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A GLOBAL REPRESENTATION OF VITAMIN D STATUS IN HEALTHY POPULATIONS

Wahl DA, Cooper C, Ebeling PR, Eggersdorfer M, Hilger J, Hoffmann K, Josse R, Kanis JA, Mithal A, Pierroz DD, Stenmark J, Stöcklin E and Dawson Hughes B*

*Corresponding author
B. Dawson-Hughes
Department of Agriculture Human Nutrition,
Research Center on Aging, Tufts University,
711 Washington Street,
Boston, MA 02111, USA
Email: bess.dawson-hughes@tufts.edu

Author affiliations

D.A. Wahl, D.D. Pierroz and J. Stenmark
International Osteoporosis Foundation, Nyon, Switzerland

C. Cooper
MRC Lifecourse Epidemiology Unit, University of Southampton and NIHR Musculoskeletal Biomedical Research Unit, University of Oxford, UK

P.R. Ebeling
NorthWest Academic Centre, University of Melbourne, Western Health, St. Albans, Victoria, Australia

M. Eggersdorfer and E. Stöcklin
Nutrition Science & Advocacy and Research & Development Human Nutrition, DSM Nutritional Products, Kaiseraugst, Switzerland

J. Hilger and K. Hoffmann
Mannheim Institute of Public Health, Social and Preventive Medicine, Mannheim Medical Faculty, Heidelberg University, Mannheim, Germany

R. Josse
Division of Endocrinology and Metabolism, University of Toronto, St Michael's Hospital Health Centre, Toronto, Canada

A. Mithal
Medanta Medicity, Sector 38, Gurgaon, India

J.A. Kanis
WHO Collaborating Centre for Metabolic Bone Diseases, University of Sheffield Medical School, UK

B. Dawson-Hughes *
Jean Mayer USDA Human Nutrition Research Center on Aging at Tufts University, Boston, USA

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 world wide 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 (25OHD) 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 mean 25OHD levels were below 50 nmol/L.

Conclusions This study provides an overview of 25OHD 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 its potential importance in other tissues, we strongly encourage new research to clearly define 25OHD status around the world.

Keywords: vitamin D status, vitamin D deficiency, 25OHD, 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 serum concentration of 25-hydroxyvitamin D levels, also known as 25OHD levels [2].

Very low levels of 25OHD have been documented in different subgroups of the population worldwide [1, 3-6], which have clinical implications. Vitamin D plays an important role in the 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], infection [14] and it may help to 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 25OHD 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 Jan 1st 1990 and 28th Feb 2011.

Abstract and full publication screening
2,566 articles were identified from both databases. Two independent researchers screened the articles were by with a good agreement for excluding studies (kappa coefficient of 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: mean or median 25OHD 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 years and > 18 years) were removed. When published repeatedly, the same cohort was not presented more than once. In contrast, studies reporting 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 examination of the database, two different age categories were selected: children and adolescents (1-18 years) and adults (>18 years). Mean serum or plasma 25OHD levels were extracted and reported as gender-specific means weighted by sample size where possible. Median levels of 25OHD were included when mean levels were not reported in a study. When data were classified by specific seasons, winter values were chosen. Values in ng/ml were converted to nmol/L by a multiple of 2.496.

Four colour codes according to mean (or median) 25OHD 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 (nmol/L) 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, 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 25OHD level (either 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.

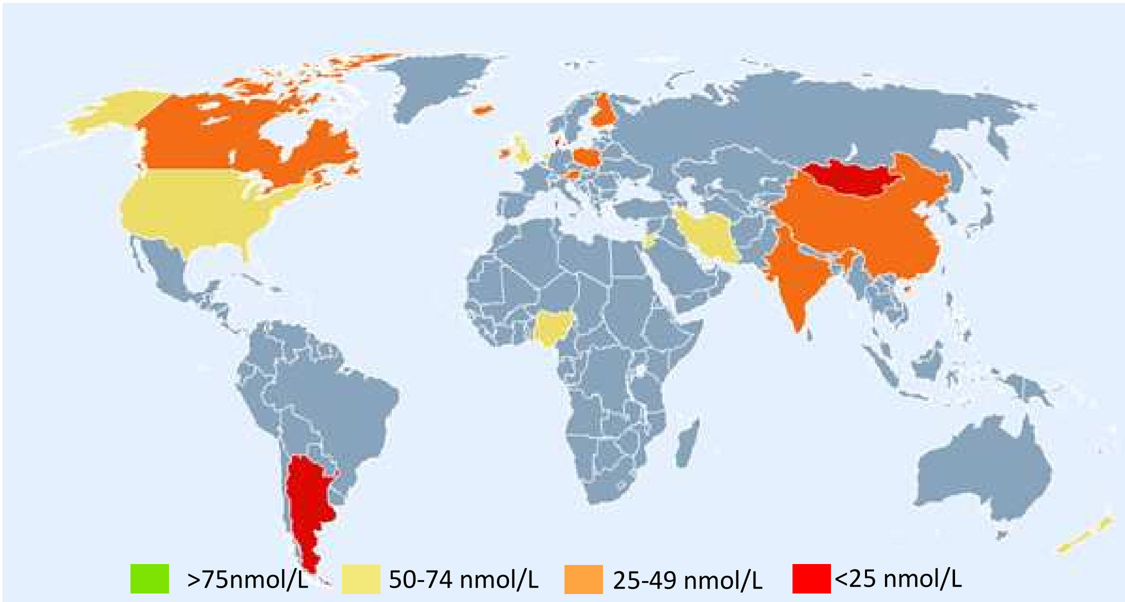
Design of the figures

The software FlashWorldMap.com was used to produce the maps

Results

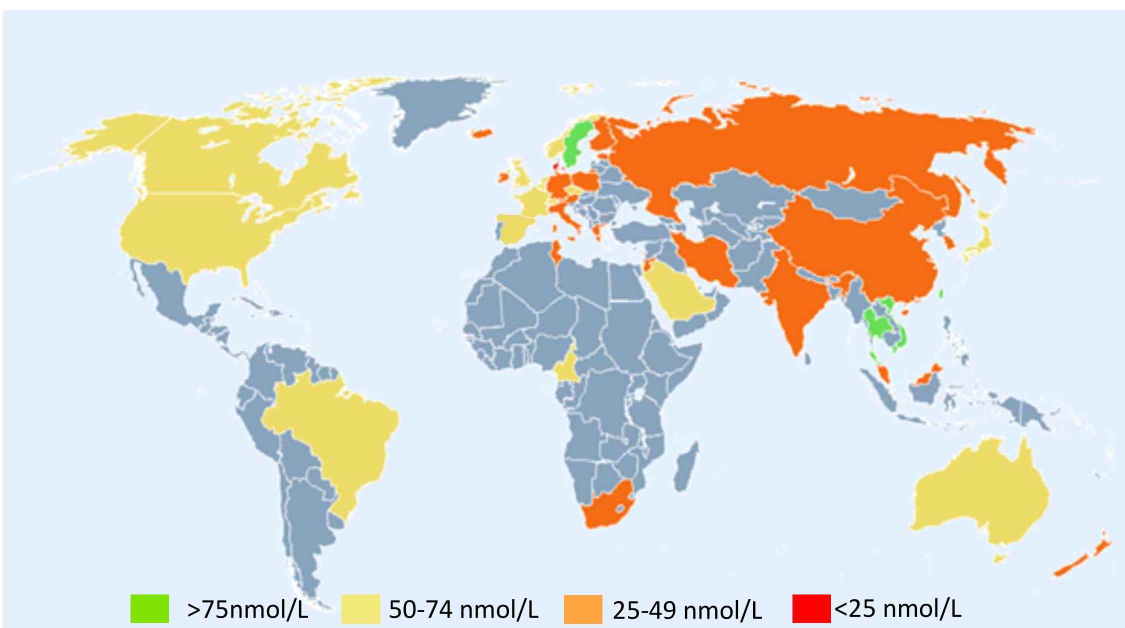
This analysis involves 200 studies from 46 countries. Forty two of the 200 studies (21%) were considered representative. Details of these studies for each contributing country are provided in Tables 1 (children and adolescents) and 2 (adults). The largest number of studies was conducted in Europe (48.0%), 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. Fig 1 and Fig 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 25OHD reported in Table 1 (children and adolescents) and Table 2 (adults) and the ranges of 25OHD represented by each colour are described in the two figures.

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 25OHD levels.

Fig 2 Vitamin D status in adults (> 18 years) around the world



when available, winter values were used to calculate the mean 25OHD levels.

Discussion

This project provides a ‘snap shot’ or summary of 25OHD 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 25OHD 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 25OHD since 1990, within regions and overall. We can expect to see rises in 25OHD 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 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 25OHD 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, 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 25OHD 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 to 49 nmol/L) and yellow (50 to 74 nmol/L). Areas where 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 25OHD 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 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 summer consistently reported higher 25OHD levels in the range of yellow and green. In view of the diversity in 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, 25OHD measurements were sometimes made in specific seasons (i.e., 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 25OHD 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 25OHD 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 25OHD levels is the well described variability in 25OHD assays. Since the first 25OHD 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, serum 25OHD levels vary by up to 20 to 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 $25OHD_2$ as effectively as they detect $25OHD_3$. As a result, in those regions where vitamin D_2 is used in most supplements, total 25OHD 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 (DEQAS) which we strongly encourage. Standard reference material consisting of known amounts of $25OHD_2$ and $25OHD_3$ 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 under way to make the measurement of 25OHD accurate and comparable over time, location and laboratory [28]. The first goal of VDSP is to standardize 25OHD values currently being measured in national health surveys to the NIST standards. Australia, Canada, Germany, Ireland, Mexico, South Korea, United Kingdom and the U.S. are participating in this process. A second goal is to design studies to cross-calibrate data from national surveys in which 25OHD measurements have already been completed. The longer range goal is to enable the use of standardized 25OHD values in individual research laboratories and in clinical care.

Conclusion

In conclusion, this study provides an overview of 25OHD 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 overall musculoskeletal health and of its potential importance in other tissues, we strongly encourage new research worldwide to define 25OHD status. Deficiency must first be identified before it can be appropriately addressed. Knowledge of specific data gaps may help to 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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Disclosure

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.

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

Country	Refs	Representative	Age	Sex	N	25OHD (nmol/L)*	Season	Study colour code&	Country colour code&	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	1143	26.4 (+)	NA	ORANGE	ORANGE	Based on a single study
Canada	[31] [32]	Yes No	3-5 9-16	M+F M F	282 878 867	48.3 45.9 45.9	Mixed Mixed	ORANGE ORANGE ORANGE	ORANGE	Representative of a region/city of the country, population-based
China	[33] [34]	Yes NA	12-14 1-2	M F F	649 131 119	33.4 42.3 25.5	Winter Mixed	ORANGE ORANGE ORANGE	ORANGE	Representative of a region/city of the country, population-based
Denmark	[35]	No	12.5	F	59	24.4	Winter	RED	RED	Based on a single study
Finland	[36] [35]	NA No	11.4 12.8	F F	64 60	39.9 29.2	Mixed Winter	ORANGE ORANGE	ORANGE	Based on a weighted average
Iceland	[37]	No	16-20	F	259	43.9	Winter	ORANGE	ORANGE	Based on a single study
India	[38]	No	11-14	M F	64 75	40.8 46.8	Winter	ORANGE ORANGE	ORANGE	Based on a single study
Iran	[39] [40] [41]	No NA No	7-18 11-15 14-18	M F F M F	424 539 414 153 165	116.3 60.4 74.9 93.2 41.9	Winter Mixed Winter	GREEN YELLOW YELLOW GREEN ORANGE	YELLOW	Based on a weighted average of females#
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] [48] [49]	No NA NA	5-14 1-2 1-2	M+F M+F M+F	1585 193 233	50.0 52.0 53.3 (+)	Mixed Mixed Mixed	YELLOW YELLOW YELLOW	YELLOW	Based on a weighted average
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] [52] [53]	Yes Yes Yes	Childs 12, 15 12-15	M+F M F M+F	854 505 510 1015	65.5 62.3 58.3 64.3	Mixed Mixed Mixed	YELLOW YELLOW YELLOW YELLOW	YELLOW	Representative of the Entire country, population-based
USA	[54] [55] [56] [57] [58] [59] [60] [61] [62]	Yes Yes Yes Yes No NA NA NA NA	1-19 1-11 12-19 6-21 4-8 9-11 7-18 4-8 12-18	M+F M+F M+F M+F F F M+F F F	8541 4558 3528 382 168 22 735 76 370	66.8 (+) 68 62.0 69.9 93.8 74.4 66.2 88.2 53.7	Mixed Mixed NA Mixed Mixed Mixed NA Mixed Mixed	YELLOW YELLOW YELLOW YELLOW GREEN YELLOW YELLOW GREEN YELLOW	YELLOW	Representative of the entire country, population-based, and based on a weighted average

(M) Males; (F) Females; (M+F) Combined data for males and females; (NA) No information available.

*Published 25OHD means (or medians if means not available) are presented with the exception of studies marked with a (+). For these studies, the 25OHD level is a mean weighted for sample size. If weighted means couldn't be calculated, a simple mean was taken.

& Colour codes: RED, < 25nmol/L; ORANGE 25-49nmol/L; YELLOW 50-74nmol/L; GREEN ≥75nmol/L

Male data from references 38 and 40 were considered outliers and were excluded from the weighted mean 25OHD levels.

Table 2 Country colour codes of vitamin D status in adults.

Country	Refs	Representative	Age	Sex	N	25OHD (nmol/L)*	Season	Study colour code[&]	Country colour code[&]	Country colour code rationale
Australia	[63] [64] [65] [66] [67]	No No No NA No	60+ 20-92 51-77 51-79 78	M F M+F M+F M+F	437 861 253 880 70	70.2 (+) 70.3 72.2 52.8 33	NA Mixed NA NA NA	YELLOW YELLOW YELLOW YELLOW ORANGE	YELLOW	Based on a weighted average
Austria	[30] [68]	NA No	65-85 21-76	M+F M+F	78 1089	9.5 52.2	NA Winter	RED YELLOW	ORANGE	Based on a weighted average
Belgium	[69] [70] [71] [72] [73]	No No NA No No	70-90 70-87 20+ 21-65 40-60	F F M F M+F M+F	245 129 270 272 126 401	56.4 43.2 71.5 73.5 48.2 35.0	NA NA NA Winter NA	YELLOW ORANGE YELLOW YELLOW ORANGE ORANGE	YELLOW	Based on a weighted average
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] [77] [78] [79]	Yes No No No	20-79 27-89 68-82 46.8	M+F M+F M+F F	3458 188 195 741	67.7 (+) 57.3 66.7 64.9	Mixed Winter Mixed Winter	YELLOW YELLOW YELLOW YELLOW	YELLOW	Representative of the entire country, population-based
China	[80] [81] [82]	NA NA No	40-70 40-65 19-40	M+F M+F F	2018 720 16	31.7 33.1 43.9	Mixed Mixed NA	ORANGE ORANGE ORANGE	ORANGE	Based on a weighted average
Czech Republic	[83]	No	62.3	F	47	58.2	NA	YELLOW	YELLOW	Based on a single study
Denmark	[84] [85] [86] [87] [35] [88] [89]	Yes NA NA No No No NA	35-65 50-82 17-87 45-58 71.6 20-29 70-74	M+F F F F F M M+F	125 315 2316 510 53 700 669	25.5 57.0 62.0 24.0 47.8 64.9 47.6	Mixed NA Mixed NA Winter Mixed Mixed	ORANGE YELLOW YELLOW RED ORANGE YELLOW ORANGE	ORANGE	Representative of a region/city of the country, population-based
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] [93] [94] [95] [96] [97] [98]	Yes Yes No No NA NA NA	30+ 30+ 30-97 30+ 40-69 31-43 20-64	M+F M+F M F M+F M+F M F M F	6937 6219 2736 3299 6241 4097 126 202 138 358	42.9 43.4 45.1 45.2 45.1 43.6 45.0 47.0 34.0 35.0	NA Mixed NA Mixed Mixed Mixed Mixed	ORANGE ORANGE ORANGE ORANGE ORANGE ORANGE ORANGE ORANGE ORANGE ORANGE	ORANGE	Representative of the entire country, population-based, and based on a weighted average
France	[99] [100] [101] [102]	NA NA No No	35-65 35-65 18-62 18-76	M+F M+F M F F	1569 1191 70 94 248	61.0 79.5 80.9 (+) 71.5 (+) 64.1	Winter Winter Mixed NA	YELLOW GREEN GREEN YELLOW YELLOW	YELLOW	Based on a weighted average
Gambia	[103]	No	25+	F	112	91.3 (+)	NA	GREEN	GREEN	Based on a single study
Germany	[104]	Yes	18-79	M F	1763 2267	45.2 44.7	NA	ORANGE ORANGE	ORANGE	Representative of the entire country,

	[105]	NA	50-80	M+F	415	42.5	Mixed	ORANGE		population-based,
	[106]	No	50-81	M	175	50.4	Winter	ORANGE		and based on a
				F	123	44.2		ORANGE		weighted average
	[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
			19-46	M+F	44	85.7		GREEN		study and on a
										weighted average
Iceland	[8]	No	30-85	M+F	944	46.1 (+)	Mixed	ORANGE	ORANGE	Based on a
	[109]	NA	70	F	308	53.1	Mixed	YELLOW		weighted average
India	[110]	NA	18+	M+F	57	36.4	Winter	ORANGE	ORANGE	Based on a
	[38]	No	41-47	M	243	52.2 (+)	NA	YELLOW		weighted average
				F	903	39.7 (+)		ORANGE		
Iran	[111]	Yes	20-74	M	520	35.0	Winter	ORANGE	ORANGE	Representative of
	[112]	Yes	40-80	F	245	73.0	NA	YELLOW		the entire country,
	[113]	NA	20-74	F	676	28.9	Winter	ORANGE		population-based,
	[114]	NA	20-79	M+F	646	31.3	NA	ORANGE		and based on a
	[115]	NA	50-80	F	300	35.4	Mixed	ORANGE		weighted average
	[116] (a)	NA	20-69	M+F	1210	32.5	NA	ORANGE		
Ireland	[117]	NA	Elderly	M+F	116	37.1	NA	ORANGE	ORANGE	Based on a
	[35]	No	72.3	F	43	43.7	Winter	ORANGE		weighted average
	[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	1006	39.9	Mixed	ORANGE	ORANGE	Representative of
	[121]	Yes	65-96	M	372	55.2	Mixed	YELLOW		the entire country,
				F	435	34.7		ORANGE		population-based,
	[122] (b)	Yes	65-102	M	976	57.9	Mixed	YELLOW		and based on a
				F	976	43.3		ORANGE		weighted average
	[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	1107	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
	[129]	No	70+	M	456	71.7	Winter	YELLOW		the entire country,
				F	638	65.8		YELLOW		population-based
	[130]	No	65-89	M	950	71.1	Mixed	YELLOW		
			65-92	F	2007	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	[132]	No	40+	M+F	1330	46.1	Mixed	ORANGE	ORANGE	Based on a single
(South)										study
Lebanon	[133]	NA	65-85	M+F	443	28.4	Mixed	ORANGE	ORANGE	Based on a
	[134]	No	30-50	M+F	316	24.2	Winter	RED		weighted average
Malaysia	[135]	No	50-65	F	101	44.4	NA	ORANGE	ORANGE	Based on a single
										study
Netherlands	[136]	Yes	65-88	M+F	1319	53.2	Mixed	YELLOW	YELLOW	Representative of
	[137] (c)	Yes	65-89	M+F	1311	50.5	Mixed	YELLOW		the entire country,
	[138]	Yes	65-85	M+F	1260	51.8	Mixed	YELLOW		population-based,
	[139]	NA	65-88	M	620	58.1	Mixed	YELLOW		and based on a
			65-88	F	635	49.1		ORANGE		weighted average
	[140]	NA	55-85	M+F	935	51.2	Mixed	YELLOW		
	[141]	NA	65-95	M+F	1282	52.4	Mixed	YELLOW		
	[142]	No	65+	M+F	1234	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	[146]	Yes	35-64	M	295	39.8	Mixed	ORANGE	ORANGE	Representative of
Zealand	[147]	No	40+	M	378	85.0	NA	GREEN		the entire country,
			55+	F	1606	51.0		YELLOW		population-based

	[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	YELLOE		
	[155]	NA	25-74	M+F	6932	58.9	NA	YELLOW		
	[156]	No	25-84	M+F	2668	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	1557	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	1194	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	3276	50.0	Mixed	YELLOW	YELLOW	Representative of the entire country, population-based
	[173]	No	66-95	M	203	91.7	Mixed	GREEN		
			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	126	133.5	NA	GREEN	GREEN	Representative of a region/city of the country, population-based
				F	125	102.7		GREEN		
	[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](e)	No	20-60	F	261	40.3	Mixed	ORANGE	ORANGE	Based on a single study
United Kingdom	[180]	Yes	65+	M	322	56.2	Mixed	YELLOW	YELLOW	Representative of the entire country, population-based
				F	320	48.4		ORANGE		
	[181]	Yes	65+	M	950	53.0	Mixed	YELLOW		
				F	1120	48.0		ORANGE		
	[182]	No	65+	M+F	1026	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	3133	54.0	Mixed	YELLOW		
	[189]	No	61.7	F	325	53.3	Mixed	YELLOW		
	[187] (d)	No	65+	M+F	924	43.5	Mixed	ORANGE		
USA	[190]	Yes	20+	M	3184	70.4 (+)	Winter	YELLOW	YELLOW	Representative of the entire country, population-based, and based on a weighted average of these studies
				F	3383	62.4 (+)		YELLOW		
	[54]	Yes	20+	M+F	11009	59.6 (+)	Winter	YELLOW		
	[191]	Yes	20+	M+F	1654	62.4	NA	YELLOW		
	[192]	Yes	20+	M+F	15068	73.7	Mixed	YELLOW		
	[11]	Yes	20+	M+F	9961	62.6	Mixed	YELLOW		
	[193]	Yes	20-49	M	3474	68.0	Mixed	YELLOW		

			50+	M	1912	69.0		YELLOW		
			20-49	F	3947	60.0		YELLOW		
			50+	F	1869	61.0		YELLOW		
	[194]	Yes	20+	M+F	8421	74.0	Mixed	YELLOW		
	[195]	Yes	20+	M+F	948	65.1	Mixed	YELLOW		
	[196]	Yes	20+	M	6097	78.0	Mixed	GREEN		
				F	6547	73.0		YELLOW		
	[197]	Yes	40+	M	1273	54.2	NA	YELLOW		
	[198]	No	65+	M+F	1917	71.9	Mixed	YELLOW		
	[199]	No	35+	M+F	3890	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	8351	61.0	NA	YELLOW		
	[207]	No	20+	F	1881	54.0	NA	YELLOW		
	[208]	No	20+	M+F	4495	49.75	NA	ORANGE		
	[209]	No	17+	M+F	-	67.4	Mixed	YELLOW		
	[210]	No	20+	M	6950	78.0	Mixed	GREEN		
				F	7729	71.6		YELLOW		
	[211]	No	65+	M+F	3408	66.0	Mixed	YELLOW		
	[212]	No	18+	M+F	16603	74.0	Mixed	YELLOW		
	[213]	No	20+	M+F	15088	75.0	Mixed	GREEN		
	[214]	No	20+	M	2939	78.8	Mixed	GREEN		
				F	3289	72.6		YELLOW		
	[215]	No	18+	M	7286	78.7	Mixed	GREEN		
				F	8104	71.1		YELLOW		
	[216]	No	55-96	M+F	654	103.7	Mixed	GREEN		
	[217]	No	74	M+F	1073	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	1179	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	205	92.0	Mixed	GREEN	GREEN	Population-based data for a region/city of the country
				F	432	75.3		GREEN		

(M) males; (F) females; (M+F) combined data for males and females; (NA) No information available.

*Published 25OHD means (or medians if means not available) are presented with the exception of studies marked with a (+). For these studies, the 25OHD level is a mean weighted for sample size. If weighted mean couldn't be calculated, a simple mean was taken.

& Colour code: RED, < 25nmol/L; ORANGE 25-49nmol/L; YELLOW 50-74nmol/L; GREEN ≥75nmol/L

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

(b) Unknown number per gender – overall study population is 976.

(c) Unknown number – subset of 1311 people measured in winter

(d) Unknown number – the entire cohort for the 4 regions in the UK represented 924 individuals.

(e) Mean 25OHD was not stated in the publication but it was calculated using the information provided.

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Figure 1

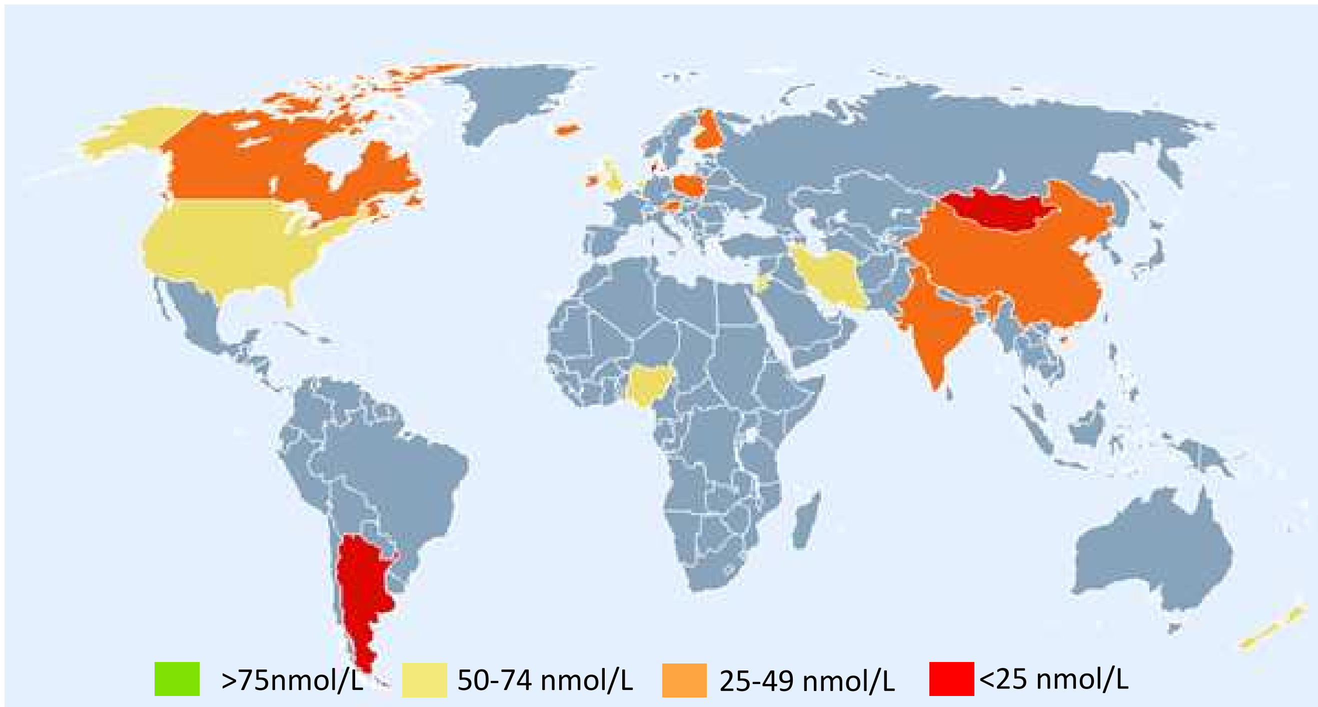

Figure 2