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A global representation of vitamin D status in healthy populations

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Abstract
Purpose This paper visualizes the available data on vitamin D status on a global map, examines the existing heterogeneities in vitamin D status and identifies research gaps.
Methods A graphical illustration of global vitamin D status was developed based on a systematic review of the worldwide literature published between 1990 and 2011. Studies were eligible if they included samples of randomly selected males and females from the general population and assessed circulating 25-hydroxyvitamin D [25(OH)D] levels. Two different age categories were selected: children and adolescents (1–18 years) and adults (>18 years). Studies were chosen to represent a country based on a hierarchical set of criteria.
Results In total, 200 studies from 46 countries met the inclusion criteria, most coming from Europe. Forty-two of these studies (21 %) were classified as representative. In children, gaps in data were identified in large parts of Africa, Central and South America, Europe, and most of the Asia/Pacific region. In adults, there was lack of information in Central America, much of South America and Africa. Large regions were identified for which the mean 25(OH)D levels were below 50 nmol/L.
Conclusions This study provides an overview of 25(OH)D levels around the globe. It reveals large gaps in information in children and adolescents and smaller but important gaps in adults. In view of the importance of vitamin D to musculoskeletal growth, development, and preservation, and of

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its potential importance in other tissues, we strongly encourage new research to clearly define 25(OH)D status around the world.

Keywords Vitamin D status · Vitamin D deficiency · 25(OH)D · IOF

Introduction

Vitamin D status in an individual is dependent on numerous genetic, lifestyle and geographical factors that include age, gender, skin pigmentation, sunlight exposure, latitude, the use of sunscreen, dietary habits and supplement intake [1]. It is best measured by the serum concentration of 25-hydroxyvitamin D levels, also known as 25(OH)D levels [2].

Very low levels of 25(OH)D have been documented in different subgroups of the population worldwide [1, 3–6], which have clinical implications. Vitamin D plays an important role in skeletal growth and development, and in bone health throughout life. It promotes calcium absorption [7] and reduces bone loss through the regulation of parathyroid hormone levels [8]. As a consequence, vitamin D deficiency has been linked to reduced bone mineral density [9, 10] and higher risk of osteoporotic fractures [11]. Although further investigation is necessary, vitamin D supplementation may reduce the risk of other diseases, such as colorectal cancer [12], diabetes [13] and infection [14], and it may help decrease fractures and falls [15, 16]. The loss of muscle mass and strength observed in vitamin D-deficient individuals puts them at higher risk of falls and, therefore, fragility fractures.

The International Osteoporosis Foundation took the initiative to describe the vitamin D status in the general population in different countries based on a systematic review and to present the data on a global map. The aims of the study were to provide a general overview of vitamin D status in countries for which data were available, examine the existing heterogeneities in vitamin D status, and identify research gaps.

Methods

The data used in this project are based on a systematic literature review conducted by the Mannheim Institute of Public Health, Germany. The methods used generally follow the PRISMA Statement (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) [17]. Here, we provide a short summary of the methods used in this review. The methods are described in more detail elsewhere [18].

Eligible criteria

A systematic search was conducted in PubMed/Medline and EMBASE to identify articles on vitamin D status in the global population. Eligible studies included samples of randomly selected persons from the general population in countries throughout the world. The outcome of interest was the mean or median 25(OH)D level measured in serum or plasma. There were no limitations based on the type of assay used. Studies were required to have a cross-sectional design or to include a population-based cohort. Other study types like clinical trials, case–control studies, case reports or case series, reviews or qualitative studies were excluded. Articles had to be written in English and published between 1st January 1990 and 28th February 2011.

Abstract and full publication screening

Two thousand five hundred sixty-six articles were identified from both databases. Two independent researchers screened the articles for excluding studies, with a good agreement (kappa coefficient, 0.719). Disagreements were discussed and resolved. After review, 273 articles were eligible and included in a large database which provided, in part, the following information: the mean or median 25(OH)D levels, population characteristics, study location, assay type, number of participants and age groups.

Data filtering

In a second review process, studies on institutionalized elderly only, those on newborn babies and those having an age range that largely overlapped the two age categories (1–18 and >18 years) were removed. When published repeatedly, the same cohort was not presented more than once. In contrast, studies reporting a sub-analysis of a cohort (number of participants and age range different from the root paper) were retained. Studies originating from England, Northern Ireland and Scotland were grouped as United Kingdom. In the end, our database included 200 studies from 46 countries.

After an examination of the database, two different age categories were selected: children and adolescents (1–18 years) and adults (>18 years). The mean serum or plasma 25(OH)D levels were extracted and reported as gender-specific means weighted by the sample size, where possible. The median levels of 25(OH)D were included when the mean levels were not reported in a study. When data were classified by specific seasons, winter values were chosen. Values in nanograms per millilitre were converted to nanomoles per litre by a multiple of 2.496.

Four colour codes according to the mean (or median) 25 (OH)D levels were used:

GREEN	>75 nmol/L
YELLOW	50-74 nmol/L
ORANGE	25-49 nmol/L
RED	<25 nmol/L

For each study, the mean or median vitamin D levels (in nanomoles per litre) were reported from the literature and a study colour code was assigned.

Rationale for the colour coding of countries

For both age categories, the rationale for assigning a colour code to a specific country was based on the following hierarchical selection criteria:

1. Representative of the entire country, population-based and based on a weighted mean of these studies
2. Representative of a region/city of the country, population-based and based on a weighted mean of these studies
3. Based on a weighted mean of multiple studies, non-population-based
4. Based on a single study

Country colour was based on the 25(OH)D level (either the weighted mean or median) of one or more representative studies, if available. If not available, it was based on one or more studies fitting the second criterion cited above, and so forth. A study was considered representative if it represented the entire population for a certain age and sex group in a certain country, region or city. Studies with a selection bias, which excluded individuals for example on the basis of health status, ethnicity, physical abilities, language, smokers and social economic status, were classified as non-representative. However, for some studies, such information was not described in the text.

Design of the figures

The software FlashWorldMap.com was used to produce the maps.

Results

This analysis involves 200 studies from 46 countries. Forty-two of the 200 studies (21 %) were considered representative. Details of these studies for each contributing country are provided in Table 1 (children and adolescents) and Table 2 (adults). The largest number of studies was conducted in Europe (48.0 %), followed by North America (27 %) and the Asia-Pacific region (16.5 %). Of the 46 countries contributing data, 20 (43 %) had at least one study that was classified as representative. Figures 1 and 2 show the vitamin D status in children and adolescents, and adults, respectively, in different countries. The countries are colour-coded according to the serum levels of 25(OH)D reported in Table 1 (children and adolescents) and Table 2 (adults), and the ranges of 25(OH)D represented by each colour are described in the two figures.

Discussion

This project provides a ‘snapshot’ or summary of the 25 (OH)D levels around the globe, as identified in publications since the year 1990. The maps form a core or platform upon which additional information can and should be added. The number of published papers describing 25(OH)D levels is escalating, and the geographic diversity of incoming data is broadening. As a result, we can anticipate having a more comprehensive picture of global vitamin D status in coming years. Updating of the accompanying tables, in which information from each country is ordered chronologically, will also allow for a qualitative assessment of secular trends in 25(OH)D since 1990, within regions and overall. We can expect to see rises in 25(OH)D levels as awareness and concern about vitamin D deficiency grows and as recommendations for vitamin D supplementation appear in more and more government documents, position statements and clinical practice guidelines for bone health [19–21]. This trend would only be accelerated should vitamin D be proven to modify the risk of non-musculoskeletal diseases, such as diabetes, infection or cancer, as has been suggested by many observational studies [22].

Examination of the current maps enables one to identify regions where information on 25(OH)D levels is lacking. The most striking gap is in children and adolescents. The systematic search did not identify studies in this age range in Central America, the northern and central regions of South America, most of Africa, much of Europe and in Australia. This information gap needs attention in view of the importance of vitamin D in bone and muscle growth and development. In regions where data were available, the predominant colour code for children and adolescents was orange, indicating mean 25(OH)D levels in the 25- to 49-nmol/L range. These values are below those recommended by the Institute of Medicine (50 nmol/L), the International Osteoporosis Foundation and the US Endocrine Society (75 nmol/L) [19–21].

Among adults, most regions offer some data, and their colour codes are approximately evenly split between orange (25–49 nmol/L) and yellow (50–74 nmol/L). Areas where

Table 1 Country colour codes of vitamin D status in children and adolescents

Country	Reference	Representative	Age (years)	Sex	*N*	25(OH)D (nmol/L)[a]	Season	Study colour code[b]	Country colour code[b]	Country colour code rationale
Argentina	[29]	No	8.5	M+F	42	24.5	Winter	RED	RED	Based on a single study
Austria	[30]	NA	4–19	M+F	1,143	26.4 (+)	NA	ORANGE	ORANGE	Based on a single study
Canada	[31]	Yes	3–5	M+F	282	48.3	Mixed	ORANGE	ORANGE	Representative of a region/city of the country, population-based
	[32]	No	9–16	M	878	45.9	Mixed	ORANGE		
				F	867	45.9		ORANGE		
China	[33]	Yes	12–14	M	649	33.4	Winter	ORANGE	ORANGE	Representative of a region/city of the country, population-based
	[34]	NA	1–2	F	131	42.3	Mixed	ORANGE		
				F	119	25.5		ORANGE		
Denmark	[35]	No	12.5	F	59	24.4	Winter	RED	RED	Based on a single study
Finland	[36]	NA	11.4	F	64	39.9	Mixed	ORANGE	ORANGE	Based on a weighted average
	[35]	No	12.8	F	60	29.2	Winter	ORANGE		
Iceland	[37]	No	16–20	F	259	43.9	Winter	ORANGE	ORANGE	Based on a single study
India	[38]	No	11–14	M	64	40.8	Winter	ORANGE	ORANGE	Based on a single study
				F	75	46.8		ORANGE		
Iran	[39]	No	7–18	M	424	116.3	Winter	GREEN	YELLOW	Based on a weighted average of females[c]
				F	539	60.4		YELLOW		
	[40]	NA	11–15	F	414	74.9	Mixed	YELLOW		
	[41]	No	14–18	M	153	93.2	Winter	GREEN		
				F	165	41.9		ORANGE		
Ireland	[42]	NA	11–13	F	15	39.0	Winter	ORANGE	ORANGE	Based on a single study
Israel	[43]	Yes	0–20	M+F	195	57.3	Mixed	YELLOW	YELLOW	Representative of the entire country, population based
Jordan	[44]	NA	4–5	M+F	93	55.8	Mixed	YELLOW	YELLOW	Based on a single study
Mongolia	[45]	No	1–3	M+F	79	24.5 (+)	NA	RED	RED	Based on a single study
Netherlands	[46]	No	8–13	M+F	307	69.7	NA	YELLOW	YELLOW	Based on a single study
New Zealand	[47]	No	5–14	M+F	1585	50.0	Mixed	YELLOW	YELLOW	Based on a weighted average
	[48]	NA	1–2	M+F	193	52.0	Mixed	YELLOW		
	[49]	NA	1–2	M+F	233	53.3 (+)	Mixed	YELLOW		
Nigeria	[50]	NA	0.6–3.9	M+F	218	66.9	Mixed	YELLOW	YELLOW	Based on a single study
Poland	[35]	No	12.6	F	61	30.6	Winter	ORANGE	ORANGE	Based on a single study
UK	[51]	Yes	Childs	M+F	854	65.5	Mixed	YELLOW	YELLOW	Representative of the entire country, population-based
	[52]	Yes	12, 15	M	505	62.3	Mixed	YELLOW		
				F	510	58.3		YELLOW		
	[53]	Yes	12–15	M+F	1,015	64.3	Mixed	YELLOW		
USA	[54]	Yes	1–19	M+F	8,541	66.8 (+)	Mixed	YELLOW	YELLOW	Representative of the entire country, population-based, and based on a weighted average
	[55]	Yes	1–11	M+F	4,558	68	Mixed	YELLOW		
	[56]	Yes	12–19	M+F	3,528	62.0	NA	YELLOW		
	[57]	Yes	6–21	M+F	382	69.9	Mixed	YELLOW		
	[58]	No	4–8	F	168	93.8	Mixed	GREEN		
	[59]	NA	9–11	F	22	74.4	Mixed	YELLOW		
	[60]	NA	7–18	M+F	735	66.2	NA	YELLOW		
	[61]	NA	4–8	F	76	88.2	Mixed	GREEN		
	[62]	NA	12–18	F	370	53.7	Mixed	YELLOW		

M males, *F* females, *M+F* combined data for males and females, *NA* no information available

[a] Published 25(OH)D means (or medians if means are not available) are presented, with the exception of studies marked with a (+). For these studies, the 25(OH)D level is a mean weighted for sample size. If weighted means could not be calculated, a simple mean was taken

[b] Colour codes: RED, <25 nmol/L; ORANGE, 25–49 nmol/L; YELLOW, 50–74 nmol/L; GREEN, ≥75 nmol/L

[c] Male data from [38,40] were considered outliers and were excluded from the weighted mean 25(OH)D levels

Table 2 Country colour codes of vitamin D status in adults

Country	Reference	Representative	Age (years)	Sex	*N*	25(OH)D (nmol/L)[a]	Season	Study colour code[b]	Country colour code[b]	Country colour code rationale
Australia	[63]	No	60+	M	437	70.2 (+)	NA	YELLOW	YELLOW	Based on a weighted average
	[64]	No	20–92	F	861	70.3	Mixed	YELLOW		
	[65]	No	51–77	M+F	253	72.2	NA	YELLOW		
	[66]	NA	51–79	M+F	880	52.8	NA	YELLOW		
	[67]	No	78	M+F	70	33	NA	ORANGE		
Austria	[30]	NA	65–85	M+F	78	9.5	NA	RED	ORANGE	Based on a weighted average
	[68]	No	21–76	M+F	1,089	52.2	Winter	YELLOW		
Belgium	[69]	No	70–90	F	245	56.4	NA	YELLOW	YELLOW	Based on a weighted average
	[70]	No	70–87	F	129	43.2	NA	ORANGE		
	[71]	NA	20+	M	270	71.5	NA	YELLOW		
				F	272	73.5		YELLOW		
	[72]	No	21–65	M+F	126	48.2	Winter	ORANGE		
	[73]	No	40–60	M+F	401	35.0	NA	ORANGE		
Brazil	[74]	Yes	65+	M+F	250	52.4	Mixed	YELLOW	YELLOW	Representative of the entire country, population-based
Cameroon	[75]	No	60–86	M+F	152	52.7	NA	YELLOW	YELLOW	Based on a single study
Canada	[76]	Yes	20–79	M+F	3458	67.7 (+)	Mixed	YELLOW	YELLOW	Representative of the entire country, population-based
	[77]	No	27–89	M+F	188	57.3	Winter	YELLOW		
	[78]	No	68–82	M+F	195	66.7	Mixed	YELLOW		
	[79]	No	46.8	F	741	64.9	Winter	YELLOW		
China	[80]	NA	40–70	M+F	2,018	31.7	Mixed	ORANGE	ORANGE	Based on a weighted average
	[81]	NA	40–65	M+F	720	33.1	Mixed	ORANGE		
	[82]	No	19–40	F	16	43.9	NA	ORANGE		
Czech Republic	[83]	No	62.3	F	47	58.2	NA	YELLOW	YELLOW	Based on a single study
Denmark	[84]	Yes	35–65	M+F	125	25.5	Mixed	ORANGE	ORANGE	Representative of a region/city of the country, population-based
	[85]	NA	50-82	F	315	57.0	NA	YELLOW		
	[86]	NA	17–87	F	2,316	62.0	Mixed	YELLOW		
	[87]	No	45–58	F	510	24.0	NA	RED		
	[35]	No	71.6	F	53	47.8	Winter	ORANGE		
	[88]	No	20–29	M	700	64.9	Mixed	YELLOW		
	[89]	NA	70–74	M+F	669	47.6	Mixed	ORANGE		
Estonia	[90]	Yes	25–70	M+F	367	43.7	Winter	ORANGE	ORANGE	Representative of a region/city of the country, population-based
Fidji Islands	[91]	NA	15–44	F	511	76.0	Winter	GREEN	GREEN	Based on a single study
Finland	[92]	Yes	30+	M+F	6937	42.9	NA	ORANGE	ORANGE	Representative of the entire country, population-based, and based on a weighted average
	[93]	Yes	30+	M+F	6219	43.4	Mixed	ORANGE		
	[94]	No	30–97	M	2736	45.1	NA	ORANGE		
				F	3299	45.2		ORANGE		
	[95]	No	30+	M+F	6241	45.1	Mixed	ORANGE		
	[96]	NA	40–69	M+F	4097	43.6	Mixed	ORANGE		
	[97]	NA	31–43	M	126	45.0	Mixed	ORANGE		
				F	202	47.0		ORANGE		
	[98]	NA	20–64	M	138	34.0	Mixed	ORANGE		
				F	358	35.0		ORANGE		
France	[99]	NA	35–65	M+F	1,569	61.0	Winter	YELLOW	YELLOW	Based on a weighted average
	[100]	NA	35–65	M+F	1,191	79.5	Winter	GREEN		
	[101]	No	18–62	M	70	80.9 (+)	Mixed	GREEN		
				F	94	71.5 (+)		YELLOW		
	[102]	No	18–76	F	248	64.1	NA	YELLOW		
Gambia	[103]	No	25+	F	112	91.3 (+)	NA	GREEN	GREEN	Based on a single study

Table 2 (continued)

Country	Reference	Representative	Age (years)	Sex	*N*	25(OH)D (nmol/L)[a]	Season	Study colour code[b]	Country colour code[b]	Country colour code rationale
Germany	[104]	Yes	18–79	M	1,763	45.2	NA	ORANGE	ORANGE	Representative of the entire country, population-based, and based on a weighted average
				F	2,267	44.7		ORANGE		
	[105]	NA	50–80	M+F	415	42.5	Mixed	ORANGE		
	[106]	No	50–81	M	175	50.4	Winter	ORANGE		
				F	123	44.2		ORANGE		
	[107]	No	25–80	M+F	41	65.6	Mixed	YELLOW		
Greece	[108]	No	60–89	M+F	279	42.9	Mixed	ORANGE	ORANGE	Based on a single study and on a weighted average
			19–46	M+F	44	85.7		GREEN		
Iceland	[8]	No	30–85	M+F	944	46.1 (+)	Mixed	ORANGE	ORANGE	Based on a weighted average
	[109]	NA	70	F	308	53.1	Mixed	YELLOW		
India	[110]	NA	18+	M+F	57	36.4	Winter	ORANGE	ORANGE	Based on a weighted average
	[38]	No	41–47	M	243	52.2 (+)	NA	YELLOW		
				F	903	39.7 (+)		ORANGE		
Iran	[111]	Yes	20–74	M	520	35.0	Winter	ORANGE	ORANGE	Representative of the entire country, population-based, and based on a weighted average
	[112]	Yes	40–80	F	245	73.0	NA	YELLOW		
	[113]	NA	20–74	F	676	28.9	Winter	ORANGE		
	[114]	NA	20–79	M+F	646	31.3	NA	ORANGE		
	[115]	NA	50–80	F	300	35.4	Mixed	ORANGE		
	[116][c]	NA	20–69	M+F	1,210	32.5	NA	ORANGE		
Ireland	[117]	NA	Elderly	M+F	116	37.1	NA	ORANGE	ORANGE	Based on a weighted average
	[35]	No	72.3	F	43	43.7	Winter	ORANGE		
	[42]	NA	70–76	F	40	47.3	Winter	ORANGE		
	[118]	NA	51–69	F	44	54.5	Winter	YELLOW		
	[119]	No	51–75	F	95	57.2	Winter	YELLOW		
Israel	[43]	Yes	20+	M+F	136	55.1 (+)	Mixed	YELLOW	YELLOW	Representative of the entire country, population-based
Italy	[120]	Yes	65+	M+F	1,006	39.9	Mixed	ORANGE	ORANGE	Representative of the entire country, population-based, and based on a weighted average
	[121]	Yes	65–96	M	372	55.2	Mixed	YELLOW		
				F	435	34.7		ORANGE		
	[122][d]	Yes	65–102	M	976	57.9	Mixed	YELLOW		
				F	976	43.3		ORANGE		
	[123]	NA	65+	M	429	48.9	Mixed	ORANGE		
				F	529	33.9		ORANGE		
	[124]	NA	20+	M	302	61.2	Mixed	YELLOW		
				F	293	48.2		ORANGE		
	[125]	No	20+	M+F	1,107	53.0	NA	YELLOW		
	[126]	No	60–80	F	697	37.9	Winter	ORANGE		
	[127]	No	36.9	M+F	90	42.7	Winter	ORANGE		
Japan	[128]	Yes	46–80	F	117	59.1	Mixed	YELLOW	YELLOW	Representative of the entire country, population-based
	[129]	No	70+	M	456	71.7	Winter	YELLOW		
				F	638	65.8		YELLOW		
	[130]	No	65–89	M	950	71.1	Mixed	YELLOW		
			65–92	F	2,007	60.4		YELLOW		
	[131]	No	42–84	F	173	79.2	Mixed	GREEN		
Jordan	[44]	NA	29–38	F	93	25.6	Mixed	ORANGE	ORANGE	Based on a single study
Korea (South)	[132]	No	40+	M+F	1,330	46.1	Mixed	ORANGE	ORANGE	Based on a single study
Lebanon	[133]	NA	65–85	M+F	443	28.4	Mixed	ORANGE	ORANGE	Based on a weighted average
	[134]	No	30–50	M+F	316	24.2	Winter	RED		
Malaysia	[135]	No	50–65	F	101	44.4	NA	ORANGE	ORANGE	Based on a single study
Netherlands	[136]	Yes	65–88	M+F	1,319	53.2	Mixed	YELLOW	YELLOW	

Table 2 (continued)

Country	Reference	Representative	Age (years)	Sex	*N*	25(OH)D (nmol/L)[a]	Season	Study colour code[b]	Country colour code[b]	Country colour code rationale
	[137][e]	Yes	65–89	M+F	1,311	50.5	Mixed	YELLOW		Representative of the entire country, population-based, and based on a weighted average
	[138]	Yes	65–85	M+F	1,260	51.8	Mixed	YELLOW		
	[139]	NA	65–88	M	620	58.1	Mixed	YELLOW		
			65–88	F	635	49.1		ORANGE		
	[140]	NA	55–85	M+F	935	51.2	Mixed	YELLOW		
	[141]	NA	65–95	M+F	1,282	52.4	Mixed	YELLOW		
	[142]	No	65+	M+F	1,234	53.9	Mixed	YELLOW		
	[143]	No	18–64	M	91	71.0	NA	YELLOW		
				F	71	70.0		YELLOW		
			65–79	M	268	40.0		ORANGE		
				F	261	38.0		ORANGE		
	[144]	NA	40–65	M	30	91.2	NA	GREEN		
			50–69	F	35	77.2		GREEN		
	[145]	No	50–75	M+F	614	53.6	Mixed	YELLOW		
New Zealand	[146]	Yes	35–64	M	295	39.8	Mixed	ORANGE	ORANGE	Representative of the entire country, population-based
	[147]	No	40+	M	378	85.0	NA	GREEN		
			55+	F	1,606	51.0		YELLOW		
	[148]	No	55.6	M	50	91.0	NA	GREEN		
			67.5	F	50	67.0		YELLOW		
	[149]	NA	46–89	F	116	54.0	NA	YELLOW		
	[150]	No	18+	M+F	273	51.0	Mixed	YELLOW		
Norway	[151]	NA	38–61	M+F	32	67.2	NA	YELLOW	YELLOW	Based on a weighted average
	[152]	No	44–59	F	300	56.9	Mixed	YELLOW		
	[153]	No	45–60	M	302	74.1	Mixed	YELLOW		
				F	278	75.9		GREEN		
	[154]	No	45–75	M+F	869	74.8	Mixed	YELLOW		
	[155]	NA	25–74	M+F	6,932	58.9	NA	YELLOW		
	[156]	No	25–84	M+F	2,668	55.3	NA	YELLOW		
Poland	[157]	Yes	60–90	F	274	33.5	Winter	ORANGE	ORANGE	Representative of the entire country, population-based
	[35]	No	71.6	F	65	32.5	Winter	ORANGE		
Russia	[158]	No	45–79	F	122	29.1	NA	ORANGE	ORANGE	Based on a single study
Saudi Arabia	[159]	No	20–45	F	1,557	66.0	Mixed	YELLOW	YELLOW	Based on a single study and on a weighted average
			62.4	F	568	55.7		YELLOW		
South Africa	[160]	No	65–92	M+F	173	37.0	NA	ORANGE	ORANGE	Based on a single study
Spain	[161]	Yes	15–70	M	126	52.7	Mixed	YELLOW	YELLOW	Representative of a region/ city of the country, population-based
				F	127	49.9		ORANGE		
	[162]	No	65–93	M + F	237	42.9	Winter	ORANGE		
	[163]	No	35	M	227	23.4	Mixed	RED		
				F	164	21.3		RED		
Sweden	[164]	No	75–76	F	986	95.0	Mixed	GREEN	GREEN	Based on a weighted average
	[165]	No	72.9	F	350	91.0	Mixed	GREEN		
	[166]	No	56–67	M	34	90.0	NA	GREEN		
	[167]	NA	61–86	F	116	69.0	Winter	YELLOW		
	[168]	No	61–83	F	100	72.0	Winter	YELLOW		
	[169]	NA	71	M	1,194	68.7	NA	YELLOW		
	[170]	NA	71	M	958	69.0	NA	YELLOW		
	[171]	No	79–95	M	23	70.0	Mixed	YELLOW		
				F	81	65.0		YELLOW		
Switzerland	[172]	Yes	25–74	M+F	3,276	50.0	Mixed	YELLOW	YELLOW	Representative of the entire country, population-based
	[173]	No	66–95	M	203	91.7	Mixed	GREEN		

Table 2 (continued)

Country	Reference	Representative	Age (years)	Sex	N	25(OH)D (nmol/L)[a]	Season	Study colour code[b]	Country colour code[b]	Country colour code rationale
			62–86	F	109	67.5		YELLOW		
Taiwan	[174]	No	40–72	W	262	76.5	Mixed	GREEN	GREEN	Based on a single study
Thailand	[175]	Yes	20–84	M F	126 125	133.5 102.7	NA	GREEN GREEN	GREEN	Representative of a region/ city of the country, population-based
	[176]	NA	20–80	M	108	126.9	NA	GREEN		
				F	121	92.8		GREEN		
	[177]	NA	60–92	F	106	83.3	Mixed	GREEN		
	[178]	NA	60–97	F	446	67.6	NA	YELLOW		
Tunisia	[179][g]	No	20–60	F	261	40.3	Mixed	ORANGE	ORANGE	Based on a single study
United Kingdom	[180]	Yes	65+	M F	322 320	56.2 48.4	Mixed	YELLOW ORANGE	YELLOW	Representative of the entire country, population-based
	[181]	Yes	65+	M	950	53.0	Mixed	YELLOW		
				F	1,120	48.0		ORANGE		
	[182]	No	65+	M+F	1,026	49.5	NA	ORANGE		
	[183]	No	18–45	M+F	32	25.5	NA	ORANGE		
	[184]	NA	40–69	M+F	524	60.2	NA	YELLOW		
	[185]	No	40–65	M	458	56.4 (+)	NA	YELLOW		
				F	599	50.1 (+)		YELLOW		
	[186]	NA	65–75	M+F	96	23.1	Winter	RED		
	[187]	No	65+	M+F	924	49.7 (+)	Mixed	ORANGE		
	[188]	No	45–54	F	3,133	54.0	Mixed	YELLOW		
	[189]	No	61.7	F	325	53.3	Mixed	YELLOW		
	[187][f]	No	65+	M+F	924	43.5	Mixed	ORANGE		
USA	[190]	Yes	20+	M F	3,184 3,383	70.4 (+) 62.4 (+)	Winter	YELLOW YELLOW	YELLOW	Representative of the entire country, population-based, and based on a weighted average of these studies
	[54]	Yes	20+	M+F	11,009	59.6 (+)	Winter	YELLOW		
	[191]	Yes	20+	M+F	1,654	62.4	NA	YELLOW		
	[192]	Yes	20+	M+F	15,068	73.7	Mixed	YELLOW		
	[11]	Yes	20+	M+F	9,961	62.6	Mixed	YELLOW		
	[193]	Yes	20–49	M	3,474	68.0	Mixed	YELLOW		
			50+	M	1,912	69.0		YELLOW		
			20–49	F	3,947	60.0		YELLOW		
			50+	F	1,869	61.0		YELLOW		
	[194]	Yes	20+	M+F	8,421	74.0	Mixed	YELLOW		
	[195]	Yes	20+	M+F	948	65.1	Mixed	YELLOW		
	[196]	Yes	20+	M	6,097	78.0	Mixed	GREEN		
				F	6,547	73.0		YELLOW		
	[197]	Yes	40+	M	1,273	54.2	NA	YELLOW		
	[198]	No	65+	M+F	1,917	71.9	Mixed	YELLOW		
	[199]	No	35+	M+F	3,890	93.0	Mixed	GREEN		
	[200]	NA	67–95	M	290	82.0	NA	GREEN		
				F	469	69.8		YELLOW		
	[201]	No	59.6	M+F	808	47.4	Mixed	ORANGE		
	[202]	No	35–89	M	843	49.0	Mixed	ORANGE		
				F	919	49.2		ORANGE		
	[203]	No	67–90	M+F	341	72.0	NA	YELLOW		
	[204]	No	69–90	M+F	328	75.0	NA	GREEN		
	[205]	NA	80–89	M+F	68	75.1	Mixed	GREEN		
	[206]	No	20+	M+F	8,351	61.0	NA	YELLOW		

Table 2 (continued)

Country	Reference	Representative	Age (years)	Sex	*N*	25(OH)D (nmol/L)[a]	Season	Study colour code[b]	Country colour code[b]	Country colour code rationale
	[207]	No	20+	F	1,881	54.0	NA	YELLOW		
	[208]	No	20+	M+F	4,495	49.75	NA	ORANGE		
	[209]	No	17+	M+F	–	67.4	Mixed	YELLOW		
	[210]	No	20+	M	6,950	78.0	Mixed	GREEN		
				F	7,729	71.6		YELLOW		
	[211]	No	65+	M+F	3,408	66.0	Mixed	YELLOW		
	[212]	No	18+	M+F	16,603	74.0	Mixed	YELLOW		
	[213]	No	20+	M+F	15,088	75.0	Mixed	GREEN		
	[214]	No	20+	M	2,939	78.8	Mixed	GREEN		
				F	3,289	72.6		YELLOW		
	[215]	No	18+	M	7,286	78.7	Mixed	GREEN		
				F	8,104	71.1		YELLOW		
	[216]	No	55–96	M+F	654	103.7	Mixed	GREEN		
	[217]	No	74	M+F	1,073	105.0	Mixed	GREEN		
	[218]	NA	50–97	M+F	615	102.0	Mixed	GREEN		
	[219]	NA	65–87	M	182	82.4	Mixed	GREEN		
				F	209	68.9		YELLOW		
	[220]	No	82.4	M+F	77	113.1	NA	GREEN		
	[221]	No	57–89	F	136	52.8	Mixed	YELLOW		
	[222]	No	55+	F	1,179	71.8	Mixed	YELLOW		
	[223]	No	20–30	F	20	75.0	NA	GREEN		
			55+	F	20	85.0		GREEN		
	[224]	NA	20–88	M+F	198	70.9	Mixed	YELLOW		
	[225]	No	20–80	F	410	54.2	Mixed	YELLOW		
	[226]	NA	21–54	F	138	77.6	NA	GREEN		
	[227]	No	64–92	M	142	67.5	NA	YELLOW		
			64–93	F	195	57.7		YELLOW		
	[228]	No	18–68	F	50	55.7	Mixed	YELLOW		
	[229]	NA	35–46	F	182	72.3	NA	YELLOW		
Vietnam	[230]	Yes	18–87	M F	205 432	92.0 75.3	Mixed	GREEN GREEN	GREEN	Population-based data for a region/city of the country

M males, *F* females, *M+F* combined data for males and females, *NA* no information available

[a] Published 25(OH)D means (or medians if means not available) are presented, with the exception of studies marked with a (+). For these studies, the 25(OH)D level is a mean weighted for the sample size. If weighted mean could not be calculated, a simple mean was taken

[b] RED, <25 nmol/L; ORANGE, 25–49 nmol/L; YELLOW, 50–74 nmol/L; GREEN, ≥75 nmol/L

[c] A previous study of the same cohort [231] reported median 25(OH)D levels of 20.6 nmol/L. This does not affect the colour of the overall country

[d] Unknown number per gender—overall study population is 976

[e] Unknown number—subset of 1,311 people measured in winter

[f] Unknown number—the entire cohort for the four regions in the UK represented 924 individuals

[g] Mean 25(OH)D was not stated in the publication, but it was calculated using the information provided

information was not identified include Central America, South America (with the exception of Brazil) and much of Africa. With the known role of vitamin D in preserving bone health, it is important to fill these gaps so that appropriate measures can be implemented to correct inadequate 25 (OH)D levels. Information gaps in both age groups would ideally be filled with survey data based on random sampling of a country or region. In the meantime, any and all data from specific regions will make some contribution to defining vitamin D status globally.

Despite using data from a systematic literature review, the maps have limitations. One limitation is that adequate

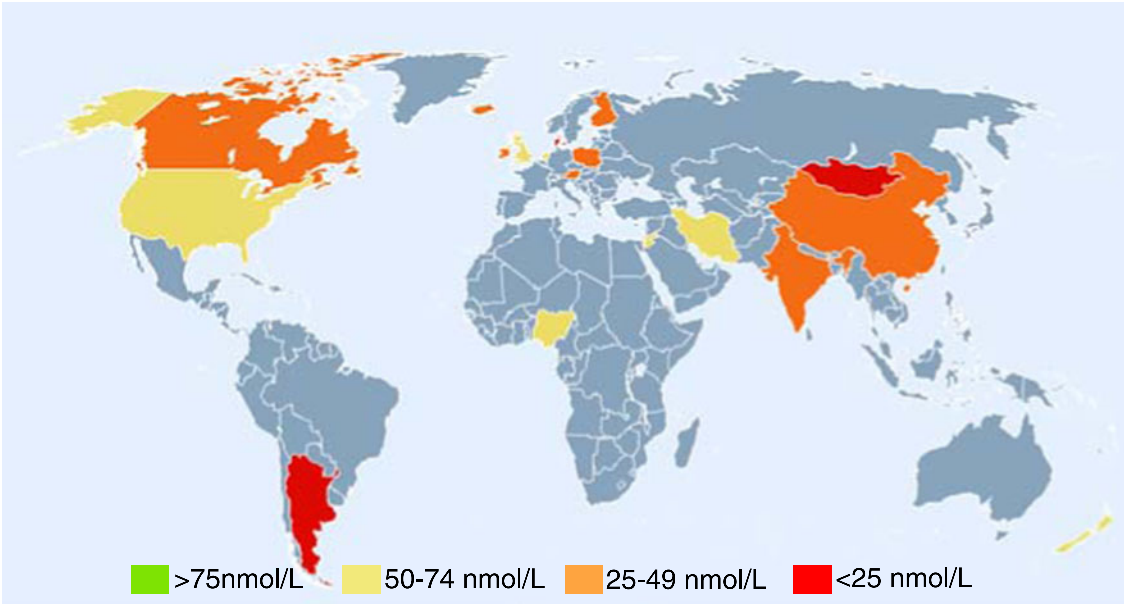

Fig. 1 Vitamin D status in children and adolescents (1–18 years) around the world when available; winter values were used to calculate the mean 25(OH)D levels

information is not available. An extreme example is that for a few countries, one single small study confined to a limited region of the country and to a narrow age range was used to colour the country (e.g. Argentina). This is of course not a complete picture of the country. Other countries have many studies, representative and non-representative. For example, New Zealand is coloured orange based on the one available representative sample of subjects residing in the city of Auckland. As indicated in the table, other studies from this country involving healthy populations and subjects measured in the summer consistently reported higher 25(OH)D levels in the range of yellow and green. In view of the diversity in the quantity and quality of data used in this study, it is important that the tables be used in conjunction with the maps and that the maps are interpreted with caution.

Several limitations are inherent in the way that the published data were presented. For example, 25(OH)D measurements were sometimes made in specific seasons (i.e.

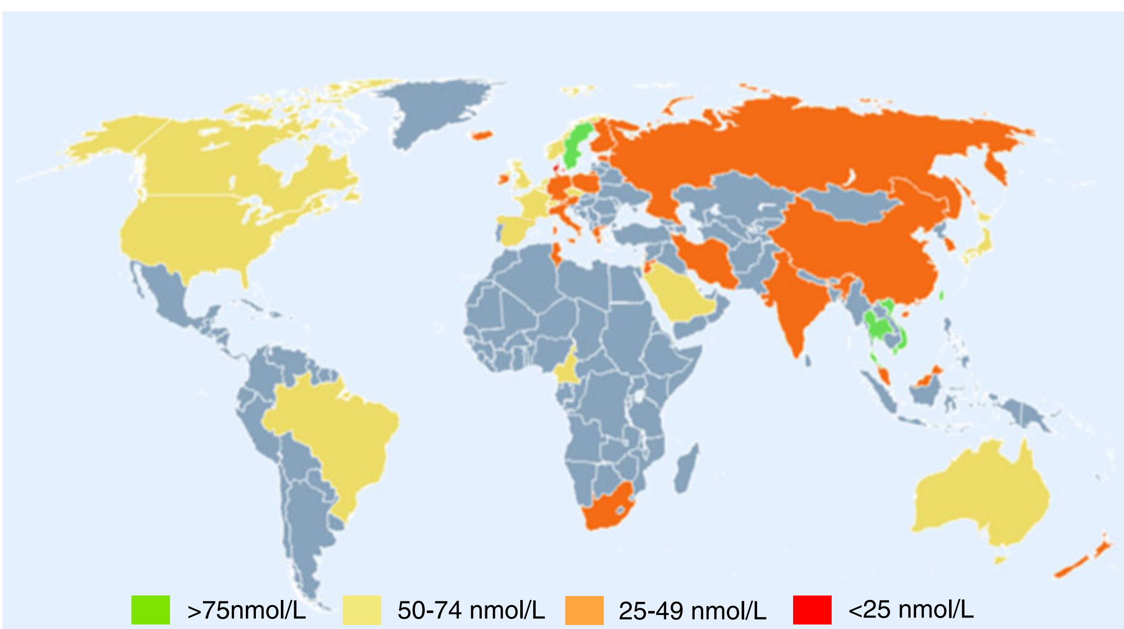

Fig. 2 Vitamin D status in adults (>18 years) around the world when available; winter values were used to calculate the mean 25(OH)D levels

winter or summer) and at other times made without reference to season. When the option was available, we used the winter measurement, representing the worst-case scenario, for the map colouration; however, 25(OH)D levels by season, when available, are provided in the table. There was inconsistency across studies in the age groupings such that we were not always able to break out the levels by our predefined age categories of children and adolescents 1–18 years and adults >18 years. Another limitation is that some of the studies represented small regions within large countries with diverse latitudes; thus, they did not fairly represent the whole nation with respect to the contribution of sun exposure (skin synthesis) to 25(OH)D levels. Additionally, information on body size, clothing habits and skin pigmentation was not consistently available.

An important limitation of this project and of any inter-study comparison of 25(OH)D levels is the well-described variability in 25(OH)D assays. Since the first 25(OH)D assay was developed 30 years ago [23], the analytical options have expanded from the original competitive protein binding assay to include radioimmunoassay, chemiluminescent assay, high-performance liquid chromatography and liquid chromatography–mass spectrometry/mass spectrometry. Unfortunately, the serum 25(OH)D levels vary by up to 20–40 %, depending upon which assay is used [24–27]. Part of the variability can be attributed to the fact that not all of the assays detect 25(OH)D2 as effectively as they detect 25(OH)D3. As a result, in those regions where vitamin D2 is used in most supplements, the total 25(OH)D levels will tend to be underestimated.

To address the assay problem, many laboratories around the world participate in a quarterly quality assurance and surveillance program, the Vitamin D External Quality Assessment Scheme, which we strongly encourage. Standard reference material consisting of known amounts of 25(OH)D2 and 25(OH)D3 in human serum is now available through the U.S. National Institute of Standards and Technology (NIST; SRM972, www.NIST.gov/srm). The use of this material should make inter-laboratory comparisons more readily interpreted and allow for the detection of intra-laboratory changes over time. An important initiative, the vitamin D standardization program (VDSP), is currently underway to make the measurement of 25(OH)D accurate and comparable over time, location and laboratory [28]. The first goal of VDSP is to standardize 25(OH)D values currently being measured in national health surveys to the NIST standards. Australia, Canada, Germany, Ireland, Mexico, South Korea, the UK and the USA are participating in this process. A second goal is to design studies to cross-calibrate data from national surveys in which 25(OH)D measurements have already been completed. The longer range goal is to enable the use of standardized 25(OH)D values in individual research laboratories and in clinical care.

Conclusion

In conclusion, this study provides an overview of 25(OH)D status around the globe. It reveals large gaps in information in children and adolescents and smaller but important gaps in adults. In view of the importance of vitamin D to the overall musculoskeletal health and of its potential importance in other tissues, we strongly encourage new research worldwide to define 25(OH)D status. Deficiency must first be identified before it can be appropriately addressed. Knowledge of specific data gaps may help motivate regional policy makers and granting agencies to define the vitamin D status of their population as they decide how to allocate scarce research resources.

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Conflicts of interest Drs. Manfred Eggersdorfer and Elisabeth Stöcklin are employed by DSM Nutritional Products, Ltd. Professor Cyrus Cooper has received honoraria and consulting fees from Amgen, Eli Lilly, Medtronic, Merck, Novartis and Servier. All the other authors have nothing to disclose.

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