, competitive protein binding protein. [f]Mean listed is for population of both men and women.

supplements or not exposed to sunlight in Europe. Wintertime and old age (>70 years) are also associated with a higher prevalence of vitamin D inadequacy.

The striking finding of this investigation is the high prevalence of vitamin D inadequacy in those with a history of osteoporosis and fracture. This is of particular concern because mounting evidence suggests that adequate vitamin D may help to prevent these conditions. Inadequate vitamin D levels are believed to contribute to high levels of parathyroid hormone, leading to excessive bone remodelling and ultimately to bone weakening, and are also associated with decreases in muscle strength and/or neuromuscular functioning and response time, which increase the risk of falls and fractures.[41,42] Flicker *et al.* also found a positive relationship between cognitive functioning and vitamin D levels, which may also influence the risk of falls and fracture.[32] A number of articles have reported that vitamin D supplementation reduces the risk of falls and fractures.[12,22,43–45] One meta-analysis reported a 22% decrease in falls associated with vitamin D supplement use.[46] Other studies have shown that vitamin D supplementation may contribute to gains in bone mineral density.[47,48] Inadequate vitamin D levels have also been associated with chronic musculoskeletal pain, and can be confused with conditions such as fibromyalgia.[49] Post-menopausal women are a primary concern for vitamin D inadequacy, as they are already predisposed to the osteoporosis associated with decreasing oestrogen levels. In these patients, supplementation may be useful in helping increase bone mineral density.[50]

The most commonly reported factors associated with inadequate vitamin D level were low sun exposure, low dietary vitamin D intake (including supplements), and older age. Lack of sun exposure from staying indoors, combined with the biological consequences of ageing, may contribute to the higher prevalence of vitamin D inadequacy in the elderly. Furthermore, PTH levels are higher in the elderly than in younger people at similar serum 25(OH)D levels, which may adversely affect the skeleton.[51] These results suggest that higher levels of vitamin D supplementation may be necessary in elderly populations to overcome high parathyroid activity, resulting perhaps from decreased renal function.

The cut-offs used to identify inadequate vitamin D level varied widely among studies, making it difficult to summarize and compare results. Further, there is inconsistent use of the terms 'deficiency' and 'insufficiency'. For example, some articles define *deficiency* as serum 25(OH)D concentrations of 20 ng/ml or 15 ng/ml and below,[25,40] while other studies term these same concentrations vitamin D *insufficiency*.[24,26] Many authors claim that the vitamin D levels are inadequate at the point when PTH starts to rise, evidence of homeostatic adaptation. Experts even disagree when advising the clinical world about the appropriate levels of sufficiency and when to provide supplementation. Some authors advise that the point at which supplementation is necessary is any serum level <32 ng/ml, and contend that others would still think that is too low,[52] while Holick recommends that a concentration of 20 ng/ml be considered sufficient.[53] Considering the wide range of cut-off values used for defining vitamin D inadequacy and the wide range of recommendations for defining a sufficient concentration of vitamin D (between $\leqslant$20 ng/ml and $\leqslant$32 ng/ml), we suggest a threshold concentration of 25(OH)D be set at 30 ng/ml for 'vitamin D inadequacy', which would encompass most of the recommendations by experts and definitions for vitamin D deficiency and insufficiency used in the most recent literature.[42,54–57] This suggested threshold to define vitamin D inadequacy is congruent with the median threshold of 75 nmol/l (~29.5 ng/ml), resulting from the consensus reported by Dawson-Hughes *et al.* to be at lower risk of fracture.[58] If this 25(OH)D cut-off of 30 ng/ml had been used to define vitamin D inadequacy in the reviewed studies, we would probably have found a higher proportion of post-menopausal women to be vitamin-D-inadequate.

As with all studies, there are some limitations to our findings. In particular, high variability in 25(OH)D assay results between laboratories for the same assay method has been reported.[59,60] As a result, some studies may have underestimated the prevalence of low 25(OH)D, whereas others may have overestimated it. It is impossible to gauge how such differences might have affected the results. Nevertheless, even if the distribution of 25(OH)D values were to be shifted by 5 or 10 ng/ml in some studies, a high proportion of people would still have values <30 ng/ml.[52,53] However, this inter-laboratory variation and the lack of consistency in defining and reporting low vitamin D precluded us from making comparisons across all the studies and performing a formal meta-analysis.

In conclusion, inadequate levels of vitamin D have been reported in post-menopausal women, and often affect a large proportion of such women. Vitamin D supplementation in this group might offer scope for prevention of falls and fracture. This may be especially important in the elderly and osteoporotic populations.

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