Systematic Review

A systematic review of vitamin D status in populations worldwide

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Abstract

Vitamin D deficiency is associated with osteoporosis and is thought to increase the risk of cancer and CVD. Despite these numerous potential health effects, data on vitamin D status at the population level and within key subgroups are limited. The aims of the present study were to examine patterns of 25-hydroxyvitamin D (25(OH)D) levels worldwide and to assess differences by age, sex and region. In a systematic literature review using the Medline and EMBASE databases, we identified 195 studies conducted in forty-four countries involving more than 168 000 participants. Mean population-level 25(OH)D values varied considerably across the studies (range 4·9–136·2 nmol/l), with 37·3 % of the studies reporting mean values below 50 nmol/l. The highest 25(OH)D values were observed in North America. Although age-related differences were observed in the Asia/Pacific and Middle East/Africa regions, they were not observed elsewhere and sex-related differences were not observed in any region. Substantial heterogeneity between the studies precluded drawing conclusions on overall vitamin D status at the population level. Exploratory analyses, however, suggested that newborns and institutionalised elderly from several regions worldwide appeared to be at a generally higher risk of exhibiting lower 25(OH)D values. Substantial details on worldwide patterns of vitamin D status at the population level and within key subgroups are needed to inform public health policy development to reduce risk for potential health consequences of an inadequate vitamin D status.

Key words: Vitamin D: Populations: Public health

Vitamin D plays an important role in bone mineralisation and other metabolic processes in the human body such as Ca and phosphate homeostasis and skeletal growth^(1,2). Vitamin D deficiency, for example, causes rickets in children, leading to skeletal abnormalities, short stature, delayed development or failure to thrive⁽³⁾. In adults, low values of vitamin D are associated with osteomalacia, osteopenia, osteoporosis and subsequent risk of fractures⁽¹⁾. In addition to beneficial effects on musculoskeletal health, observational studies have suggested that low 25-hydroxyvitamin D (25(OH)D) values are associated with an increased risk for several extraskeletal diseases including cancer, infections, autoimmune diseases and CVD⁽⁴⁾. In light of the global ageing population⁽⁵⁾, an almost fourfold increase in osteoporotic hip fractures since $1990^{(6)}$ and the possible risk of other chronic diseases, patterns of low 25(OH)D levels are of substantial public health interest.

Vitamin D status is traditionally measured through assays of 25(OH)D, the major circulating form of vitamin D⁽⁷⁾. Although 25(OH)D levels below 25 nmol/l have been associated with disorders of bone metabolism⁽⁸⁾ and are used to indicate severe vitamin D deficiency, the threshold for defining adequate stores of vitamin D in humans has not been established clearly⁽⁹⁾. The Institute of Medicine has suggested, for example, that approximately 97.5% of the population across all age groups meet their requirements for vitamin D, having serum 25(OH)D values higher than 50 nmol/l⁽¹⁰⁾. However, others consider 25(OH)D values of 75 nmol/l or higher to be adequate^(11,12).

Abbreviations: 25(OH)D, 25-hydroxyvitamin D.

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Given the absence of uniformly accepted definitions, previous reviews have reported substantial variations in the prevalence of vitamin D deficiency across countries throughout the world, with estimates ranging from 2 to 90% depending on the cut-off value and study population selected^(8,13-16). Insights from these earlier studies are limited, however, due to a focus on specific geographical regions, age or risk groups. Moreover, use of a binary approach to define the presence of vitamin D deficiency in some studies might have also obscured important relationships with chronic disease that might exist across a broader spectrum of values.

To provide a basis for future efforts to limit the health consequences of vitamin D deficiency and insufficiency worldwide, we conducted a systematic literature review of studies performed worldwide using continuous values for 25(OH)D to enable comparisons across studies and between different subgroups within the population. The specific objective of the present study, therefore, was to assess vitamin D status across a range of values at the population level and within key population subgroups defined by age, sex and region.

Methods

Literature search

We searched the Medline and EMBASE databases for original articles on vitamin D status in the general population. Keywords were chosen from the Medical Subject Headings terms and the EMTREE thesaurus, respectively, using the following search strategy: (vitamin D/D3 OR 25-hydroxyvitamin D/D3 OR 25(OH)D/D3 OR calcidiol) AND (epidemiologic studies OR population-based OR population OR survey OR representative OR cross-sectional OR observational) NOT (dihydroxycholecalciferols OR case reports OR case–control studies OR clinical trials OR reviews) AND humans. Search terms for vitamin D included the controlled term 'vitamin D' (including calcifediol and 25-hydroxycholecalciferol) and several free-text terms taking different notations of 25(OH)D into account.

Articles published in English between 1 January 1990 and 28 February 2011 (date of the final screen) were considered. We excluded articles published before 1990 because of a general shift in lifestyle, particularly in industrialised nations (e.g. spending less time outdoors), that might have affected mean population-level 25(OH)D values⁽¹⁷⁾. The final screen produced 2566 hits from both databases after excluding 449 exact duplicates identified using EndNote X6 (Thomson Reuters). Wherever possible, the methods used in the present review follow the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement⁽¹⁸⁾.

Study selection

Studies were included in the present review if they met the following criteria defined *a priori*: (1) outcomes – report of mean or median plasma level for 25(OH)D; (2) study participants – randomly selected samples from the general population as well as subgroups defined by age, sex and specific areas within a country; (3) study designs – cross-sectional

studies or baseline data from population-based cohorts. Studies were excluded if vitamin D status was estimated (e.g. through self-reported nutritional intake) or if data were available only on vitamin D₂. We also did not consider studies using a binary indicator for vitamin D deficiency or insufficiency as the sole outcome measure, given differing thresholds used in the literature to define either state⁽⁵⁾. Furthermore, clinical samples or studies restricted to subgroups with specific characteristics (e.g. ethnicity, job and skin colour) were excluded, as they were not randomly selected from the general population.

All studies were independently screened and evaluated for selection by two of the authors (R. H. and A. F.). Inter-rater agreement was good to moderate, and disagreements were discussed and resolved by consensus in each case (abstract selection: $\kappa = 0.719$; full-text selection: $\kappa = 0.544$). Following the application of exclusion criteria to information contained in the study abstract, we reduced the 2566 screened records to 601 (Fig. 1); application of these criteria following review of each full-text article reduced the pool of potentially eligible articles to 272. Given the presence of multiple reports based on the same data, our final analytical sample comprised 195 unique studies. In several instances, multiple articles from single studies were retained for analysis as they provided separate 25(OH)D values for subgroups with the characteristics of interest (age, sex and region).

Data extraction, data elements and quality assessment

Each study was evaluated using a standardised data extraction form. In each case, we assessed a wide range of variables including vitamin D values, assays used and study characteristics as well as characteristics of the study population and method of recruitment. Data from most studies were represented in the dataset by a single entry for the total study population. Multiple subentries for a single study were included if data were presented by age, sex or region. All 25(OH)D values were expressed in nmol/l, following conversion from ng/ml (multiplied by a factor of 2.496) as necessary.

Based on the WHO recommendations, we classified geographical regions as follows: Latin America; North America; Europe; Asia/ Pacific; Middle East/Africa⁽¹⁹⁾. To determine age-related differences, we defined four age groups: newborns/infants (0–1 years); children/adolescents (>1–17 years); adults (>17–65 years); elderly (>65 years). In instances where details about age were not provided, we created a separate category ('other'). Where possible, we also distinguished elderly living in nursing homes (institutionalised elderly) from those living in the community.

We assessed study quality using data reported in each study on representativeness, validity and reliability. A study was considered representative if (1) this feature of the study was explicitly addressed in the corresponding full-text article or (2) any statement made by the authors suggested that the actual sample reflected the target population. A study was classified as non-representative if the corresponding full-text article contained information about an existing selection bias, which might also occur in a randomly selected sample (e.g. overestimation of females). Measurement validity was



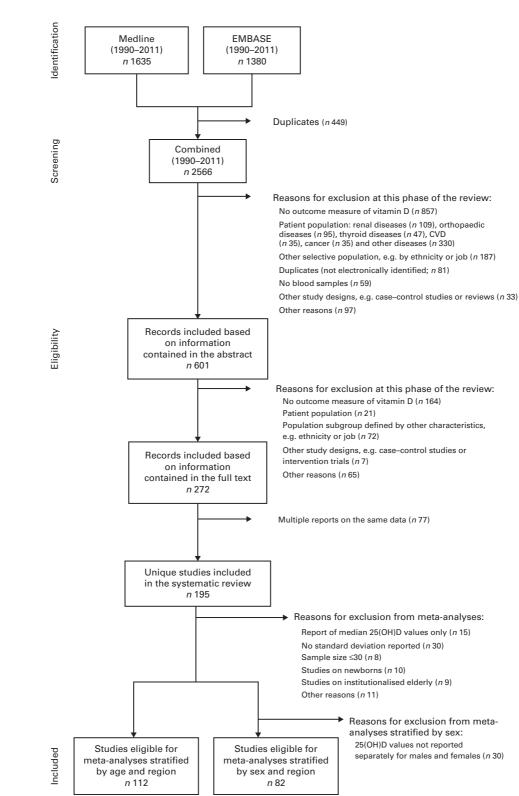


Fig. 1. Flow chart of the study selection (1990-2011). 25(OH)D, 25-Hydroxyvitamin D.

evaluated using information about the 25(OH)D measure (e.g. participation of the laboratory in the International Vitamin D Quality Assessment Scheme)⁽²⁰⁾. Finally, a study was classified as reliable if the intra- and inter-assay coefficients of variation

were below 10 and 15%, respectively. In instances where details about representativeness, validity or reliability were not provided, we created a separate category ('unknown') for each quality criterion.

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Table 1. Characteristics and main results from single studies on 25-hydroxyvitamin D (25(OH)D)*

Region and country	City/region within the country	Reference	n	Male (%)	Age group	Season	25(OH)D (nmol/l)	Reliability	Representativenes
Europe									
Austria									
	Whole country	Koenig & Elmadfa ⁽³³⁾	1452	NA	0	NA	27.5	Unknown	Unknown
	Whole country	Kudlacek et al. (34)	1048	38.2	А	Winter	52.2	Unknown	No
Belgium									
	Brabant	Boonen <i>et al.</i> ⁽³⁵⁾	245	0.0	E	NA	56.4	Unknown	No
	Brussels	MacFarlane et al. ⁽³⁶⁾	126	31.0	А	Winter	48-4	Unknown	No
	Brussels	Moreno-Reyes et al. ⁽³⁷⁾	401	50.1	А	NA	35.0	Yes	No
	Northern Belgium	Richart et al. (38)	542	49.8	NA	NA	71.4†; 73.4‡	Unknown	Unknown
Czech Republic									
	Prague	Zofkova & Hill ⁽³⁹⁾	47	0.0	А	NA	58.2	Unknown	No
Denmark									
	Copenhagen	Andersen et al. ⁽⁴⁰⁾	112	NA	C; E	Winter	24·4§; 47·8§	Yes	No
	Copenhagen	Brot et al. ⁽⁴¹⁾	510	0.0	А	NA	24.0§	Yes	No
	Faroe Islands	Dalgard et al. ⁽⁴²⁾	669	51.1	E	Mixed	47.6	Unknown	Unknown
	Odense	Frost et al. ⁽⁴³⁾	700	100.0	А	Whole year	64·9	Unknown	No
	Aarhus	Rejnmark <i>et al.</i> ⁽⁴⁴⁾	315	0.0	А	NA	57.0§	Unknown	No
	Aarhus	Reinmark et al. ⁽⁴⁵⁾	2316	0.0	А	Mixed	62·0§	Unknown	Yes
	Copenhagen	Rudnicki et al. (46)	125	42.4	А	Whole year	25·5	Yes	Yes
Estonia									
	Vaike-Maarja	Kull <i>et al.</i> ⁽⁴⁷⁾	367	45.5	А	Winter	43.7	Yes	Yes
Finland	2								
	Porvoo (region)	Andersen <i>et al.</i> ⁽⁴⁰⁾	120	NA	A; E	Winter	29·2§; 45·2§	Yes	No
	Whole country	Kauppi <i>et al.</i> ⁽⁴⁸⁾	6035	45.3	A	NA	45.11; 45.2	Yes	No
	Whole country	Lamberg-Allardt et al. (49)	328	38.4	А	Mixed	45.0†; 47.0‡	Yes	Unknown
	Whole country	Matilla et al. ⁽⁵⁰⁾	4097	47.0	А	Whole year	43.6	Yes	Unknown
	Whole country	Partti et al. ⁽⁵¹⁾	6241	45.0	А	Mixed	45.1	Unknown	No
	North Savo	Parviainen et al. ⁽⁵²⁾	776	53.9	А	Mixed	34.0†; 35.0‡	Unknown	Unknown
	Turku	Piirainen <i>et al</i> ⁽⁵³⁾	82	NA	C	Mixed	54.7	Unknown	Unknown
	Helsinki	Viljakainen <i>et al.</i> ⁽⁵⁴⁾	64	0.0	c	Summer; winter	59.5; 37.3	Yes	Unknown
	Helsinki	Viljakainen <i>et al.</i> ⁽⁵⁵⁾	125	52.8	l	Winter	50·7	Yes	Unknown
France									
	Montpellier	Blain <i>et al.</i> ⁽⁵⁶⁾	248	0.0	А	NA	64·1§	Yes	No
	Caen	Bougle et al. ⁽⁵⁷⁾	82	NA	1 I	NA	74.9	Unknown	No
	France	Chapuy et al. ⁽⁵⁸⁾	1569	48.8	A	Winter	61.0	Yes	Unknown
	Burgundy	De Carvalho <i>et al.</i> ⁽⁵⁹⁾	164	42.7	A	Whole year	74.4†; 52.8‡	Unknown	No
	Poitiers	Deplas <i>et al.</i> ⁽⁶⁰⁾	64	31.3	E	Spring	21.4	Unknown	No
	Whole country	Malvy <i>et al.</i> ⁽⁶¹⁾	1191	42.7	Ā	Winter	79.5	Unknown	Unknown
Germany		many or an						0	erina i erina
contaily	Bonn	Braemswig et al. ⁽⁶²⁾	21	100.0	А	Mixed	51.3	Unknown	Unknown
	Whole country	Hintzpeter <i>et al.</i> ⁽⁶³⁾	4030	43.7	0	NA	45.2§†; 44.7§‡	Yes	Yes
	Southern Germany	Scharla <i>et al.</i> ⁽⁶⁴⁾	415	50.4	Ă	Summer; winter	67.4; 42.4	Yes	Unknown
	Southern Germany	Woitge <i>et al.</i> ⁽⁶⁵⁾	41	36.6	0	Mixed	65·6	Unknown	No
	Bonn	Zittermann <i>et al.</i> ⁽⁶⁶⁾	76	0.0	A	Summer; winter	69.8; 30.3	Unknown	No
Greece	Boilit	Entermann et al.	,0	0.0				Shidowi	
	Athens	Nicolaidou <i>et al.</i> ⁽⁶⁷⁾	123	57.7	1	Whole year	50·9§	Yes	Yes
	/ 1110110	Papapetrou <i>et al.</i> ⁽⁶⁸⁾	120	57.7		venoie year	00.03	103	100

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Table 1. Continued

Region and country	City/region within the country	Reference	n	Male (%)	Age group	Season	25(OH)D (nmol/l)	Reliability	Representativeness
Iceland									
	Reykjavik	Kristinsson <i>et al.</i> ⁽⁶⁹⁾	259	0.0	С	Winter	43.9	Yes	No
	Reykjavik	Sigurdsson <i>et al.</i> ⁽⁷⁰⁾	308	0.0	Ē	Mixed	53.1	Yes	NA
	Reykjavik	Steingrimsdottir <i>et al.</i> ⁽⁷¹⁾	944	52.0	Ā	Whole year	45.7	Yes	No
Ireland			• • •			,			
	Cork (region)	Andersen <i>et al.</i> ⁽⁴⁰⁾	62	NA	C; E	Winter	41.3§; 43.7§	Yes	No
	Cork (city)	Hill <i>et al.</i> ⁽⁷²⁾	44	0.0	A	Winter	54.5	Yes	Unknown
	Dublin	Keane <i>et al</i> ⁽⁷³⁾	116	NA	E	NA	37.1	Unknown	Unknown
Israel									
	Whole country	Oren <i>et al.</i> ⁽⁷⁴⁾	195	48.7	0	Whole year	57.2	Unknown	Yes
Italy	,					,			
,	Whole country	Adami <i>et al.</i> ⁽⁷⁵⁾	697	0.0	E	Winter	37.9	Unknown	No
	Southern Italy	Carnevale et al. ⁽⁷⁶⁾	90	35.6	А	Winter	42.7	Yes	No
	Rome	Romagnoli <i>et al.</i> ⁽⁷⁷⁾	135	NA	А	Summer; winter	90.1; 45.9	Yes	No
	Greve, Bagno a Ripoli	Vezzoli <i>et al.</i> ⁽⁷⁸⁾	595	50.8	0	NA	61.2†; 48.2‡	Yes	Unknown
Netherlands									
	Bilthoven, Utrecht	Al-Delaimy et al. ⁽⁷⁹⁾	65	46.2	А	NA	91·2†; 77·2‡	Unknown	Unknown
	Zutphen	Baynes <i>et al.</i> ⁽⁸⁰⁾	142	100.0	E	Spring	42.0	Yes	No
	Rotterdam	Fang et al. ⁽⁸¹⁾	1317	NA	E	Whole year	65.5	Yes	No
	Whole country	Kuchuk et al. ⁽⁸²⁾	1319	48.7	E	Whole year	53.2	Yes	Yes
	Whole country	Löwik <i>et al.</i> ⁽⁸³⁾	529	50.7	E	NA	40.01; 38.01	Unknown	No
	Hoorn	Pilz et al. ⁽⁸⁴⁾	614	NA	E	Whole year	56.51; 50.8‡	Yes	No
	Amsterdam	Van Summeren et al. ⁽⁸⁵⁾	307	50.8	С	NA	69.6	Unknown	No
Norway									
•	Skjervoy	Brustad et al. ⁽⁸⁶⁾	32	65.6	А	NA	67.2	Unknown	No
	Northern Norway	Brustad <i>et al.</i> ⁽⁸⁷⁾	300	0.0	А	Mixed	56.9	Yes	Unknown
	Tromso	Grimnes et al. ⁽⁸⁸⁾	6932	39.0	А	NA	58.9	Yes	No
	Oslo	Meyer <i>et al.</i> ⁽⁸⁹⁾	869	42.8	А	Mixed	74.8	No	No
Poland									
	Sadyba (Warsaw)	Andersen <i>et al.</i> ⁽⁴⁰⁾	126	NA	C; E	Winter	30.6§; 32.5§	Yes	No
	Warsaw	Napiorkowska <i>et al.</i> ⁽⁹⁰⁾	274	0.0	E	Winter	33.7	Yes	Yes
Russia									
	NA	Sapir-Koren <i>et al.</i> ⁽⁹¹⁾	122	0.0	E	NA	29.1	Unknown	No
Spain		•							
	Sabadell	Almirall et al. ⁽⁹²⁾	237	46.8	E	Winter	42.9	Unknown	No
	L'Hospitalet de Llobregat	Gomez et al. ⁽⁹³⁾	253	49.8	А	Whole year	52.7†; 49.9‡	Unknown	Yes
	Betanzos	Moreiras <i>et al.</i> ⁽⁹⁴⁾	55	45.5	E	Spring	25.3	Unknown	Unknown
	Lleida	Muray <i>et al.</i> ⁽⁹⁵⁾	391	58.1	А	Autumn	23.4†; 21.3‡	Unknown	No
	Murica	Perez-Llamas et al. (96)	86	33.7	E	Mixed	50.1	Yes	Unknown
Sweden									
	Central Sweden	Burgaz <i>et al.</i> ⁽⁹⁷⁾	116	0.0	E	Winter	69.0	Yes	Unknown
	Uppsala, Västmanland	Burgaz <i>et al.</i> ⁽⁹⁸⁾	100	0.0	E	Winter	72.0	Unknown	No
	Malmo	Gerdhem et al. ⁽²⁸⁾	986	0.0	E	Whole year	95.0	Yes	No
	Uppsala	Hagström <i>et al.</i> ⁽⁹⁹⁾	958	100.0	E	NA	69.0	Unknown	Unknown
	Uppsala	Lind <i>et al.</i> ⁽¹⁰⁰⁾	34	100.0	А	NA	90.0	Unknown	No
	Stockholm	Melin <i>et al.</i> ⁽¹⁰¹⁾	104	22.1	E	Spring	69.9†; 64.9‡	Yes	No
	Stockholm	Salminen <i>et al.</i> ⁽¹⁰²⁾	350	0.0	E	Whole year	91.0§	Yes	No

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Table 1. Continued

Region and country	City/region within the country	Reference	n	Male (%)	Age group	Season	25(OH)D (nmol/l)	Reliability	Representativeness
Switzerland	-						. ,	-	-
Ownzenand	Vaud, Fribourg, Ticino	Burnand et al. ⁽¹⁰³⁾	3276	51.7	0	Mixed	50.0	Unknown	Yes
	Lausanne	Krieg <i>et al.</i> ⁽¹⁰⁴⁾	349	29.5	Ē	NA	26.5†; 23.2‡	Unknown	Unknown
	Basel	Theiler et al. ⁽²⁹⁾	505	57.4	E	Mixed	17·5† ; 18·2‡ ; 91·6†; 67·4‡	Yes	No
UK		(105)							
	Central, South, West England, Wales	Bates et al. ⁽¹⁰⁵⁾	924	NA	E	Mixed	51.9	Unknown	No
	East Kent	Carter et al.(106)	188	25.5	E	Mixed	31.2§	Unknown	No
	Northern Ireland	Cashman <i>et al.</i> ⁽¹⁰⁷⁾	1015	49.8	С	Mixed	61·1†§; 59·0‡§	Yes	Yes
	Great Britain	Davies <i>et al.</i> ⁽¹⁰⁸⁾	756	NA	С	Mixed	51.8	Unknown	Yes
	South England	Elia <i>et al.</i> ⁽¹⁰⁹⁾	1026	NA	E	NA	52.5	Unknown	No
	Isle of Ely	Forouhi <i>et al.</i> ⁽¹¹⁰⁾	524	40.8	Α	NA	60.2	Yes	Unknown
	Cambridge	Hegarty <i>et al.</i> ⁽¹¹¹⁾	96	49.0	E	Winter	23.1	Yes	Unknown
	Northern Ireland	Hill et al. ⁽¹¹²⁾	1015	49.8	С	Whole year	64.3	Yes	Yes
	England	Hirani & Primatesta ⁽¹¹³⁾	1297	40.3	E	Whole year	40·0† ; 37·4‡ 58·3†; 49·4‡	Unknown	Yes
	Great Britain	Hypponen & Power ⁽¹¹⁴⁾	7437	50.1	А	Summer; winter	60.3; 41.1	Yes	No
	Grampian	Macdonald et al. (115)	2905	0.0	А	Mixed	53.9	Yes	No
	Aberdeen	Mavroeidi et al.(116)	325	0.0	E	Mixed	53.3	No	No
	Isle of Ely	Wareham et al. ⁽¹¹⁷⁾	1057	43.3	NA	Whole year	54.4†; 46.2‡	Yes	No
North America Canada						,	., .		
	Quebec	Barake et al. ⁽¹¹⁸⁾	404	51·2	E	Mixed	74.0	Yes	No
	Nunavut	El Havek <i>et al.</i> ⁽¹¹⁹⁾	282	46.8	c	Mixed	48·3§	No	Yes
	Whole country	Langlois <i>et al.</i> ⁽¹²⁰⁾	5306	48.4	0	Whole year	67.7	Yes	Yes
	St Theresa Point, Garden Hill	Lebrun <i>et al.</i> ⁽¹²¹⁾	76	NA	1	Summer	26.2	Unknown	Unknown
	Toronto	Liu <i>et al.</i> ⁽¹²²⁾	155	49.7	E	Autumn	44.9	Unknown	Unknown
	Quebec	Mark <i>et al.</i> ⁽¹²³⁾	1753	50.3	С	Mixed	46.0	Yes	No
	Avalon Peninsula	Newhook et al. ⁽¹²⁴⁾	51	NA	I	Summer; winter	63.6; 48.6	Unknown	No
	Edmonton	Overton & Basu ⁽¹²⁵⁾	36	100.0	E	Summer	122.0	Unknown	No
	Calgary	Rucker et al.(126)	188	31.9	E	Winter	57.3	No	No
	Quebec	Sinotte et al. ⁽¹²⁷⁾	741	0.0	Ā	Winter	64.9	Yes	No
USA									
	NA	Alvarez et al.(128)	50	0.0	А	Mixed	55.7	Unknown	No
	New York	Arunabh <i>et al.</i> ⁽¹²⁹⁾	410	0.0	А	Whole year	54.2	Yes	No
	Connecticut	Averv et al. ⁽¹³⁰⁾	114	NA	E	NA	113⋅1; 81⋅8∥	Yes	No
	Honolulu	Chai <i>et al.</i> ⁽¹³¹⁾	182	0.0	А	NA	72.3	Unknown	Unknown
	Framingham	Cheng et al. ⁽¹³²⁾	3890	46.0	А	Whole year	92.9	No	No
	Boston	Dawson-Hughes et al.(133)	391	46.5	E	Whole year	82.41; 68.9	Yes	Unknown
	Oakland	Dror <i>et al.</i> ⁽¹³⁴⁾	199	NA	1	Mixed	43.7	Unknown	Unknown
	Whole country	Looker et al. ⁽¹³⁵⁾	18462	47.2	0	Summer, winter	77.3; 67.2	No	Yes
	Framingham	Hannan <i>et al.</i> ⁽¹³⁶⁾	341	NA	E	NA	71.9	Yes	No
	Boston, Houston, West Lafayette	Hill <i>et al.</i> ⁽¹³⁷⁾	735	30.5	С	NA	66-2	Unknown	Unknown
	Whole country	lannuzzi-Sucich <i>et al.</i> ⁽¹³⁸⁾	337	42.1	Е	NA	67·4†: 57·7‡	Yes	No
	Connecticut	llich <i>et al.</i> ⁽¹³⁹⁾	136	0.0	Ē	Whole year	52·8	Unknown	No
	Framingham	Jaques <i>et al.</i> ⁽¹⁴⁰⁾	759	38.2	Ē	NA	82.0†; 71.0‡	Yes	Unknown
	Northern Georgia	Johnson <i>et al.</i> ⁽¹⁴¹⁾	317	20.2	Ē	Whole year	66·7	Yes	Unknown
	Rochester	Khosla <i>et al.</i> ⁽¹⁴²⁾	138	0.0	Ā	NA	77.6	Unknown	Unknown
	Whole country	Kim <i>et al.</i> ⁽¹⁴³⁾	8351	0.0	0	NA	61.0	Unknown	No

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Table 1. Continued

Region and country	City/region within the country	Reference	n	Male (%)	Age group	Season	25(OH)D (nmol/l)	Reliability	Representativeness
	California	Kremer et al. ⁽¹⁴⁴⁾	90	0.0	А	Summer	75·1	Unknown	No
	Eastern Nebraska	Lappe <i>et al.</i> ⁽¹⁴⁵⁾	1179	0.0	E	Whole year	71.8	Yes	No
	Whole country	Mansbach <i>et al.</i> ⁽¹⁴⁶⁾	4558	49.6	Č	Whole year	68.0	Unknown	Yes
	Farmington	Mirza <i>et al.</i> ⁽¹⁴⁷⁾	40	0.0	А; Е	NA	74.9; 84.9	Yes	No
	Rancho Bernardo	Reis <i>et al.</i> ⁽¹⁴⁸⁾	654	36.4	E, E	NA	103.6	Yes	No
	Marion County	Rock et al. ⁽¹⁴⁹⁾	1042	39.4	0	Mixed	31.9†; 29.3‡	Yes	Yes
	Greenwich	Sabetta <i>et al.</i> ⁽¹⁵⁰⁾	198	42.9	0	Autumn	70.9	Unknown	Unknown
		Shea et al. ⁽¹⁵¹⁾	1381	42.9 48.4	A	NA	49·4	Unknown	No
	Framingham	Stein <i>et al.</i> ⁽¹⁵²⁾	168	40·4 0·0			93·8		
	Athens	Sullivan <i>et al.</i> ⁽¹⁵³⁾			С	Whole year		Yes	No
	Bangor	Sullivan <i>et al.</i> (154)	22	0.0	С	Summer	74.4	Yes	Unknown
A : (D :0	Philadelphia	Weng et al. ⁽¹⁵⁴⁾	382	47.6	С	Whole year	69·9§	Yes	Yes
Asia/Pacific									
Australia		(155)							
	Sydney	Bowyer et al. ⁽¹⁵⁵⁾	901	NA	I	Winter	60∙0§	Unknown	No
	Sydney	Brock et al. ⁽¹⁵⁶⁾	186	NA	E	NA	36.0; 33.0	Yes	No
	Dubbo	Center et al. ⁽¹⁵⁷⁾	437	100.0	E	NA	70.7	Yes	No
	Tasmania	Ding <i>et al.</i> ⁽¹⁵⁸⁾	1002	NA	Α	Mixed	52.8	Yes	Unknown
	North-Western Adelaide	Ngo <i>et al.</i> ⁽¹⁵⁹⁾	253	43.5	E	NA	72.2	Yes	No
	Barwon	Pasco <i>et al.</i> ⁽¹⁶⁰⁾	861	0.0	Α	Whole year	70.0	Yes	No
	Melbourne	Stein et al.(161)	99	26.3	E	Winter	26·0§	Yes	No
	Sydney	Zochling et al. (162)	584	21.2	E	Mixed	21.4†; 16.9‡	Unknown	No
China	, , , , , , , , , , , , , , , , , , ,	0					•/ •		
	Linxian	Abnet et al. ⁽¹⁶³⁾	720	42.2	А	Spring	33.1	Yes	Unknown
	Hong Kong	Chan <i>et al.</i> ⁽¹⁶⁴⁾	53	0.0	Е	NA	57.7	Unknown	No
	Linxian	Chen <i>et al.</i> ⁽¹⁶⁵⁾	2018	54.0	Ā	Spring	31.7	Unknown	Unknown
	Beijing	Du <i>et al.</i> ⁽¹⁶⁶⁾	649	0.0	C	Winter	33.5	Yes	Yes
	Shanxi	Strand et al. ⁽¹⁶⁷⁾	250	52.4	Č	Spring	42.3†; 25.5‡	Unknown	Unknown
	Taipei	Tsai <i>et al.</i> ⁽¹⁶⁸⁾	262	0.0	Ă	Mixed	76.6	Yes	No
Fiji Islands	Taper		202	0.0	7.	Mixed	10.0	105	
i iji lolando	Whole country	Heere et al. ⁽¹⁶⁹⁾	511	0.0	А	Winter	76.0	Unknown	Unknown
India	whole country	Tieere et al.	511	0.0	~	WIIIICH	70.0	Onknown	OTIKTOWT
mula	Agota	Goswami <i>et al.</i> ⁽¹⁷⁰⁾	57	56.1	А	Winter	36.4	Unknown	Unknown
	Tirupati	Harinarayan <i>et al.</i> ⁽¹⁷¹⁾	1146	21.2	A	NA	46·3†; 38·7‡	Unknown	No
	Lucknow	Sachan <i>et al.</i> ⁽¹⁷²⁾	1140	NA	Î	Mixed	21.0	Yes	No
Indonasia	LUCKHOW	Sachan et al.	117	INA	1	wixeu	21.0	Tes	NO
Indonesia	lakarta Dakasi	Rinaldi <i>et al.</i> ⁽¹⁷³⁾	<u></u>	0.0	E	C	<u> </u>		
	Jakarta, Bekasi		62	0.0		Summer	68·2	Unknown	Unknown
	Jakarta, Bekasi	Setiati et al.(174)	74	0.0	E	NA	38.7	No	Yes
Japan		(175)			_				
	NA	Kuwabra <i>et al.</i> ⁽¹⁷⁵⁾	50	30.0	E	NA	27.7§	Unknown	Unknown
	Tokyo	Kwon <i>et al.</i> ⁽¹⁷⁶⁾	1094	41.7	E	Winter	71.7†; 65.8‡	Unknown	No
	Toyosaka	Nakamura et al.(177)	160	0.0	E	Summer	78.3	Yes	No
	Toyosaka	Nakamura <i>et al.</i> ⁽¹⁷⁸⁾	117	0.0	E	Summer	59.1	Yes	Yes
	Tokyo	Suzuki <i>et al.</i> ⁽¹⁷⁹⁾	2957	32.1	E	Autumn	71.1†; 60.4‡	Unknown	No
Malaysia									
	Kuala Lumpur	Rahman <i>et al.</i> ⁽¹⁸⁰⁾	101	0.0	А	NA	44.4	Yes	No
Mongolia	-								
	Ulaanbaatar	Lander et al.(181)	98	72.4	С	Autumn	24.1	Yes	No

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Table 1. Continued

Region and country	City/region within the country	Reference	п	Male (%)	Age group	Season	25(OH)D (nmol/l)	Reliability	Representativeness
New Zealand	-								
How Zoalana	Auckland	Bolland et al. ⁽¹⁸²⁾	1984	19.1	A; E	NA	84.0†; 51.0‡	Yes	No
	Auckland	Bolland <i>et al.</i> ⁽¹⁸³⁾	116	0.0	A	NA	54·0	Unknown	Unknown
	Auckland	Bolland <i>et al.</i> ⁽¹⁸⁴⁾	100	50.0	A; E	NA	91·0†; 51·0‡	Yes	No
	Wellington; Christchurch	Camargo <i>et al.</i> ⁽¹⁸⁵⁾	922	50.7	л, с I	Whole year	44·0§	Yes	Unknown
	Auckland	Grant <i>et al.</i> (186)	353	47.6	1	Whole year	55·0	Yes	Unknown
	Dunedin	Houghton <i>et al.</i> ⁽¹⁸⁷⁾	193	47.0 57.5	C	Mixed	52·0	Yes	Unknown
	Auckland	Ley et al. ⁽¹⁸⁸⁾	39	0.0	E	Winter	26·1		
		Lucas et al. ⁽¹⁸⁹⁾						Unknown	No
	Auckland	Rockell <i>et al.</i> ⁽¹⁹⁰⁾	1606	0.0	E	Whole year	51.2	Unknown	No
	Whole country		1585	50.5	С	Mixed	50.0	Yes	No
	Dunedin; Invercargill	Rockell <i>et al.</i> ⁽¹⁹¹⁾	342	34.8	A	Summer	85.0	Unknown	Unknown
	Auckland	Scragg et al. ⁽¹⁹²⁾	295	100.0	A	Whole year	39.8	No	Yes
South Korea		(100)							
	Chungju	Kim <i>et al.</i> ⁽¹⁹³⁾	1330	38.0	E	Whole year	46.1	Unknown	No
	Seoul	Namgung et al. ⁽¹⁹⁴⁾	71	50.7	I	Summer; winter	74.9; 26.7	Yes	Unknown
Thailand									
	NA	Chailurkit <i>et al.</i> ⁽¹⁹⁵⁾	158	48.7	0	NA	168·2†; 105·8‡	Unknown	Unknown
	Khon Kaen	Chailurkit et al.(196)	251	50.2	0	NA	128.3†; 93.6‡	No	Yes
	Bangkok	Chailurkit <i>et al.</i> ⁽¹⁹⁷⁾	229	47.2	0	NA	135.0†; 72.6‡	No	Unknown
	Bangkok	Chailurkit <i>et al.</i> ⁽²⁶⁾	446	0.0	E	NA	67.6	Yes	Unknown
	Khon Kaen	Soontrapa <i>et al.</i> ⁽¹⁹⁸⁾	65	0.0	Е	Summer	83-2	No	Unknown
Vietnam									
	Ho Chi Minh (city)	Ho-Pham <i>et al.</i> ⁽¹⁹⁹⁾	637	32.2	А	Mixed	91.9†; 75.1‡	Yes	Yes
Middle East/				02 2			0.01,.0.14		
Africa									
Cameroon									
Carrieroon	Ntam	Niemini <i>et al.</i> ⁽²⁰⁰⁾	152	60.5	Е	NA	52.7	Unknown	No
Iran	Man	Njerinin et al.	102	00.0	-	14/4	0L I	Onknown	110
Iran	Tehran	Bassir <i>et al.</i> ⁽²⁰¹⁾	44	NA	1	Mixed	4.9	Unknown	Unknown
	Tehran	Dahifar <i>et al.</i> (202)	414	0.0	C	Mixed	74.9	Unknown	Unknown
	Tehran	Hashemipour <i>et al.</i> ⁽²⁰³⁾	1210	59·1	õ	NA	20·7§	Yes	No
		Hossein-Nezhad et al. ⁽²⁰⁴⁾				NA	31.3	Yes	Unknown
	Tehran		646	24.8	A				
	Tehran	Hosseinpanah <i>et al.</i> ⁽²⁰⁵⁾ Kazemi <i>et al.</i> ⁽²⁰⁶⁾	245	0.0	A	NA	73.0	Yes	Yes
	Zanjan		61	NA	1	Mixed	16.7	Unknown	Unknown
	Shiraz	Masoompour et al. ⁽²⁰⁷⁾	520	100.0	A	Winter	35.0	Yes	Yes
	Tehran	Mirsaeid Ghazi <i>et al.</i> ⁽²⁰⁸⁾	1171	41.8	0	Mixed	87.4†; 52.4‡	Yes	No
	Isfahan	Moussavi <i>et al.</i> ⁽²⁰⁹⁾	318	48.1	С	Winter	93·1†; 41·8‡	Yes	No
	Tabriz	Niafar <i>et al.</i> ⁽²¹⁰⁾	300	0.0	A	Mixed	35·4§	Yes	Unknown
	Tehran	Rabbani <i>et al.</i> ⁽²¹¹⁾	963	44.0	С	Winter	116·1†; 60·3‡	Yes	No
	Isfahan	Salek et al. ⁽²¹²⁾	88	NA	I	Summer	68.4	Yes	Unknown
Jordan									
	Northern Jordan	Gharaibeh & Stoecker ⁽²²⁾	186	27.4	A	Summer	25.6	Unknown	Unknown
Lebanon									
	NA	Arabi <i>et al.</i> ⁽²¹³⁾	443	64.6	E	Spring	28.5	Unknown	Unknown
	Beirut, Bekaa	Gannage-Yared et al. ⁽²¹⁴⁾	316	31.3	А	Winter	24.2	Yes	No

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Table 1. Continued

Region and country	City/region within the country	Reference	u	Male (%)	Male (%) Age group Season	Season	25(OH)D (nmol/l)	Reliability	Reliability Representativeness
Nigeria	sol	Pfitzner <i>et al.</i> ⁽²¹⁵⁾	218	45.0	v	Mixed	66.8	Unknown	Unknown
South Africa	Cape Town	Charlton <i>et al.</i> ⁽²¹⁶⁾	173	48.0	ш		36.9	Unknown	No
Gambia	Whole country	Asprav <i>et al.</i> ⁽²¹⁷⁾	113	0.0	0	AN	2.79	No	oZ
Latin America		-							
	Ushuaia	Oliveri <i>et al.</i> ⁽²¹⁸⁾	42	57.1	O	Winter	24.5	Unknown	No
Drazii	Sao Paulo Sao Paulo	Canto-Costa <i>et al.</i> ⁽²¹⁹⁾ Saraiva <i>et al.</i> ⁽²²⁰⁾	11 250	36.4 30.8	шш	NA Whole year	61 :2 52 :4	Yes No	No Yes

VA, not available; O, others; A, adults; E, elderly; C, children and adolescents; I, newborns/infants. Data from three studies not indicating geographical region have been excluded^(221–223), data from a single study⁽⁴⁰⁾ providing country-specific data on four nations in Europe are represented separately. In some cases, 25(OH)D mean values were available by age, sex or region only. For some studies, multiple reports have been published, which are not listed in this table^(23,27,30,224–237).

r 25(OH)D mean values for men. t 25(OH)D mean values for women. § 25(OH)D median values. [25(OH)D mean values for institutionalised elderly.

Statistical analyses

Descriptive statistics were calculated for baseline characteristics of all the included studies. If mean 25(OH)D values were not reported in an article, we used median values (9.2% of the studies) in our descriptive analyses.

Meta-analyses were performed for subgroups stratified by age, sex and geographical region using random-effects models. Studies reporting median 25(OH)D values (n 15) or mean values without a corresponding standard deviation (n 30) were not included in this phase of the analyses (Fig. 1). In addition, our focus in the meta-analyses was limited to studies/subgroups with sample sizes greater than 30, given concerns about the precision of estimates. Studies on newborns $(n \ 10)$ and institutionalised elderly $(n \ 9)$ were also not included in the meta-analyses. For analyses stratified by sex, we also excluded studies that did not report separate 25(OH)D values for males and females (n 30).

Heterogeneity between the studies was assessed by visual inspection of forest plots and calculation of I^2 statistics. Because we found substantial heterogeneity across the studies, we decided to further explore potential explanatory factors. Therefore, we conducted heterogeneity analyses within each subgroup by accounting for a range of characteristics other than age and sex, which included season, assay type, distance from the equator⁽⁵⁾ and components of study quality. Studies were grouped by study characteristics (e.g. season and assay type) to assess whether heterogeneity was reduced as indicated by the I^2 statistics and the inspection of forest plots.

Supplementary analyses explored patterns of vitamin D status within specific subgroups (e.g. institutionalised elderly) and for selected associations reported in previous work. The purpose of these exploratory analyses was to support further research in this area by generating hypotheses that might be tested more thoroughly in future studies. All statistical analyses were conducted using STATA version 12.1 (StataCorp).

Results

Description of studies

Studies included in the present review (Table 1) contained data on a total of 168 389 participants from forty-four countries. The sample size of individual studies ranged from 11 to 18462 participants with a median of 316 (interquartile range 117-861). While the majority of studies contained data on males and females, nine studies (47%) restricted their focus to males, while fifty-four studies (28.0%) contained data on only females. The overall proportions of males and females were 33.3 and 66.7%, respectively, and the mean age of the participants was 51.7 (sp 24.3) years. Most studies were conducted in Europe (45.1%), followed by the Asia/Pacific region (23.8%) and North America (19.7%). In terms of the country in which studies were conducted, most were carried out in the USA $(n \ 28)$, followed by Iran $(n \ 12)$, New Zealand $(n \ 11)$ and Canada (n 10).

The assays reported to measure 25(OH)D values included RIA (55.9%), competitive protein-binding assays (14.0%) and other methods such as chemiluminescence immunoassay and HPLC.

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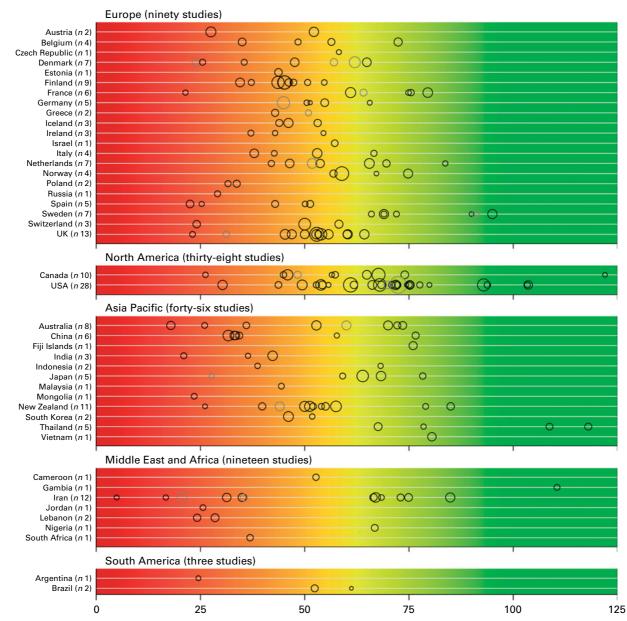


Fig. 2. Mean/median 25-hydroxyvitamin D (25(OH)D) values, by geographical region and country. Note: medians ($_{\bigcirc}$) are shown where mean values ($_{\bigcirc}$) are not reported; Study size is indicated by circle size. The background colour scheme is intended to reflect the current uncertainty around the definition of thresholds for deficient, insufficient and adequate 25(OH)D levels. Mean/median values falling within the intensely red zone are most consistent with severe vitamin D deficiency; those in the green zone reflect adequate vitamin D levels. Values within the yellow zone are those thought to be indicative of insufficiency. Data from three studies not indicating geographical region have been excluded⁽²²¹⁻²²³⁾; data from a single study⁽⁴⁰⁾ providing country-specific data on four nations in Europe are represented separately. One study⁽¹⁹⁵⁾ reported a mean 25(OH)D value of 136-2 nmol/l and therefore is not presented in the figure due to graphical reasons.

In terms of study quality, more than half of the studies (50·2%) were classified as non-representative of the target population and 14·9% qualified as representative according to the criteria defined previously. Evidence of representativeness could not be established in $34\cdot9\%$ of the studies due to missing information. Information on assay reliability was provided in $61\cdot0\%$ of the studies with $52\cdot8\%$ classified as providing reliable 25(OH)D measurements. Assay validity was reported in a minority of studies (9.7%).

Global vitamin D status

There was a significant variability in the estimates of 25(OH)D values across the studies with mean and median values ranging from 4.9 to $136\cdot2\,nmol/1$ and $20\cdot7$ to $91\cdot0\,nmol/1$, respectively. We found that $88\cdot1\%$ of the samples presented in the present review had mean 25(OH)D values below 75 nmol/1, $37\cdot3\%$ had mean values below 50 nmol/1 and $6\cdot7\%$ had mean values below 25 nmol/1. Fig. 2 provides an overview

Systematic review of vitamin D status

References	Country the	stance from e equator (°)	Season	Age group	Number of participants			ES (95 % CI)	Weig (%)
	-								
^s emale Brustad <i>et al.</i> (2004) ⁽⁸⁷⁾	Norway	68	Mixed	Adults	300			56-90 (54-77, 59-03)	1.91
Kauppi <i>et al.</i> (2009) ⁽⁴⁸⁾	Finland	65	wixeu	Adults	3299			45.20 (44.30, 46.10)	1.91
Sigurdsson et al. (2009)		64	Missai			그는 것을 수 있는 것이 없다.			
ristinsson <i>et al.</i> (1998) ⁽⁶⁹⁾	Iceland		Mixed	Elderly	308			53.10 (50.87, 55.33)	1.91
ristinsson <i>et al.</i> (1998)	lceland Finland	64	Winter Mixed	Children/adolescents	118			45.80 (42.14, 49.46)	1.88
arviainen <i>et al.</i> (1992) ⁽⁵²⁾		63		Adults	358			35.00 (33.24, 36.76)	1.91
iljakainen <i>et al.</i> (2006) ⁽⁵⁴⁾	Finland	60 60	Winter	Children/adolescents	35			41.90 (36.47, 477.33)	1.84
ull et al. (2009) ⁽⁴⁷⁾	Estonia Finland	60	Winter	Adults	200	and the second		44.60 (42.41, 46.79)	1.91
amberg-Allardt <i>et al.</i> (2001) ⁽⁴⁹⁾			Mixed	Adults	202 100			47.00 (42.31, 51.69)	1.86
urgaz et al. (2009) ⁽⁹⁸⁾	Sweden	60	Winter	Elderly				72.00 (67.49, 76.51)	1.86
urgaz et al. (2007) ⁽⁹⁷⁾	Sweden	60	Winter	Elderly	116			69·00 (64·81, 73·19)	1.87
lelin et al. (1999) ⁽¹⁰¹⁾	Sweden	59	Spring	Elderly	81			64.90 (58.37, 71.42)	1.80
lavroeidi et al. (2010) ⁽¹¹⁶⁾	UK	57	Mixed	Elderly	325			53.30 (51.20, 55.40)	1.91
acdonald et al. (2006) ⁽¹¹⁵⁾	Scotland	57		Adults	2905			53·91 (53·12, 54·70)	1.92
erdhem <i>et al.</i> (2005) ⁽²⁸⁾	Sweden	56	Whole year	Elderly	986			95.00 (93.13, 96.87)	1.91
ill et al. (2008) ⁽¹¹²⁾	Ireland	54.5	Whole year	Children/adolescents	510			62.80 (60.46, 65.14)	1.90
irani & Primatesta (2005) ⁽¹¹³⁾	England	54	Whole year	Elderly	320			48.40 (45.85, 50.95)	1.90
prouhi <i>et al.</i> (2008) ⁽¹¹⁰⁾	England	52		Adults	310			57.10 (54.50, 59.70)	1.90
I-Delaimy et al. (2006) ⁽⁷⁹⁾	Netherlands	52		Adults	35			77.20 (75.25, 79.15)	1.91
uchuk et al. (2009) ⁽⁸²⁾	Netherlands	52	Whole year	Elderly	676			48.80 (47.08, 50.52)	1.91
öwik <i>et al.</i> (1990) ⁽⁸³⁾	Netherlands	52		Elderly	261			38.00 (36.06, 39.94)	1.91
ill et al. (2005) ⁽⁷²⁾	Ireland	51	Winter	Adults	44			54·50 (46·29, 62·71)	1.74
lacfarlane <i>et al.</i> (2004) ⁽³⁶⁾	Belgium	51	Winter	Adults	87			60·40 (56·63, 64·18)	1.88
ttermann <i>et al.</i> (1998) ⁽⁶⁶⁾	Germany	51	Winter	Adults	38			30.30 (24.23, 36.37)	1.82
oonen <i>et al.</i> (1996a) ⁽³⁰⁾	Belgium	51		Elderly	245			56·40 (52·57, 60·23)	1.88
ofkova & Hill (2008) ⁽³⁹⁾	Czech Republic			Adults	47		_	58·23 (32·93, 83·54)	0.98
neiler <i>et al.</i> (1999a) ⁽²⁹⁾	Switzerland	47	Summer	Elderly	109			67·39 (59·66, 75·12)	1.76
hapuy <i>et al.</i> (1997) ⁽⁵⁸⁾	France	47	Winter	Adults	804	· · · · · · · · · · · · · · · · · · ·		60·00 (57·93, 62·07)	1.91
e Carvalho <i>et al.</i> (1996) ⁽⁵⁹⁾	France	47	Whole year	Adults	39			81·10 (67·00, 98·20)	1.34
dami <i>et al.</i> (2008) ⁽⁷⁵⁾	Italy	46	Winter	Elderly	697			37.90 (35.32, 40.48)	1.90
ezzoli et al. (2005) ⁽⁷⁸⁾	Italy	43		Elderly	293			48.20 (44.46, 51.94)	1.88
iomez <i>et al.</i> (2004) ⁽⁹³⁾	Spain	41	Whole year	Adults	127			49.90 (46.16, 53.64)	1.88
arnevale <i>et al.</i> (2001) ⁽⁷⁶⁾	Italy	40	Winter	Adults	58			38.00 (34.35, 41.65)	1.88
apapetrou <i>et al.</i> (2007) ⁽⁶⁸⁾	Greece	38	Winter	Elderly	231			41.60 (39.09, 44.11)	1.90
apir-Koren <i>et al.</i> (2003) ⁽⁹¹⁾	Russia			Elderly	122			29·13 (26·09, 32·17)	1.89
ubtotal ($I^2 = 99.3$ %, $P = 0.000$)						$\neg \diamond$		53.30 (48.66, 57.94)	62-4
ale						1			
auppi <i>et al.</i> (2009) ⁽⁴⁸⁾	Finland	65		Adults	2736			45·10 (44·06, 46·14)	1.92
arviainen <i>et al.</i> (1992) ⁽⁵²⁾	Finland	63	Mixed	Adults	418			34.00 (32.56, 35.44)	1.91
amberg-Allardt et al. (2001) ⁽⁴⁹⁾	Finland	60	Mixed	Adults	126			45·00 (38·89, 51·11)	1.82
ull et al. (2009) ⁽⁴⁷⁾	Estonia	60	Winter	Adults	167			42.70 (40.58, 44.82)	1.91
nd <i>et al.</i> (1995) ⁽¹⁰⁰⁾	Sweden	59.8		Adults	34	— 1	_	90.00 (83.61, 96.39)	1.81
agstrom et al. (2009) ⁽⁹⁹⁾	Sweden	59		Elderly	958	I		69.00 (67.80, 70.20)	1.92
ost et al. (2010) ⁽⁴³⁾	Denmark	55	Whole year	Adults	700			64-90 (62-85, 66-95)	1.91
ill et al. (2008) ⁽⁷²⁾	Ireland	54.5	Whole year	Children/adolescents	505			65·80 (63·40, 68·20)	1.90
rani & Primatesta (2005) ⁽¹¹³⁾	England	54	Whole year	Elderly	322			56.20 (53.26, 59.14)	1.89
avnes <i>et al.</i> (1997) ⁽⁸⁰⁾	Netherlands	53	Spring	Elderly	142	and the second sec		42.00 (37.21, 46.79)	1.86
owik <i>et al.</i> (1990) ⁽⁸³⁾	Netherlands	52		Elderly	268			40.00 (37.73, 42.27)	1.90
prouhi et al. (2008) ⁽¹¹⁰⁾	England	52		Adults	214	二 二 一 一 一 一 一 一 一 一 一 一 一 一 一 一 一 一 一 一		64.70 (61.04, 68.36)	1.88
uchuk et al. (2009) ⁽⁸²⁾	Netherlands	52	Whole year	Elderly	643			57.90 (56.01, 59.79)	1.91
acFarlane et al. (2004) ⁽³⁶⁾	Belgium	51	Winter	Adults	39			34.44 (32.02, 36.87)	1.90
neiler et al. (1999a) ⁽²⁹⁾	Switzerland	47	Summer	Elderly	203		_	91.60 (83.67, 99.53)	1.75
apuy et al. (1997) ⁽⁵⁸⁾	France	47	Winter	Adults	765			62.00 (59.87, 64.13)	1.9
zzoli et al. (2005) ⁽⁷⁸⁾	Italy	47		Elderly	302			61.20 (57.61, 64.79)	1.8
omez et al. (2004) ⁽⁹³⁾	Spain	43	Whole year	Adults	126			52·70 (49·05, 56·35)	1.8
arnevale <i>et al.</i> (2004)	Italy	40	Winter	Adults	32			51·20 (46·52, 55·88)	1.86
apapetrou <i>et al.</i> (2007) ⁽⁶⁸⁾	Greece	38	Winter	Elderly	48			51-20 (46-52, 55-88) 49-20 (42-82, 55-58)	1.8
ibtotal ($I^2 = 99.3 \%$, $P = 0.000$)	Greece	30	winter	Elderly	40	\Leftrightarrow		49·20 (42·82, 55·58) 55·82 (49·75, 61·89)	37-5
verall (I ² = 99·3 %, P = 0·000)								54-24 (50-65, 57-82)	100
ote: weights are from random	effects analysis				1		1		

Fig. 3. Forest plot for Europe stratified by sex. ES, effect estimator.

of the distribution of country- and study-specific mean 25(OH)D values, stratified by region. In addition, a visualisation of the available data on a global map can be found elsewhere⁽²¹⁾.

Vitamin D status by age, sex and region

Due to a limited number of studies being identified from Latin America, it was not possible to perform meta-analyses for this region. Depending on the stratifying variable, I^2 values ranged from 84.5 to 99.7%, indicating substantial heterogeneity between the studies.

No significant age- or sex-related differences in 25(OH)D values were observed in the sample of eligible studies worldwide (data not shown). However, we observed differences by region with values being significantly higher in North America than in Europe or the Middle East/Africa region (Figs. 3–6). In an analysis stratified by age and region, we did not find age-related differences for Europe and North America (Table 2). However, in the Asia/Pacific region, children/adolescents were found to have significantly lower 25(OH)D values than adults and elderly. In contrast, children/ adolescents from the Middle East/Africa region had significantly higher values than the other two age groups. No significant sex-related differences were observed in any of the regions (Figs. 3–6). However, reports of 25(OH)D values in women tended to be lower, especially in the Asia/Pacific and Middle East/Africa regions.

Heterogeneity analyses

The substantial heterogeneity that we observed within the different geographical regions could not be explained by the characteristics of the study population or features of study quality. Grouping studies by age category and sex, assay type,

References	Country	Distance from the equator (°)	Season	Age group	Number of participants		ES (95 % CI)	Weight (%)
Female						1		
Sinotte et al. 2009 ⁽¹²⁷⁾	Canada	54	Winter	Adults	741		64.90 (63.49, 66.31)	4.76
Khosla <i>et al.</i> 1997 ⁽¹⁴²⁾	USA	43		Adults	138	! - ⊫−	77.60 (71.74, 83.46)	4.48
Dawson-Hughes <i>et al.</i> 1997 ⁽¹³³⁾	USA	42	Whole year	Elderly	209		68.90 (64.55, 73.25)	4.61
Shea <i>et al.</i> 2009 ⁽²⁹⁰⁾	USA	42		Elderly	919	i i	49.20 (47.95, 50.45)	4.76
Jaques <i>et al.</i> 1997 ⁽¹⁴⁰⁾	USA	42		Elderly	469	-	71.00 (68.38, 73.62)	4.71
llich <i>et al.</i> 2003 ⁽¹³⁹⁾	USA	41	Whole year	Adults	136		52.80 (50.65, 54.95)	4.73
Lappe <i>et al.</i> 2006 ⁽¹⁴⁵⁾	USA	41	Whole year	Elderly	1179	i i	71.80 (70.64, 72.96)	4.76
lannuzzi-Sucich et al. 2002 ⁽¹³⁸⁾	USA	40		Elderly	195	e i	57.66 (54.82, 60.50)	4.70
Arunabh <i>et al.</i> 2003 ⁽¹²⁹⁾	USA	40	Whole year	Adults	410		54.20 (50.84, 57.56)	4.67
Kremer <i>et al.</i> 2009 ⁽¹⁴⁴⁾	USA	37	Summer	Children/adolescents	90		75.13 (68.43, 81.83)	4.40
Hill et al. (2010) ⁽¹³⁷⁾	USA	36		Children/adolescents	511		66.20 (63.85, 68.55)	4.72
Stein et al. (2006) ⁽¹⁵²⁾	USA	34	Whole year	Children/adolescents	168	1	- 93.80 (89.55, 98.05)	4.62
Johnson <i>et al.</i> (2008) ⁽¹⁴¹⁾	USA	32.5	Whole year	Elderly	200		67.90 (63.04, 72.76)	4.57
Chai <i>et al.</i> . (2010) ⁽¹³¹⁾	Hawaii	21		Adults	182	i i i i i i i i i i i i i i i i i i i	72.30 (68.45, 76.15)) 4.64
Alvarez et al. (2010) ⁽¹²⁸⁾	USA		Mixed	Adults	50	i	55.66 (46.18, 65.14)) 4.08
Subtotal ($I^2 = 98.8 \%$, $P = 0.000$)						\diamond	66.57 (60.94, 72.20)	69.23
Male						I I		
Overton & Basu (1999) ⁽¹²⁵⁾	Canada	53	Summer	Elderly	36	I	122.00 (106.32, 137	·683·26
Jaques <i>et al.</i> (1997) ⁽¹⁴⁰⁾	USA	42		Elderly	290		82.00 (78.66, 85.34)	4.68
Shea <i>et al.</i> (2009) ⁽²⁹⁰⁾	USA	42		Elderly	843		49.00 (47.81, 50.19)) 4.78
Dawson-Hughes <i>et al.</i> (1997) ⁽¹³³⁾	USA	42	Whole year	Elderly	182	i -	82.40 (77.20, 87.60)) 4.54
lannuzzi-Sucich <i>et al.</i> (2002) ⁽¹³⁸⁾	USA	40		Elderly	142		67.39 (64.03, 70.76)	4.67
Hill et al. (2010) ⁽¹³⁷⁾	USA	36		Children/adolescents	224		65.70 (62.83, 68.57)) 4.70
Johnson <i>et al.</i> (2008) ⁽¹⁴¹⁾	USA	32.5	Whole year	Elderly	37		60.50 (51.70, 69.30)) 4.16
Subtotal ($I^2 = 99.0 \%$, $P = 0.000$)						$\langle \rangle$	74.44 (61.65, 87.24)) 30.77
Overall ($I^2 = 98.9$ %, $P = 0.000$)						\diamond	68.73 (63.71, 73.75)) 100.00
Note: weights are from random-e	ffects analy	sis		1	L		1	
				0	25	50 75	100	

Fig. 4. Forest plot for North America stratified by sex. ES, effect estimator.

season, distance from the equator or representativeness, for example, did not significantly reduce heterogeneity across the studies in our sample, as measured by the I^2 statistics.

Exploratory analyses

We found that mean 25(OH)D values for institutionalised elderly were lower than those for non-institutionalised elderly, especially in Europe and the Asia/Pacific region. Moreover, in specific subgroups in single countries within Europe, we observed differences, with Swedish elderly having higher 25(OH)D mean values than the elderly in other European countries. In addition, we found that newborns had lower 25(OH)D values than the other three age groups in several countries worldwide.

Discussion

Summary of the main findings

The published evidence on vitamin D status at the population level, as assessed by mean or median 25(OH)D values, is characterised by a high degree of variability across studies, countries and regions. Although no age- or sex-related significant differences in 25(OH)D values were observed across the sample of studies that we reviewed, we did observe differences by region with values being significantly higher in North America than in Europe or the Middle East/Africa region. In stratified analyses, significant age-related differences were observed in the Asia/Pacific and Middle East/ Africa regions, but not elsewhere. However, exploratory analyses suggested that newborns and institutionalised elderly were more likely to have lower reported 25(OH)D values in several regions worldwide. We found substantial heterogeneity between the studies in our sample from each geographical region that could not be explained in a detailed analysis.

Interpretation and comparison with previous studies

In contrast to previous reviews^(5,13,14), we could not find differences in 25(OH)D values for children/adolescents, adults and elderly. However, in analyses stratified by geographical region, significant age-related differences could be observed for the Asia/Pacific region, with children/adolescents having lower 25(OH)D values than older groups. This might be primarily due to the low 25(OH)D values found for Chinese children/ adolescents as reported in previous work⁽¹³⁾, who were observed to have low dietary Ca intake and limited sunlight exposure as possible reasons. In contrast, in the Middle East/

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References	Country	Distance from the equator (°)	Season	Age group	Number of participants		ES (95 % CI)	Weigh (%)
Female						1		
Bolland <i>et al.</i> (2006b) ⁽¹⁸³⁾	New Zealand	40		Adults	116		54.00 (50.00, 58.00)	4·21
Du et al. (2001) ⁽¹⁶⁶⁾	China	40	Winter	Children/adolescents	649	i	33-45 (32-01, 34-89)	4.31
Nakamuta <i>et al.</i> (2001) ⁽¹⁷⁸⁾	Japan	38	Winter	Elderly	117		59.10 (56.18, 65.02)	4.26
Nakamuta <i>et al.</i> (1999) ⁽¹⁷⁷⁾	Japan	38	Summer	Adults	160	1 1	78.30 (75.54, 81.06)	4.27
Lucas <i>et al.</i> (2005) ⁽¹⁸⁹⁾	New Zealand	37	Whole year	Adults	1606		51.20 (50.25, 52.15)	4.32
Bolland <i>et al.</i> (2007a) ⁽¹⁸⁴⁾	New Zealand	37		Adults	50		67.00 (60.62, 73.38)	4.04
Bolland et al. (2006a) ⁽¹⁸²⁾	New Zealand	37		Adults	1606		51.00 (50.07, 51.93)	4.32
Strand et al. (2009) ⁽¹⁶⁷⁾	China	37	Spring	Children/adolescents	119	1	25.48 (19.69, 31.27)	4.09
Suzuki <i>et al.</i> (2008) ⁽¹⁷⁹⁾	Japan	36	Autumn	Elderly	2007		60.40 (59.87, 60.94)	4.32
Kwon <i>et al.</i> (2007) ⁽¹⁷⁶⁾	Japan	35	Winter	Elderly	638		65.80 (64.83, 66.77)	4.32
Tsai <i>et al.</i> (1997) ⁽¹⁶⁸⁾	China	25	Mixed	Adults	262		76-63 (74-15, 79-11)	4·28
Soontrapa et al. (2005) ⁽²⁹¹⁾	Thailand	16	Summer	Elderly	48	1.1.1	80.10 (75.44, 84.79)	4·17
Chailurkit et al. (2011) ⁽²⁶⁾	Thailand	13		Elderly	446	; = ; =	67.60 (66.14, 69.06)	4.31
Harinarayan <i>et al.</i> (2007) ⁽¹⁷¹⁾	India	13			807		38.69 (37.22, 40.15)	4.31
Ho-Pham <i>et al.</i> (2011) ⁽¹⁹⁹⁾	Vietnam	11	Mixed	Adults	432		75·13 (73·74, 76·52)	4.31
Rahman <i>et al.</i> (2004) ⁽¹⁸⁰⁾	Malaysia	3		Adults	101		44-40 (42-33, 46-47)	4·29
Subtotal ($I^2 = 99 \%$, $P = 0.000$)						\sim	58.03 (52.27, 63.79)	68·10
Male					_			
Strand et al. (2009) ⁽¹⁶⁷⁾	China	37	Spring	Children/adolescents	131		42.33 (27.59. 57.07)	3.14
Bolland <i>et al.</i> (2006a) ⁽¹⁸²⁾	New Zealand	37		Adults	378		84.00 (80.87, 87.13)	4.25
Bolland <i>et al.</i> (2007a) ⁽¹⁸⁴⁾	New Zealand	37		Adults	50		91.00 (80.19, 101.81)) 3.59
Suzuki <i>et al.</i> (2008) ⁽¹⁷⁹⁾	Japan	36	Autumn	Elderly	950	1 E E	71.14 (70.34, 71.93)	4.32
Kwon <i>et al.</i> (2007) ⁽¹⁷⁶⁾	Japan	35	Winter	Elderly	456	- i -	71.70 (70.49, 72.91)	4.31
Goswami <i>et al.</i> (2008) ⁽¹⁷⁰⁾	India	29	Winter	Adults	32	÷ 1	44-20 (35-75, 52-65)	3.85
Harinarayan <i>et al.</i> (2007) ⁽¹⁷¹⁾	India	13			134		46.28 (42.35, 50.21)	4·21
Ho-Pham <i>et al.</i> (2011) ⁽¹⁹⁹⁾	Vietnam	11	Mixed	Adults	205	\diamond	91.85 (88.37, 95.34)	4.23
Subtotal ($I^2 = 98.6$ %, $P = 0.000$))						60.00 (62.43, 75.57)	31.90
Overall (I ² = 99.6 %, P = 0.000)						\diamond	61·39 (56·40, 66·37)	100.00
Note: weights are from randor	m-effects analys	sis			I			

Fig. 5. Forest plot for the Asia/Pacific region stratified by sex. ES, effect estimator.

Africa region, children/adolescents were found to have significantly higher 25(OH)D values than adults and elderly, a finding consistent with at least one previous study⁽⁸⁾. One potential explanation for this pattern in the Middle East/Africa region could be that children/adolescents from this region generally spend more time outdoors compared with the other age groups (e.g. indoor working by the adult population)⁽²²⁾. However, others have also found age-related differences in other regions^(5,13,14), which could not be confirmed in the present meta-analyses. A reduction in differences and thus greater similarities across age groups might be attributable to lifestyle changes over the course of time in which younger individuals from industrialised countries spend more time indoors watching television, using computers and playing video games compared with older adults⁽²³⁾.

In contrast to previous reviews, we were also unable to find significant sex-related differences^(8,13,16). On examining our data by region, however, we observed that females tended to have lower 25(OH)D values, especially in the Middle East/Africa and Asia/Pacific regions. Some have suggested that this finding may be related to cultural factors such as differences in clothing styles that may impede vitamin D conversion in the skin⁽²⁴⁾.

The highest mean 25(OH)D values were generally observed in North America, a finding that might be explained by the routine fortification of several foods (e.g. milk, juice and cereals) in the USA⁽²⁵⁾. The absence of significant differences between studies conducted in North America and those carried out in the Asia/Pacific region, however, may have been influenced by relatively high values found in Thailand, a country located near the equator with significant year-round sunlight exposure and higher daytime temperatures, resulting in the use of lighter-weight clothes, which afford less UV protection⁽²⁶⁾. Studies conducted in Japan and other Asian countries may have further contributed to somewhat higher regional values, resulting from diets rich in vitamin D foods such as oily fish⁽²⁷⁾.

Previous reviews^(5,8,15) have reported an apparent north– south gradient for 25(OH)D in Europe, with Scandinavian countries showing generally higher values than the Southern European countries. This finding is thought to result, in part, from population-based differences in skin pigmentation, diets rich in oily fish, the common use of cod-liver oil and a higher degree of vitamin D supplementation in Scandinavian countries^(14,15). Although we did not find such a gradient in the present review, we observed generally higher 25(OH)D

References	Country	Distance from the equator (°)	Season	Age group	Number o participan			ES (95% CI)	Weight (%)
Female							1		
Rabbani <i>et al.</i> (2009) ⁽²¹¹⁾	Iran	36	Winter	Children/adolescents	539		-88-	60.34 (56.45, 64.23)	6.67
Hossein-Nezhad et al. (2009) ⁽²⁰⁴⁾	Iran	36		Adults	486			30.92 (29.31, 32.53)	6.75
Hosseinpanah et al. (2008) ⁽²⁰⁵⁾	Iran	35		Adults	245			73.00 (65.20, 80.80)	6.39
Charlton et al. (1996) ⁽²¹⁶⁾	South Afri	ica 34	Winter	Elderly	90	-	1	37.69 (35.06, 40.32)	6.72
Gannage-Yared et al. (2000) ⁽²¹⁴⁾	Lebanon	34	Winter	Adults	217		1	18.62 (16.70, 20.54)	6.74
Moussavi et al. (2005) ⁽²⁰⁹⁾	Iran	32	Winter	Children/adolescents	165	-	1	41.83 (38.65, 45.02)	6.70
Gharaibeh & Stoecker (2009) ⁽²²⁾	Jordan	31	Summer	Adults	93		1	25.60 (23.65, 27.55)	6.74
Dahifar et al. (2007) ⁽²⁰²⁾	Iran	30.5	Other	Children/adolescents	414			74.88 (71.08, 78.68)	6.67
Omrani <i>et al.</i> (2006) ⁽²⁸⁵⁾	Iran	29	Winter	Adults	676		1	28.90 (27.17, 30.63)	6.75
Subtotal ($I^2 = 990.3 \%$, $P = 0.000$)						\sim	- A	43-24 (33-80, 52-67)	60.13
							1		
Male							1		
Rabbani <i>et al.</i> (2009) ⁽²¹¹⁾	Iran	36	Winter	Children/adolescents	424		1	> 116.14 (111.00, 121.28)	6.60
Hossein-Nezhad et al. (2009) ⁽²⁰⁴⁾	Iran	36		Adults	160	-		32.57 (29.21, 35.93)	6.69
Gannage-Yared et al. (2000) ⁽²¹⁴⁾	Lebanon	34	Winter	Adults	96	-		35.74 (32.01, 39.48)	6.68
Charlton et al. (1996) ⁽²¹⁶⁾	South Afri	ica 34	Winter	Elderly	83	-		36.19 (33.67, 38.72)	6.72
Moussavi <i>et al.</i> (2005) ⁽²⁰⁹⁾	Iran	32	Winter	Children/adolescents	153		1	→ 93·08 (85·66, 100·50)	6.43
Masoompour <i>et al.</i> (2008) ⁽²⁰⁷⁾	Iran	29	Winter	Adults	520		1	35.00 (33.54, 36.46)	6.75
Subtotal ($I^2 = 99.6$ %, $P = 0.000$)						<		57.91 (39.19, 76.63)	39.87
Overall (I ² = 99·4 %, P = 0·000)						<	5	49.05 (40.61, 57.48)	100.00
							1		
Note: weights are from random-e	ffects analys	sis					i – –	I	

Fig. 6. Forest plot for the Middle East/Africa region stratified by sex. ES, effect estimator.

values in Swedish elderly than in those from other European countries. Some have suggested that this finding can be explained by the routine fortification of oil and low-fat milk products with vitamin D in Sweden⁽²⁸⁾.

In accordance with other reviews^(5,8,15), our exploratory analyses also suggested that institutionalised elderly in Europe and the Asia/Pacific region had lower mean 25(OH)D values than the elderly living in the community. It is possible that such a finding may result from less time spent outdoors due to poorer

health status⁽²⁹⁾, although similar findings in other groups of institutionalised individuals could be expected elsewhere. Further investigations of the patterns of vitamin D deficiency and insufficiency are needed in this vulnerable subgroup. Another interesting finding from our exploratory analyses was that newborns/infants were reported to have lower 25(OH)D values than the members of other age groups in several countries worldwide. Because newborn vitamin D status is mainly determined by maternal vitamin D status⁽³⁰⁾, this finding may be

Table 2. Effect estimators (ES) from the meta-analyses stratified by age and region* (ES and 95% confidence intervals)

Regions	l² (%)	n (studies)	n (participants)	ES	95 % CI
Europe					
Children/adolescents (>1-17 years)	99.5	6	1816	50.56	34.35, 66.77
Adults (>17-65 years)	99.4	35	28844	52.98	45.01, 56.58
Elderly (>65 years)	99.4	30	10894	51.74	45.81, 57.66
North America					
Children/adolescents (>1-17 years)	98.5	3	993	78.35	59.44, 97.25
Adults (>17-65 years)	99.7	8	6201	71.83	57.71, 86.00
Elderly (>65 years)	99.3	15	5307	71.70	64·84, 78·57
Asia/Pacific					
Children/adolescents (>1-17 years)	85.4	3	899	31.89†	24.94, 38.84
Adults (>17-65 years)	99.5	13	3709	67.99	59.73, 76.25
Elderly (>65 years)	98.8	9	4965	66.16	62.16, 70.22
Middle East/Africa					
Children/adolescents (>1-17 years)	99.2	6	1913	75.41†	56.43, 94.38
Adults (>17-65 years)	98.5	6	2079	34.66	29.32, 40.01
Elderly (>65 years)	99-2	4	874	38.20	29.15, 47.25

* Meta-analyses were not conducted for studies carried out in Latin America due to the limited number of eligible studies.

† Values were significantly different from those of the other age groups.

explained by generally inadequate vitamin D levels in pregnant women as suggested in previous work⁽³¹⁾. Future research in these groups is needed to confirm these findings and test interventions aimed at interrupting this putative mechanism.

Strengths and limitations

To our knowledge, the present systematic review, conducted in accordance with the PRISMA statement⁽¹⁸⁾, is among the first to focus on patterns of vitamin D status worldwide and in key population subgroups. We purposefully sought to identify studies with randomly selected samples from the general population to reduce sources of bias, which may otherwise obscure the public health importance of vitamin D status across the world. Use of continuous 25(OH)D values in our analyses is another important strength of the present study, given the inconsistent application of thresholds to indicate 25(OH)D deficiency, insufficiency and adequacy. A systematic search strategy based on two of the largest biomedical literature databases also reduced the probability of missing relevant articles. Besides the detailed data on 25(OH)D values among important subgroups by age, sex and region, the present review adds to the current understanding of vitamin D status in both developed and developing countries worldwide. We used the randomeffects model to account for the substantial heterogeneity that we observed across the studies. Between-study heterogeneity is common in systematic reviews, especially in observational epidemiology where unobserved characteristics at both the study and individual levels affect the outcomes of interest. The random-effects model adjusts for this heterogeneity by incorporating a between-study component of variance in the weights used for calculating the summary estimate⁽³²⁾.

It is important to consider the findings of the present review in the context of several potential limitations. First, we cannot fully exclude publication bias as studies reporting vitamin D deficiency might have been more likely to be published than those reporting mean or median levels within the normal range. Second, language bias may have affected the results, as we limited the present review to articles written in English. This may have accounted, for example, for the relative under-representation of studies conducted in Latin America in our sample. Efforts to identify and review studies published in languages other than English are needed in the future to gain a clear understanding of the full scope of vitamin D deficiency worldwide. Third, our strict inclusion criteria (e.g. inclusion of studies with randomly selected samples) might also explain the limited number of studies identified from some regions. However, previous reviews using more liberal inclusion criteria have also identified a limited number of studies conducted in these regions^(8,16). Fourth, recruitment strategies in the studies that we sampled may have focused to an extent on healthier populations, resulting in an overestimation of the prevalence of adequate vitamin D levels and a consequent minimisation of observable differences between the sexes or age-related subgroups. Fifth, we observed substantial heterogeneity between the studies in our sample that could not be explained by variables such as age, sex, season, distance from the equator, assay type or representativeness. Other unmeasured factors influencing vitamin D status (e.g. dietary intake, clothing style, time spent outdoors and use of sunscreen) may have contributed to the heterogeneity of results. Differences across the studies in study quality, adjustment for potential confounders and the definition of some characteristics or factors such as season may have contributed substantially to the heterogeneity that we observed. Finally, the precision of the estimates of vitamin D status in the subgroups of interest in the present review was probably affected by their relative under-representation in studies conducted in many regions of the world. High-quality population-based studies that assess and report all relevant data on 25(OH)D levels and central covariates including lifestyle factors to enable comparison of 25(OH)D values in the future, at least for population subgroups within the same country, have to be conducted.

Conclusion

Although we found a high degree of variability in reports of vitamin D status at the population level, more than one-third of the studies in the present systematic review reported mean 25(OH)D values below 50 nmol/l. Given the substantial heterogeneity of published evidence to date, further research on worldwide patterns of vitamin D deficiency at the population level and within key subgroups is needed to inform public health policy development to reduce risk for potential health consequences of an inadequate vitamin D status. The present review further suggests the importance of developing and implementing research designs that minimise potential sources of bias and consequently strengthen our understanding on vitamin D status in key subgroups worldwide.

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All authors declare that they have no conflicts of interest.

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