

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 extra-skeletal 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).

Abbreviation: 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



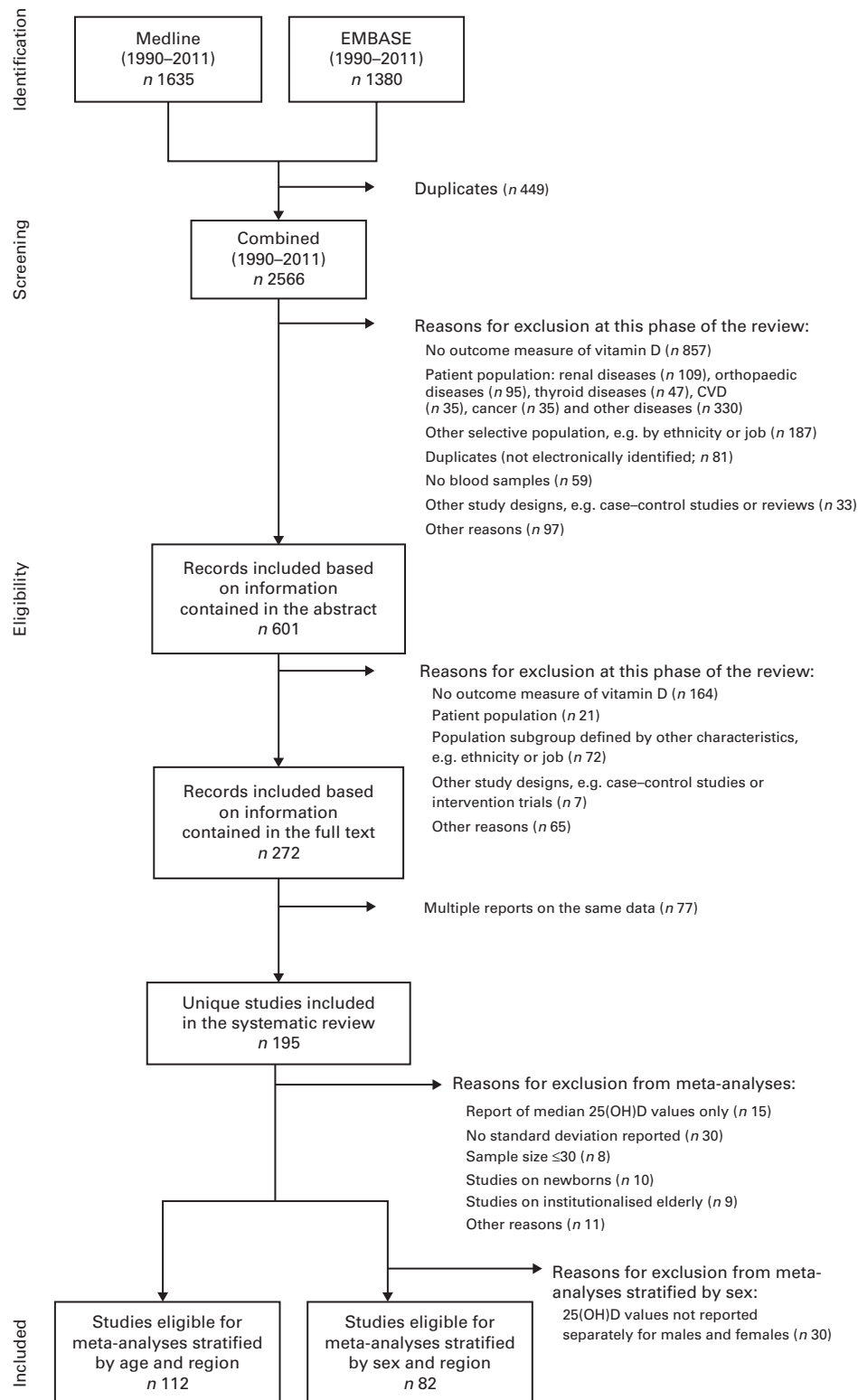


Fig. 1. Flow chart of the study selection (1990–2011). 25(OH)D, 25-Hydroxyvitamin D.

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.

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	Representativeness
Europe									
Austria	Whole country	Koenig & Elmadfa ⁽³³⁾	1452	NA	O	NA	27.5	Unknown	Unknown
	Whole country	Kudlacek <i>et al.</i> ⁽³⁴⁾	1048	38.2	A	Winter	52.2	Unknown	No
Belgium	Brabant	Boonen <i>et al.</i> ⁽³⁵⁾	245	0.0	E	NA	56.4	Unknown	No
	Brussels	MacFarlane <i>et al.</i> ⁽³⁶⁾	126	31.0	A	Winter	48.4	Unknown	No
	Brussels	Moreno-Reyes <i>et al.</i> ⁽³⁷⁾	401	50.1	A	NA	35.0	Yes	No
	Northern Belgium	Richart <i>et al.</i> ⁽³⁸⁾	542	49.8	NA	NA	71.4†; 73.4‡	Unknown	Unknown
Czech Republic	Prague	Zofkova & Hill ⁽³⁹⁾	47	0.0	A	NA	58.2	Unknown	No
Denmark	Copenhagen	Andersen <i>et al.</i> ⁽⁴⁰⁾	112	NA	C; E	Winter	24.4§; 47.8§	Yes	No
	Copenhagen	Brot <i>et al.</i> ⁽⁴¹⁾	510	0.0	A	NA	24.0§	Yes	No
	Faroe Islands	Dalgard <i>et al.</i> ⁽⁴²⁾	669	51.1	E	Mixed	47.6	Unknown	Unknown
	Odense	Frost <i>et al.</i> ⁽⁴³⁾	700	100.0	A	Whole year	64.9	Unknown	No
	Aarhus	Rejnmark <i>et al.</i> ⁽⁴⁴⁾	315	0.0	A	NA	57.0§	Unknown	No
	Aarhus	Rejnmark <i>et al.</i> ⁽⁴⁵⁾	2316	0.0	A	Mixed	62.0§	Unknown	Yes
	Copenhagen	Rudnicki <i>et al.</i> ⁽⁴⁶⁾	125	42.4	A	Whole year	25.5	Yes	Yes
Estonia	Vaike-Maarja	Kull <i>et al.</i> ⁽⁴⁷⁾	367	45.5	A	Winter	43.7	Yes	Yes
Finland	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	45.1†; 45.2‡	Yes	No
	Whole country	Lamberg-Allardt <i>et al.</i> ⁽⁴⁹⁾	328	38.4	A	Mixed	45.0†; 47.0‡	Yes	Unknown
	Whole country	Matilla <i>et al.</i> ⁽⁵⁰⁾	4097	47.0	A	Whole year	43.6	Yes	Unknown
	Whole country	Partti <i>et al.</i> ⁽⁵¹⁾	6241	45.0	A	Mixed	45.1	Unknown	No
	North Savo	Parviainen <i>et al.</i> ⁽⁵²⁾	776	53.9	A	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	I	Winter	50.7	Yes	Unknown
	France	Montpellier	Blain <i>et al.</i> ⁽⁵⁶⁾	248	0.0	A	NA	64.1§	Yes
Caen		Bougle <i>et al.</i> ⁽⁵⁷⁾	82	NA	I	NA	74.9	Unknown	No
France		Chapuy <i>et al.</i> ⁽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	A	Winter	79.5	Unknown	Unknown
Germany	Bonn	Braemswig <i>et al.</i> ⁽⁶²⁾	21	100.0	A	Mixed	51.3	Unknown	Unknown
	Whole country	Hintzpeter <i>et al.</i> ⁽⁶³⁾	4030	43.7	O	NA	45.2§†; 44.7§‡	Yes	Yes
	Southern Germany	Scharla <i>et al.</i> ⁽⁶⁴⁾	415	50.4	A	Summer; winter	67.4; 42.4	Yes	Unknown
	Southern Germany	Woitge <i>et al.</i> ⁽⁶⁵⁾	41	36.6	O	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	Athens	Nicolaidou <i>et al.</i> ⁽⁶⁷⁾	123	57.7	I	Whole year	50.9§	Yes	Yes
	Athens	Papapetrou <i>et al.</i> ⁽⁶⁸⁾	279	17.2	E	Mixed	42.9	Unknown	No

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	C	Winter	43.9	Yes	No
	Reykjavik	Sigurdsson <i>et al.</i> ⁽⁷⁰⁾	308	0.0	E	Mixed	53.1	Yes	NA
	Reykjavik	Steingrimsdottir <i>et al.</i> ⁽⁷¹⁾	944	52.0	A	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	O	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 <i>et al.</i> ⁽⁷⁶⁾	90	35.6	A	Winter	42.7	Yes	No
	Rome	Romagnoli <i>et al.</i> ⁽⁷⁷⁾	135	NA	A	Summer; winter	90.1; 45.9	Yes	No
	Greve, Bagno a Ripoli	Vezzoli <i>et al.</i> ⁽⁷⁸⁾	595	50.8	O	NA	61.2‡; 48.2‡	Yes	Unknown
Netherlands	Bilthoven, Utrecht	Al-Delaimy <i>et al.</i> ⁽⁷⁹⁾	65	46.2	A	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 <i>et al.</i> ⁽⁸¹⁾	1317	NA	E	Whole year	65.5	Yes	No
	Whole country	Kuchuk <i>et al.</i> ⁽⁸²⁾	1319	48.7	E	Whole year	53.2	Yes	Yes
	Whole country	Löwik <i>et al.</i> ⁽⁸³⁾	529	50.7	E	NA	40.0‡; 38.0‡	Unknown	No
	Hoorn	Pilz <i>et al.</i> ⁽⁸⁴⁾	614	NA	E	Whole year	56.5‡; 50.8‡	Yes	No
	Amsterdam	Van Summeren <i>et al.</i> ⁽⁸⁵⁾	307	50.8	C	NA	69.6	Unknown	No
Norway	Skjervoy	Brustad <i>et al.</i> ⁽⁸⁶⁾	32	65.6	A	NA	67.2	Unknown	No
	Northern Norway	Brustad <i>et al.</i> ⁽⁸⁷⁾	300	0.0	A	Mixed	56.9	Yes	Unknown
	Tromso	Grimnes <i>et al.</i> ⁽⁸⁸⁾	6932	39.0	A	NA	58.9	Yes	No
	Oslo	Meyer <i>et al.</i> ⁽⁸⁹⁾	869	42.8	A	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 <i>et al.</i> ⁽⁹²⁾	237	46.8	E	Winter	42.9	Unknown	No
	L'Hospitalet de Llobregat	Gomez <i>et al.</i> ⁽⁹³⁾	253	49.8	A	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	Murray <i>et al.</i> ⁽⁹⁵⁾	391	58.1	A	Autumn	23.4‡; 21.3‡	Unknown	No
	Murica	Perez-Llamas <i>et al.</i> ⁽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
	Malmö	Gerdhem <i>et al.</i> ⁽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	A	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

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	Vaud, Fribourg, Ticino	Burnand <i>et al.</i> ⁽¹⁰³⁾	3276	51.7	O	Mixed	50.0	Unknown	Yes
	Lausanne	Krieg <i>et al.</i> ⁽¹⁰⁴⁾	349	29.5	E	NA	26.5†; 23.2‡	Unknown	Unknown
	Basel	Theiler <i>et al.</i> ⁽²⁹⁾	505	57.4	E	Mixed	17.5† ; 18.2‡ ; 91.6†; 67.4‡	Yes	No
UK	Central, South, West England, Wales	Bates <i>et al.</i> ⁽¹⁰⁵⁾	924	NA	E	Mixed	51.9	Unknown	No
	East Kent	Carter <i>et al.</i> ⁽¹⁰⁶⁾	188	25.5	E	Mixed	31.2§	Unknown	No
	Northern Ireland	Cashman <i>et al.</i> ⁽¹⁰⁷⁾	1015	49.8	C	Mixed	61.1†§; 59.0‡§	Yes	Yes
	Great Britain	Davies <i>et al.</i> ⁽¹⁰⁸⁾	756	NA	C	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	A	NA	60.2	Yes	Unknown
	Cambridge	Hegarty <i>et al.</i> ⁽¹¹¹⁾	96	49.0	E	Winter	23.1	Yes	Unknown
	Northern Ireland	Hill <i>et al.</i> ⁽¹¹²⁾	1015	49.8	C	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	A	Summer; winter	60.3; 41.1	Yes	No
	Grampian	Macdonald <i>et al.</i> ⁽¹¹⁵⁾	2905	0.0	A	Mixed	53.9	Yes	No
	Aberdeen	Mavroei <i>et al.</i> ⁽¹¹⁶⁾	325	0.0	E	Mixed	53.3	No	No
	Isle of Ely	Wareham <i>et al.</i> ⁽¹¹⁷⁾	1057	43.3	NA	Whole year	54.4†; 46.2‡	Yes	No
North America Canada	Quebec	Barake <i>et al.</i> ⁽¹¹⁸⁾	404	51.2	E	Mixed	74.0	Yes	No
	Nunavut	El Hayek <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	O	Whole year	67.7	Yes	Yes
	St Theresa Point, Garden Hill	Lebrun <i>et al.</i> ⁽¹²¹⁾	76	NA	I	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	C	Mixed	46.0	Yes	No
	Avalon Peninsula	Newhook <i>et al.</i> ⁽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 <i>et al.</i> ⁽¹²⁶⁾	188	31.9	E	Winter	57.3	No	No
	Quebec	Sinotte <i>et al.</i> ⁽¹²⁷⁾	741	0.0	A	Winter	64.9	Yes	No
	USA	NA	Alvarez <i>et al.</i> ⁽¹²⁸⁾	50	0.0	A	Mixed	55.7	Unknown
New York		Arunabh <i>et al.</i> ⁽¹²⁹⁾	410	0.0	A	Whole year	54.2	Yes	No
Connecticut		Avery <i>et al.</i> ⁽¹³⁰⁾	114	NA	E	NA	113.1; 81.8	Yes	No
Honolulu		Chai <i>et al.</i> ⁽¹³¹⁾	182	0.0	A	NA	72.3	Unknown	Unknown
Framingham		Cheng <i>et al.</i> ⁽¹³²⁾	3890	46.0	A	Whole year	92.9	No	No
Boston		Dawson-Hughes <i>et al.</i> ⁽¹³³⁾	391	46.5	E	Whole year	82.4†; 68.9‡	Yes	Unknown
Oakland		Dror <i>et al.</i> ⁽¹³⁴⁾	199	NA	I	Mixed	43.7	Unknown	Unknown
Whole country		Looker <i>et al.</i> ⁽¹³⁵⁾	18462	47.2	O	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	C	NA	66.2	Unknown	Unknown
Whole country		Iannuzzi-Sucich <i>et al.</i> ⁽¹³⁸⁾	337	42.1	E	NA	67.4†; 57.7‡	Yes	No
Connecticut		Ilich <i>et al.</i> ⁽¹³⁹⁾	136	0.0	E	Whole year	52.8	Unknown	No
Framingham		Jaques <i>et al.</i> ⁽¹⁴⁰⁾	759	38.2	E	NA	82.0†; 71.0‡	Yes	Unknown
Northern Georgia		Johnson <i>et al.</i> ⁽¹⁴¹⁾	317	20.2	E	Whole year	66.7	Yes	Unknown
Rochester		Khosla <i>et al.</i> ⁽¹⁴²⁾	138	0.0	A	NA	77.6	Unknown	Unknown
Whole country		Kim <i>et al.</i> ⁽¹⁴³⁾	8351	0.0	O	NA	61.0	Unknown	No

J. Hilger *et al.*

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 <i>et al.</i> ⁽¹⁴⁴⁾	90	0.0	A	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	C	Whole year	68.0	Unknown	Yes	
	Farmington	Mirza <i>et al.</i> ⁽¹⁴⁷⁾	40	0.0	A; E	NA	74.9; 84.9	Yes	No	
	Rancho Bernardo	Reis <i>et al.</i> ⁽¹⁴⁸⁾	654	36.4	E	NA	103.6	Yes	No	
	Marion County	Rock <i>et al.</i> ⁽¹⁴⁹⁾	1042	39.4	O	Mixed	31.9†; 29.3‡	Yes	Yes	
	Greenwich	Sabetta <i>et al.</i> ⁽¹⁵⁰⁾	198	42.9	O	Autumn	70.9	Unknown	Unknown	
	Framingham	Shea <i>et al.</i> ⁽¹⁵¹⁾	1381	48.4	A	NA	49.4	Unknown	No	
	Athens	Stein <i>et al.</i> ⁽¹⁵²⁾	168	0.0	C	Whole year	93.8	Yes	No	
	Bangor	Sullivan <i>et al.</i> ⁽¹⁵³⁾	22	0.0	C	Summer	74.4	Yes	Unknown	
	Philadelphia	Weng <i>et al.</i> ⁽¹⁵⁴⁾	382	47.6	C	Whole year	69.9§	Yes	Yes	
	Asia/Pacific									
	Australia									
	Sydney	Bowyer <i>et al.</i> ⁽¹⁵⁵⁾	901	NA	I	Winter	60.0§	Unknown	No	
	Sydney	Brock <i>et al.</i> ⁽¹⁵⁶⁾	186	NA	E	NA	36.0; 33.0	Yes	No	
	Dubbo	Center <i>et al.</i> ⁽¹⁵⁷⁾	437	100.0	E	NA	70.7	Yes	No	
	Tasmania	Ding <i>et al.</i> ⁽¹⁵⁸⁾	1002	NA	A	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	A	Whole year	70.0	Yes	No	
	Melbourne	Stein <i>et al.</i> ⁽¹⁶¹⁾	99	26.3	E	Winter	26.0§	Yes	No	
	Sydney	Zochling <i>et al.</i> ⁽¹⁶²⁾	584	21.2	E	Mixed	21.4†; 16.9‡	Unknown	No	
China										
	Linxian	Abnet <i>et al.</i> ⁽¹⁶³⁾	720	42.2	A	Spring	33.1	Yes	Unknown	
	Hong Kong	Chan <i>et al.</i> ⁽¹⁶⁴⁾	53	0.0	E	NA	57.7	Unknown	No	
	Linxian	Chen <i>et al.</i> ⁽¹⁶⁵⁾	2018	54.0	A	Spring	31.7	Unknown	Unknown	
	Beijing	Du <i>et al.</i> ⁽¹⁶⁶⁾	649	0.0	C	Winter	33.5	Yes	Yes	
	Shanxi	Strand <i>et al.</i> ⁽¹⁶⁷⁾	250	52.4	C	Spring	42.3†; 25.5‡	Unknown	Unknown	
	Taipei	Tsai <i>et al.</i> ⁽¹⁶⁸⁾	262	0.0	A	Mixed	76.6	Yes	No	
Fiji Islands										
	Whole country	Heere <i>et al.</i> ⁽¹⁶⁹⁾	511	0.0	A	Winter	76.0	Unknown	Unknown	
India										
	Agota	Goswami <i>et al.</i> ⁽¹⁷⁰⁾	57	56.1	A	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⁾	117	NA	I	Mixed	21.0	Yes	No	
Indonesia										
	Jakarta, Bekasi	Rinaldi <i>et al.</i> ⁽¹⁷³⁾	62	0.0	E	Summer	68.2	Unknown	Unknown	
	Jakarta, Bekasi	Setiati <i>et al.</i> ⁽¹⁷⁴⁾	74	0.0	E	NA	38.7	No	Yes	
Japan										
	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 <i>et al.</i> ⁽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	A	NA	44.4	Yes	No	
Mongolia										
	Ulaanbaatar	Lander <i>et al.</i> ⁽¹⁸¹⁾	98	72.4	C	Autumn	24.1	Yes	No	

Table 1. Continued

Region and country	City/region within the country	Reference	n	Male (%)	Age group	Season	25(OH)D (nmol/l)	Reliability	Representativeness
New Zealand	Auckland	Bolland <i>et al.</i> ⁽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	I	Whole year	44.0§	Yes	Unknown
	Auckland	Grant <i>et al.</i> ⁽¹⁸⁶⁾	353	47.6	I	Whole year	55.0	Yes	Unknown
	Dunedin	Houghton <i>et al.</i> ⁽¹⁸⁷⁾	193	57.5	C	Mixed	52.0	Yes	Unknown
	Auckland	Ley <i>et al.</i> ⁽¹⁸⁸⁾	39	0.0	E	Winter	26.1	Unknown	No
	Auckland	Lucas <i>et al.</i> ⁽¹⁸⁹⁾	1606	0.0	E	Whole year	51.2	Unknown	No
	Whole country	Rockell <i>et al.</i> ⁽¹⁹⁰⁾	1585	50.5	C	Mixed	50.0	Yes	No
	Dunedin; Invercargill	Rockell <i>et al.</i> ⁽¹⁹¹⁾	342	34.8	A	Summer	85.0	Unknown	Unknown
	Auckland	Scragg <i>et al.</i> ⁽¹⁹²⁾	295	100.0	A	Whole year	39.8	No	Yes
South Korea	Chungju	Kim <i>et al.</i> ⁽¹⁹³⁾	1330	38.0	E	Whole year	46.1	Unknown	No
	Seoul	Namgung <i>et al.</i> ⁽¹⁹⁴⁾	71	50.7	I	Summer; winter	74.9; 26.7	Yes	Unknown
Thailand	NA	Chailurkit <i>et al.</i> ⁽¹⁹⁵⁾	158	48.7	O	NA	168.2†; 105.8‡	Unknown	Unknown
	Khon Kaen	Chailurkit <i>et al.</i> ⁽¹⁹⁶⁾	251	50.2	O	NA	128.3†; 93.6‡	No	Yes
	Bangkok	Chailurkit <i>et al.</i> ⁽¹⁹⁷⁾	229	47.2	O	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	E	Summer	83.2	No	Unknown
Vietnam	Ho Chi Minh (city)	Ho-Pham <i>et al.</i> ⁽¹⁹⁹⁾	637	32.2	A	Mixed	91.9†; 75.1‡	Yes	Yes
Middle East/ Africa									
Cameroon	Ntam	Njemini <i>et al.</i> ⁽²⁰⁰⁾	152	60.5	E	NA	52.7	Unknown	No
Iran	Tehran	Bassir <i>et al.</i> ⁽²⁰¹⁾	44	NA	I	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	O	NA	20.7§	Yes	No
	Tehran	Hosseini-Nezhad <i>et al.</i> ⁽²⁰⁴⁾	646	24.8	A	NA	31.3	Yes	Unknown
	Tehran	Hosseini-panah <i>et al.</i> ⁽²⁰⁵⁾	245	0.0	A	NA	73.0	Yes	Yes
	Zanjan	Kazemi <i>et al.</i> ⁽²⁰⁶⁾	61	NA	I	Mixed	16.7	Unknown	Unknown
	Shiraz	Masoompour <i>et al.</i> ⁽²⁰⁷⁾	520	100.0	A	Winter	35.0	Yes	Yes
	Tehran	Mirsaeid Ghazi <i>et al.</i> ⁽²⁰⁸⁾	1171	41.8	O	Mixed	87.4†; 52.4‡	Yes	No
	Isfahan	Moussavi <i>et al.</i> ⁽²⁰⁹⁾	318	48.1	C	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	C	Winter	116.1†; 60.3‡	Yes	No
Isfahan	Salek <i>et al.</i> ⁽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 <i>et al.</i> ⁽²¹⁴⁾	316	31.3	A	Winter	24.2	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
Nigeria	Jos	Pfützner <i>et al.</i> ⁽²¹⁵⁾	218	45.0	C	Mixed	66.8	Unknown	Unknown
South Africa	Cape Town	Charlton <i>et al.</i> ⁽²¹⁶⁾	173	48.0	E		36.9	Unknown	No
Gambia	Whole country	Aspray <i>et al.</i> ⁽²¹⁷⁾	113	0.0	O	NA	97.7	No	No
Latin America									
Argentina	Ushuaia	Oliveri <i>et al.</i> ⁽²¹⁸⁾	42	57.1	C	Winter	24.5	Unknown	No
Brazil	Sao Paulo	Canto-Costa <i>et al.</i> ⁽²¹⁹⁾	11	36.4	E	NA	61.2	Yes	No
	Sao Paulo	Saraiva <i>et al.</i> ⁽²²⁰⁾	250	30.8	E	Whole year	52.4	No	Yes

NA, 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^(23,27,30,224–287).

† 25(OH)D mean values for men.

‡ 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 18 462 participants with a median of 316 (interquartile range 117–861). While the majority of studies contained data on males and females, nine studies (4.7%) 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 (SD 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.

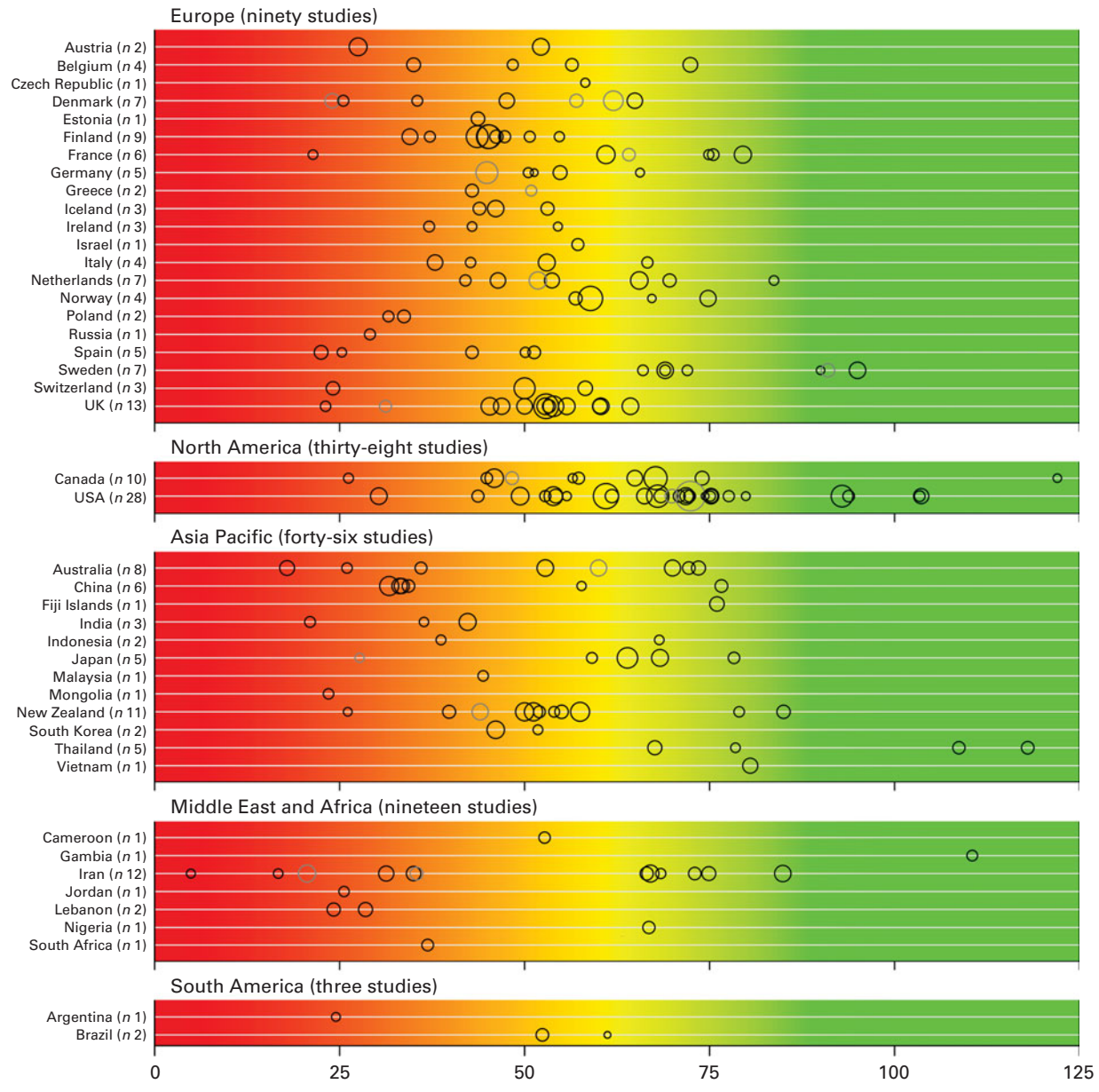


Fig. 2. Mean/median 25-hydroxyvitamin D (25(OH)D) values, by geographical region and country. Note: medians (○) are shown where mean values (○) are not reported; Study size is indicated by circle size. The background colour scheme is intended to reflect the current uncertainty around the definition of 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 34.9% of the studies due to missing information. Information on assay reliability was provided in 61.0% of the studies with 52.8% 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 136.2 nmol/l and 20.7 to 91.0 nmol/l, respectively. We found that 88.1% of the samples presented in the present review had mean 25(OH)D values below 75 nmol/l, 37.3% had mean values below 50 nmol/l and 6.7% had mean values below 25 nmol/l. Fig. 2 provides an overview

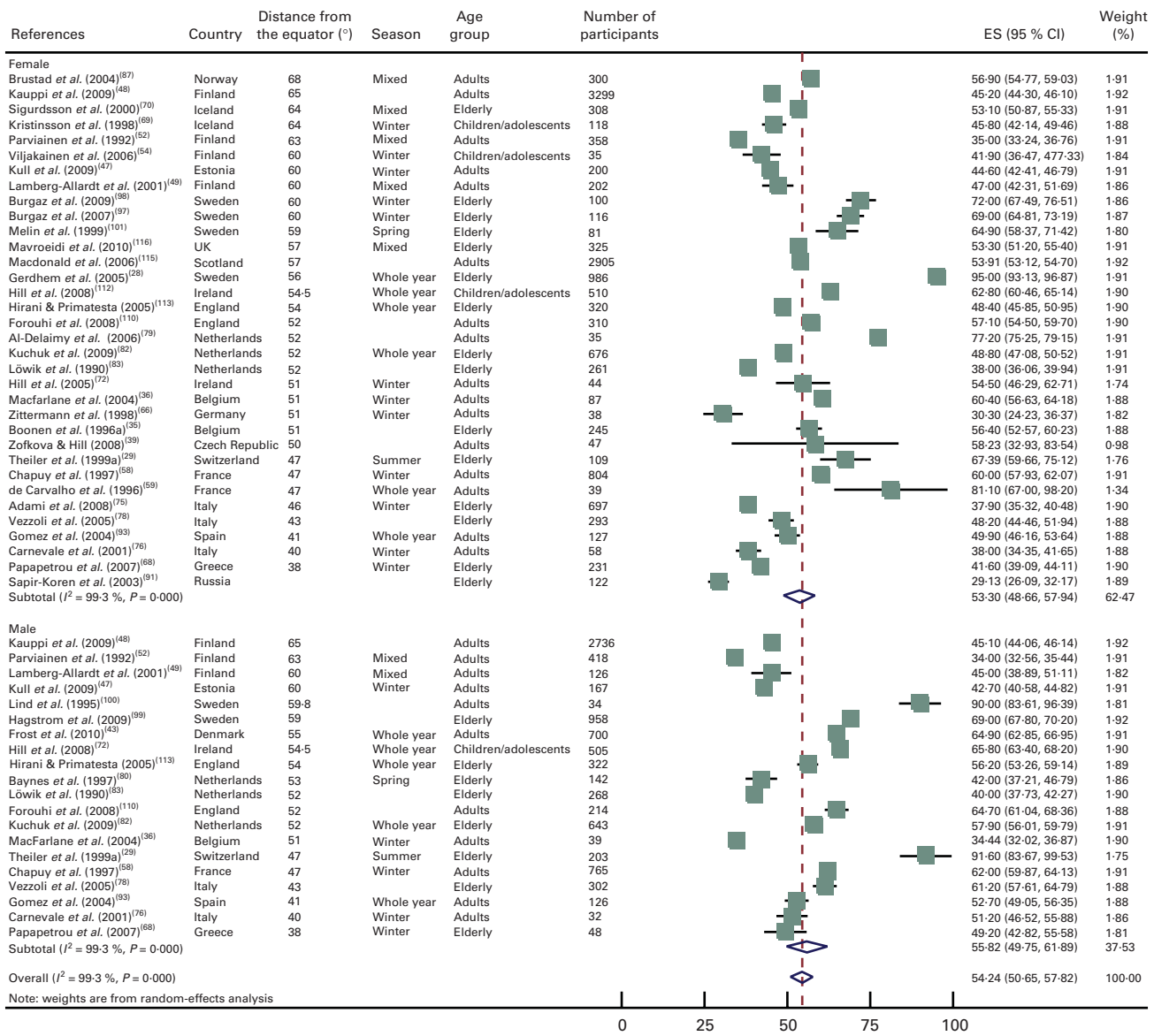


Fig. 3. Forest plot for Europe stratified by sex. ES, effect estimator. (A colour version of this figure can be found online at <http://www.journals.cambridge.org/bjn>)

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,

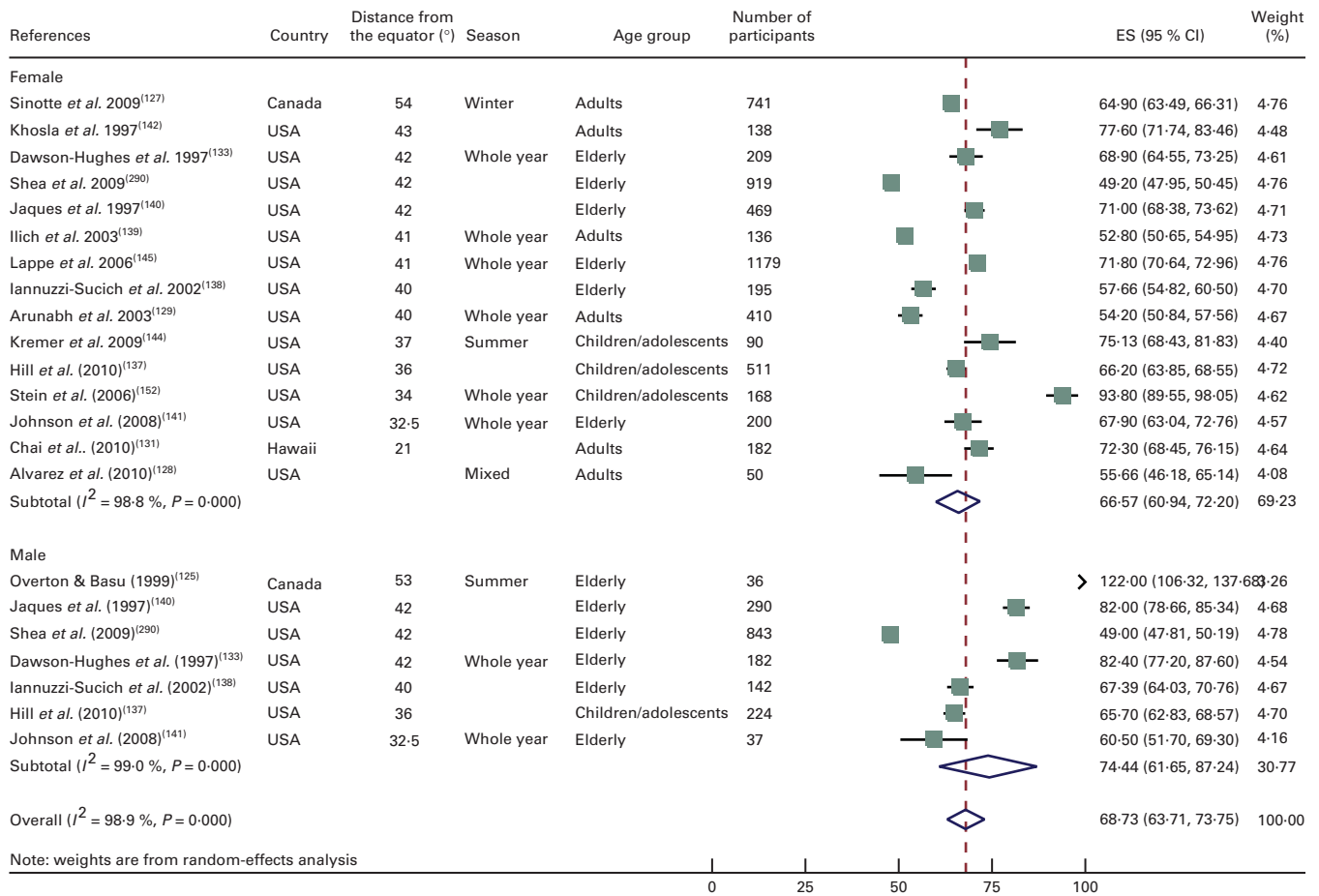


Fig. 4. Forest plot for North America stratified by sex. ES, effect estimator. (A colour version of this figure can be found online at <http://www.journals.cambridge.org/bjn>)

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/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

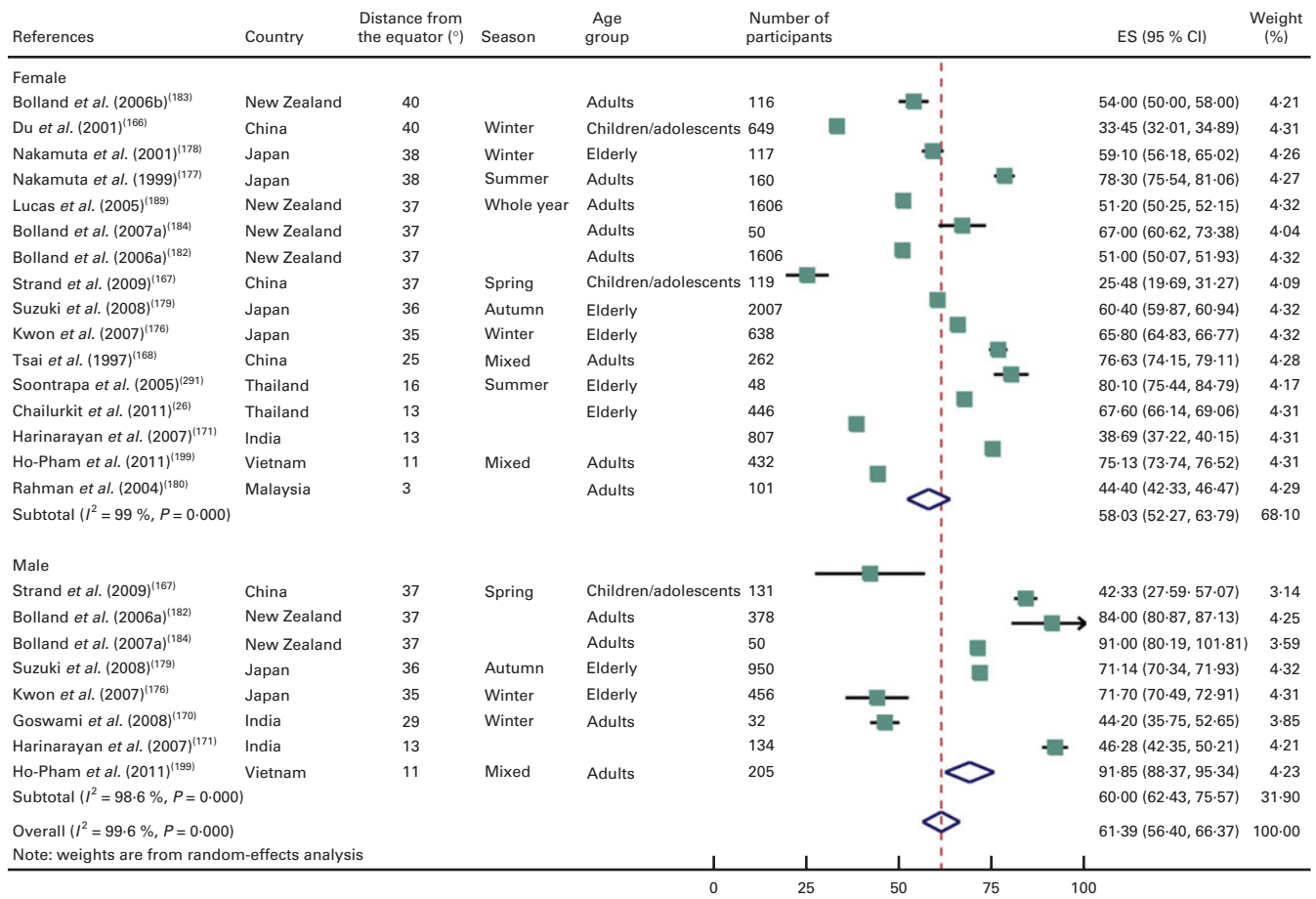


Fig. 5. Forest plot for the Asia/Pacific region stratified by sex. ES, effect estimator. (A colour version of this figure can be found online at <http://www.journals.cambridge.org/bjn>)

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 cer-

eals) 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 values in Swedish elderly than in those from other European countries. Some have suggested that this finding can be

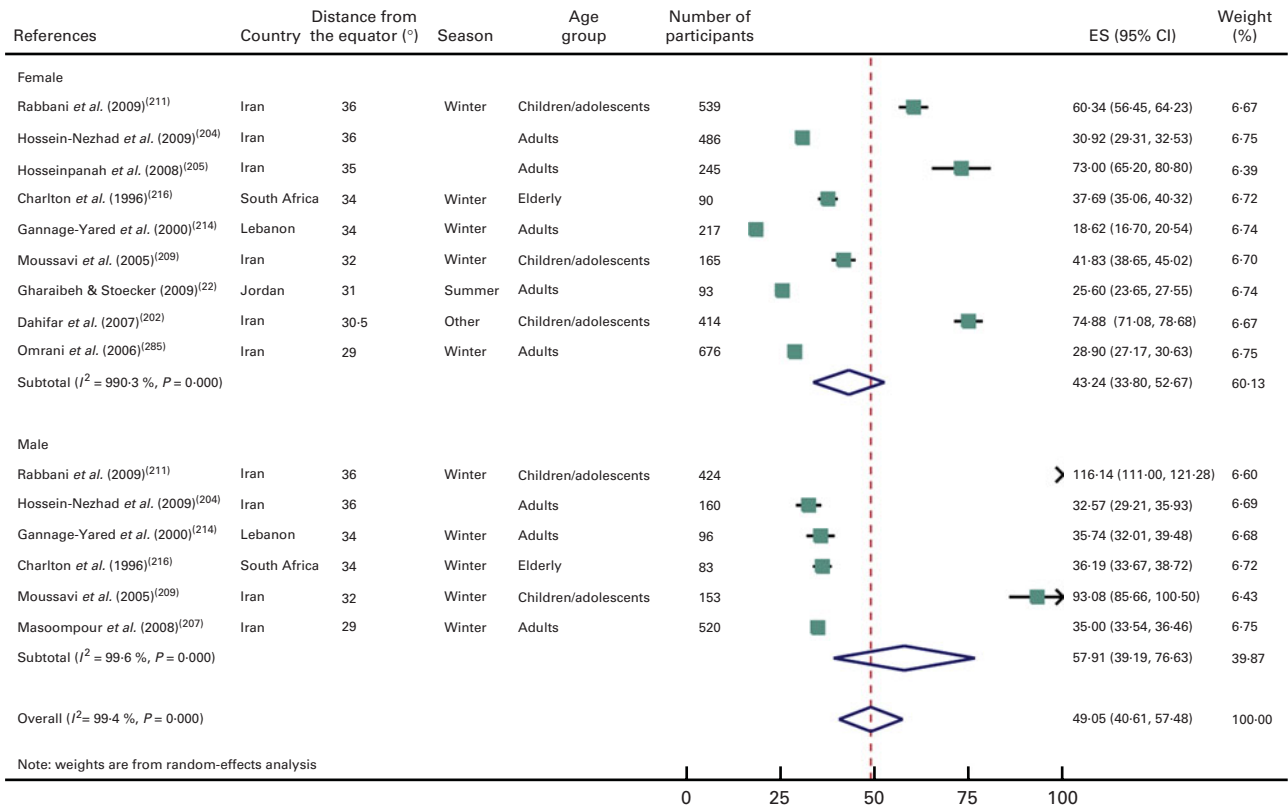


Fig. 6. Forest plot for the Middle East/Africa region stratified by sex. ES, effect estimator. (A colour version of this figure can be found online at <http://www.journals.cambridge.org/bjn>)

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	I^2 (%)	<i>n</i> (studies)	<i>n</i> (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	28 844	52.98	45.01, 56.58
Elderly (> 65 years)	99.4	30	10 894	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 random-effects 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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References

1. Tsiaras WG & Weinstock MA (2011) Factors influencing vitamin D status. *Acta Derm Venereol* **91**, 115–124.
2. Haroon M & Regan MJ (2010) Vitamin D deficiency: the time to ignore it has passed. *Int J Rheum Dis* **13**, 318–323.
3. Holick MF (2004) Sunlight and vitamin D for bone health and prevention of autoimmune diseases, cancers, and cardiovascular disease. *Am J Clin Nutr* **80**, 1678–1688.
4. Pilz S, Kienreich K, Tomaschitz A, *et al.* (2012) Vitamin D and cardiovascular disease: update and outlook. *Scand J Clin Lab Invest Suppl* **72**, 83–91.
5. Mithal A, Wahl DA, Bonjour JP, *et al.* (2009) Global vitamin D status and determinants of hypovitaminosis D. *Osteoporos Int* **20**, 1807–1820.
6. World Health Organization (2011) *Noncommunicable Diseases Country Profiles – WHO Global Report*. Geneva: WHO.
7. Holick MF (2009) Vitamin D status: measurement, interpretation, and clinical application. *Ann Endocrinol* **19**, 73–78.
8. van Schoor NM & Lips P (2011) Worldwide vitamin D status. *Best Pract Res Clin Endocrinol Metab* **25**, 671–680.
9. Thacher TD & Clarke BL (2011) Vitamin D insufficiency. *Mayo Clin Proc* **86**, 50–60.
10. Ross AC, Manson JE, Abrams SA, *et al.* (2011) The 2011 report on dietary reference intakes for calcium and vitamin D from the Institute of Medicine: what clinicians need to know. *J Clin Endocrinol Metab* **96**, 53–58.
11. Holick MF (2007) Vitamin D deficiency. *N Engl J Med* **357**, 266–281.
12. Holick MF, Binkley NC, Bischoff-Ferrari HA, *et al.* (2011) Evaluation, treatment, and prevention of vitamin D deficiency: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab* **96**, 1911–1930.
13. Arabi A, El Rassi R & El-Hajj Fuleihan G (2010) Hypovitaminosis D in developing countries – prevalence, risk factors and outcomes. *Nat Rev Endocrinol* **6**, 550–561.
14. Hagenau T, Vest R, Gissel TN, *et al.* (2009) Global vitamin D levels in relation to age, gender, skin pigmentation and latitude: an ecologic meta-regression analysis. *Osteoporos Int* **20**, 133–140.
15. Lips P (2007) Vitamin D status and nutrition in Europe and Asia. *J Steroid Biochem Mol Biol* **103**, 620–625.
16. McKenna MJ (1992) Differences in vitamin D status between countries in young adults and the elderly. *Am J Med* **93**, 69–77.
17. Nair R & Maseeh A (2012) Vitamin D: the “sunshine” vitamin. *J Pharmacol Pharmacother* **3**, 118–126.
18. Moher D, Liberati A, Tetzlaff J, *et al.* (2009) Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med* **6**, 100097.
19. World Health Organization (2002) *The World Health Report – Reducing Risks, Promoting Healthy Life*. Geneva: WHO.
20. Carter GD (2011) Accuracy of 25-hydroxyvitamin D assays: confronting the issues. *Curr Drug Targets* **12**, 19–28.
21. Wahl DA, Cooper C, Ebeling PR, *et al.* (2012) A global representation of vitamin D status in healthy populations. *Arch Osteoporos* **7**, 155–172.
22. Gharaibeh MA & Stoecker BJ (2009) Assessment of serum 25(OH)D concentration in women of childbearing age and their preschool children in Northern Jordan during summer. *Eur J Clin Nutr* **63**, 1320–1326.
23. Ginde AA, Liu MC, Camargo CA, *et al.* (2009) Demographic differences and trends of vitamin D insufficiency in the US population, 1988–2004. *Arch Intern Med* **169**, 626–632.
24. Batieha A, Khader Y, Jaddou H, *et al.* (2011) Vitamin D status in Jordan: dress style and gender discrepancies. *Ann Nutr Metab* **58**, 10–18.
25. Prentice A (2008) Vitamin D deficiency: a global perspective. *Nutr Rev* **66**, 153–164.
26. Chailurkit LO, Kruavit A & Rajatanavin R (2011) Vitamin D status and bone health in healthy Thai elderly women. *Nutrition* **27**, 160–164.
27. Nakamura K, Nashimoto M, Hori Y, *et al.* (2000) Serum parathyroid hormone in healthy Japanese women in relation to serum 25-hydroxyvitamin D. *Int J Vitam Nutr Res* **70**, 287–292.
28. Gerdhem P, Ringsberg KA, Obrant KJ, *et al.* (2005) Association between 25-hydroxy vitamin D levels, physical activity, muscle strength and fractures in the prospective population-based OPRA Study of Elderly Women. *Osteoporos Int* **16**, 1425–1431.
29. Theiler R, Stahelin HB, Tyndall A, *et al.* (1999) Calcidiol, calcitriol and parathyroid hormone serum concentrations in institutionalized and ambulatory elderly in Switzerland. *Int J Vitam Nutr Res* **69**, 96–105.
30. Ginde AA, Sullivan AF, Mansbach JM, *et al.* (2010) Vitamin D insufficiency in pregnant and nonpregnant women of childbearing age in the United States. *Am J Obstet Gynecol* **202**, 436.
31. Dror DK (2011) Vitamin D status during pregnancy: maternal, fetal, and postnatal outcomes. *Curr Opin Obstet Gynecol* **23**, 422–426.
32. DerSimonian R & Laird N (1986) Meta-analysis in clinical trials. *Control Clin Trials* **7**, 177–188.
33. Koenig J & Elmadfa I (2000) Status of calcium and vitamin D of different population groups in Austria. *Int J Vitam Nutr Res* **70**, 214–220.
34. Kudlacek S, Schneider B, Peterlik M, *et al.* (2003) Assessment of vitamin D and calcium status in healthy adult Austrians. *Eur J Clin Invest* **33**, 323–331.
35. Boonen S, Lesaffre E, Aerssens J, *et al.* (1996) Deficiency of the growth hormone-insulin-like growth factor-I axis potentially involved in age-related alterations in body composition. *Gerontology* **42**, 330–338.
36. MacFarlane GD, Sackrison JL Jr, Body JJ, *et al.* (2004) Hypovitaminosis D in a normal, apparently healthy urban European population. *J Steroid Biochem Mol Biol* **89–90**, 621–622.
37. Moreno-Reyes R, Carpentier YA, Boelaert M, *et al.* (2009) Vitamin D deficiency and hyperparathyroidism in relation to ethnicity: a cross-sectional survey in healthy adults. *Eur J Nutr* **48**, 31–37.
38. Richart T, Thijs L, Nawrot T, *et al.* (2011) The metabolic syndrome and carotid intima-media thickness in relation to the parathyroid hormone to 25-OH-D(3) ratio in a general population. *Am J Hypertens* **24**, 102–109.
39. Zofkova I & Hill M (2008) Biochemical markers of bone remodeling correlate negatively with circulating TSH in postmenopausal women. *Endocr Regul* **42**, 121–127.
40. Andersen R, Molgaard C, Skovgaard LT, *et al.* (2005) Teenage girls and elderly women living in northern Europe have low winter vitamin D status. *Eur J Clin Nutr* **59**, 533–541.
41. Brot C, Jorgensen N, Madsen OR, *et al.* (1999) Relationships between bone mineral density, serum vitamin D metabolites and calcium:phosphorus intake in healthy perimenopausal women. *J Intern Med* **245**, 509–516.
42. Dalgard C, Petersen MS, Schmedes AV, *et al.* (2010) High latitude and marine diet: vitamin D status in elderly Faroese. *Br J Nutr* **104**, 914–918.

43. Frost M, Abrahamsen B, Nielsen TL, *et al.* (2010) Vitamin D status and PTH in young men: a cross-sectional study on associations with bone mineral density, body composition and glucose metabolism. *Clin Endocrinol (Oxf)* **73**, 573–580.
44. Rejnmark L, Vestergaard P, Heickendorff L, *et al.* (2008) Plasma 1,25(OH)₂D levels decrease in postmenopausal women with hypovitaminosis D. *Eur J Endocrinol* **158**, 571–576.
45. Rejnmark L, Vestergaard P, Heickendorff L, *et al.* (2011) Determinants of plasma PTH and their implication for defining a reference interval. *Clin Endocrinol (Oxf)* **74**, 37–43.
46. Rudnicki M, Thode J, Jorgensen T, *et al.* (1993) Effects of age, sex, season and diet on serum ionized calcium, parathyroid hormone and vitamin D in a random population. *J Intern Med* **234**, 195–200.
47. Kull M Jr, Kallikorm R, Tamm A, *et al.* (2009) Seasonal variance of 25-(OH) vitamin D in the general population of Estonia, a Northern European country. *BMC Public Health* **9**, 22.
48. Kauppi M, Impivaara O, Maki J, *et al.* (2009) Vitamin D status and common risk factors for bone fragility as determinants of quantitative ultrasound variables in a nationally representative population sample. *Bone* **45**, 119–124.
49. Lamberg-Allardt CJ, Outila TA, Karkkainen MU, *et al.* (2001) Vitamin D deficiency and bone health in healthy adults in Finland: could this be a concern in other parts of Europe? *J Bone Miner Res* **16**, 2066–2073.
50. Mattila C, Knekt P, Mannisto S, *et al.* (2007) Serum 25-hydroxyvitamin D concentration and subsequent risk of type 2 diabetes. *Diabetes Care* **30**, 2569–2570.
51. Partti K, Heliovaara M, Impivaara O, *et al.* (2010) Skeletal status in psychotic disorders: a population-based study. *Psychosom Med* **72**, 933–940.
52. Parviainen MT, Kumpusalo E, Halonen P, *et al.* (1992) Epidemiology of vitamins A, E, D and C in rural villages in Finland: biochemical, nutritional and socioeconomic aspects. *Int J Vitam Nutr Res* **62**, 238–243.
53. Piirainen T, Laitinen K & Isolauri E (2007) Impact of national fortification of fluid milks and margarines with vitamin D on dietary intake and serum 25-hydroxyvitamin D concentration in 4-year-old children. *Eur J Clin Nutr* **61**, 123–128.
54. Viljakainen HT, Palssa A, Karkkainen M, *et al.* (2006) A seasonal variation of calcitropic hormones, bone turnover and bone mineral density in early and mid-puberty girls – a cross-sectional study. *Br J Nutr* **96**, 124–130.
55. Viljakainen HT, Saarnio E, Hytinantti T, *et al.* (2010) Maternal vitamin D status determines bone variables in the newborn. *J Clin Endocrinol Metab* **95**, 1749–1757.
56. Blain H, Jaussent A, Thomas E, *et al.* (2009) Low sit-to-stand performance is associated with low femoral neck bone mineral density in healthy women. *Calcif Tissue Int* **84**, 266–275.
57. Bougle D, Sabatier JP, Bureau F, *et al.* (1998) Relationship between bone mineralization and aluminium in the healthy infant. *Eur J Clin Nutr* **52**, 431–435.
58. Chapuy MC, Preziosi P, Maamer M, *et al.* (1997) Prevalence of vitamin D insufficiency in an adult normal population. *Osteoporos Int* **7**, 439–443.
59. de Carvalho MJ, Guillard JC, Moreau D, *et al.* (1996) Vitamin status of healthy subjects in Burgundy (France). *Ann Nutr Metab* **40**, 24–51.
60. Deplas A, Debais F, Alcalay M, *et al.* (2004) Bone density, parathyroid hormone, calcium and vitamin D nutritional status of institutionalized elderly subjects. *J Nutr Health Aging* **8**, 400–404.
61. Malvy DJ, Guinot C, Preziosi P, *et al.* (2000) Relationship between vitamin D status and skin phototype in general adult population. *Photochem Photobiol* **71**, 466–469.
62. Bramswig S, Zittermann A & Berthold HK (2003) Carbamazepine does not alter biochemical parameters of bone turnover in healthy male adults. *Calcif Tissue Int* **73**, 356–360.
63. Hintzpeter B, Mensink GB, Thierfelder W, *et al.* (2008) Vitamin D status and health correlates among German adults. *Eur J Clin Nutr* **62**, 1079–1089.
64. Scharla SH, Scheidt-Nave C, Leidig G, *et al.* (1996) Lower serum 25-hydroxyvitamin D is associated with increased bone resorption markers and lower bone density at the proximal femur in normal females: a population-based study. *Exp Clin Endocrinol Diabetes* **104**, 289–292.
65. Woitge HW, Knothe A, Witte K, *et al.* (2000) Circannual rhythms and interactions of vitamin D metabolites, parathyroid hormone, and biochemical markers of skeletal homeostasis: a prospective study. *J Bone Miner Res* **15**, 2443–2450.
66. Zittermann A, Scheld K & Stehle P (1998) Seasonal variations in vitamin D status and calcium absorption do not influence bone turnover in young women. *Eur J Clin Nutr* **52**, 501–506.
67. Nicolaidou P, Hatzistamatiou Z, Papadopoulou A, *et al.* (2006) Low vitamin D status in mother–newborn pairs in Greece. *Calcif Tissue Int* **78**, 337–342.
68. Papapetrou PD, Triantaphyllopoulou M, Karga H, *et al.* (2007) Vitamin D deficiency in the elderly in Athens, Greece. *J Bone Miner Metab* **25**, 198–203.
69. Kristinnsson JO, Valdimarsson O, Sigurdsson G, *et al.* (1998) Serum 25-hydroxyvitamin D levels and bone mineral density in 16–20 years-old girls: lack of association. *J Intern Med* **243**, 381–388.
70. Sigurdsson G, Franzson L, Steingrimsdottir L, *et al.* (2000) The association between parathyroid hormone, vitamin D and bone mineral density in 70-year-old Icelandic women. *Osteoporos Int* **11**, 1031–1035.
71. Steingrimsdottir L, Gunnarsson O, Indridason OS, *et al.* (2005) Relationship between serum parathyroid hormone levels, vitamin D sufficiency, and calcium intake. *J Am Med Assoc* **294**, 2336–2341.
72. Hill T, Collins A, O'Brien M, *et al.* (2005) Vitamin D intake and status in Irish postmenopausal women. *Eur J Clin Nutr* **59**, 404–410.
73. Keane EM, Healy M, O'Moore R, *et al.* (1995) Hypovitaminosis D in the healthy elderly. *Br J Clin Pract* **49**, 301–303.
74. Oren Y, Shapira Y, Agmon-Levin N, *et al.* (2010) Vitamin D insufficiency in a sunny environment: a demographic and seasonal analysis. *Israel Med Assoc J* **12**, 751–756.
75. Adami S, Viapiana O, Gatti D, *et al.* (2008) Relationship between serum parathyroid hormone, vitamin D sufficiency, age, and calcium intake. *Bone* **42**, 267–270.
76. Carnevale V, Modoni S, Pileri M, *et al.* (2001) Longitudinal evaluation of vitamin D status in healthy subjects from southern Italy: seasonal and gender differences. *Osteoporos Int* **12**, 1026–1030.
77. Romagnoli E, Caravella P, Scarnecchia L, *et al.* (1999) Hypovitaminosis D in an Italian population of healthy subjects and hospitalized patients. *Br J Nutr* **81**, 133–137.
78. Vezzoli G, Soldati L, Arcidiacono T, *et al.* (2005) Urinary calcium is a determinant of bone mineral density in elderly men participating in the InCHIANTI study. *Kidney Int* **67**, 2006–2014.
79. Al-Delaimy WK, Jansen EH, Peeters PH, *et al.* (2006) Reliability of biomarkers of iron status, blood lipids,

- oxidative stress, vitamin D, C-reactive protein and fructosamine in two Dutch cohorts. *Biomarkers* **11**, 370–382.
80. Baynes KC, Boucher BJ, Feskens EJ, *et al.* (1997) Vitamin D, glucose tolerance and insulinaemia in elderly men. *Diabetologia* **40**, 344–347.
81. Fang Y, van Meurs JB, Arp P, *et al.* (2009) Vitamin D binding protein genotype and osteoporosis. *Calcif Tissue Int* **85**, 85–93.
82. Kuchuk NO, Pluijm SM, van Schoor NM, *et al.* (2009) Relationships of serum 25-hydroxyvitamin D to bone mineral density and serum parathyroid hormone and markers of bone turnover in older persons. *J Clin Endocrinol Metab* **94**, 1244–1250.
83. Löwik MR, Schrijver J, Odink J, *et al.* (1990) Nutrition and aging: nutritional status of “apparently healthy” elderly (Dutch nutrition surveillance system). *J Am Coll Nutr* **9**, 18–27.
84. Pilz S, Dobnig H, Nijpels G, *et al.* (2009) Vitamin D and mortality in older men and women. *Clin Endocrinol (Oxf)* **71**, 666–672.
85. van Summeren MJ, van Coeverden SC, Schurgers LJ, *et al.* (2008) Vitamin K status is associated with childhood bone mineral content. *Br J Nutr* **100**, 852–858.
86. Brustad M, Sandanger T, Aksnes L, *et al.* (2004) Vitamin D status in a rural population of northern Norway with high fish liver consumption. *Public Health Nutr* **7**, 783–789.
87. Brustad M, Alsaker E, Engelsen O, *et al.* (2004) Vitamin D status of middle-aged women at 65–71 degrees N in relation to dietary intake and exposure to ultraviolet radiation. *Public Health Nutr* **7**, 327–335.
88. Grimnes G, Emaus N, Joakimsen RM, *et al.* (2010) Baseline serum 25-hydroxyvitamin D concentrations in the Tromsø Study 1994–95 and risk of developing type 2 diabetes mellitus during 11 years of follow-up. *Diabet Med* **27**, 1107–1115.
89. Meyer HE, Falch JA, Sogaard AJ, *et al.* (2004) Vitamin D deficiency and secondary hyperparathyroidism and the association with bone mineral density in persons with Pakistani and Norwegian background living in Oslo, Norway, The Oslo Health Study. *Bone* **35**, 412–417.
90. Napiorkowska L, Budlewski T, Jakubas-Kwiatkowska W, *et al.* (2009) Prevalence of low serum vitamin D concentration in an urban population of elderly women in Poland. *Pol Arch Med Wewn* **119**, 699–703.
91. Sapir-Koren R, Livshits G & Kobylansky E (2003) Genetic effects of estrogen receptor alpha and collagen IA1 genes on the relationships of parathyroid hormone and 25 hydroxyvitamin D with bone mineral density in Caucasian women. *Metabolism* **52**, 1129–1135.
92. Almirall J, Vaqueiro M, Bare ML, *et al.* (2010) Association of low serum 25-hydroxyvitamin D levels and high arterial blood pressure in the elderly. *Nephrol Dial Transplant* **25**, 503–509.
93. Gomez JM, Maravall FJ, Gomez N, *et al.* (2004) Relationship between 25-(OH) D₃, the IGF-I system, leptin, anthropometric and body composition variables in a healthy, randomly selected population. *Horm Metab Res* **36**, 48–53.
94. Moreiras O, Carbajal A, Perea I, *et al.* (1992) The influence of dietary intake and sunlight exposure on the vitamin D status in an elderly Spanish group. *Int J Vitam Nutr Res* **62**, 303–307.
95. Muray S, Marco MP, Craver L, *et al.* (2006) Influence of mineral metabolism parameters on pulse pressure in healthy subjects. *Clin Nephrol* **66**, 411–417.
96. Perez-Llamas F, Lopez-Contreras MJ, Blanco MJ, *et al.* (2008) Seemingly paradoxical seasonal influences on vitamin D status in nursing-home elderly people from a Mediterranean area. *Nutrition* **24**, 414–420.
97. Burgaz A, Akesson A, Oster A, *et al.* (2007) Associations of diet, supplement use, and ultraviolet B radiation exposure with vitamin D status in Swedish women during winter. *Am J Clin Nutr* **86**, 1399–1404.
98. Burgaz A, Akesson A, Michaelsson K, *et al.* (2009) 25-Hydroxyvitamin D accumulation during summer in elderly women at latitude 60 degrees N. *J Intern Med* **266**, 476–483.
99. Hagstrom E, Hellman P, Larsson TE, *et al.* (2009) Plasma parathyroid hormone and the risk of cardiovascular mortality in the community. *Circulation* **119**, 2765–2771.
100. Lind L, Hanni A, Lithell H, *et al.* (1995) Vitamin D is related to blood pressure and other cardiovascular risk factors in middle-aged men. *Am J Hypertens* **8**, 894–901.
101. Melin A, Wilske J, Ringertz H, *et al.* (2001) Seasonal variations in serum levels of 25-hydroxyvitamin D and parathyroid hormone but no detectable change in femoral neck bone density in an older population with regular outdoor exposure. *J Am Geriatr Soc* **49**, 1190–1196.
102. Salminen H, Saaf M, Ringertz H, *et al.* (2008) The role of IGF-I and IGFBP-1 status and secondary hyperparathyroidism in relation to osteoporosis in elderly Swedish women. *Osteoporos Int* **19**, 201–209.
103. Burnand B, Sloutskis D, Gianoli F, *et al.* (1992) Serum 25-hydroxyvitamin D: distribution and determinants in the Swiss population. *Am J Clin Nutr* **56**, 537–542.
104. Krieg MA, Cornuz J, Jacquet AF, *et al.* (1998) Influence of anthropometric parameters and biochemical markers of bone metabolism on quantitative ultrasound of bone in the institutionalized elderly. *Osteoporos Int* **8**, 115–120.
105. Bates CJ, Carter GD, Mishra GD, *et al.* (2003) In a population study, can parathyroid hormone aid the definition of adequate vitamin D status? A study of people aged 65 years and over from the British National Diet and Nutrition Survey. *Osteoporos Int* **14**, 152–159.
106. Carter JL, O’Riordan SE, Eaglestone GL, *et al.* (2008) Bone mineral metabolism and its relationship to kidney disease in a residential care home population: a cross-sectional study. *Nephrol Dial Transplant* **23**, 3554–3565.
107. Cashman KD, Hill TR, Cotter AA, *et al.* (2008) Low vitamin D status adversely affects bone health parameters in adolescents. *Am J Clin Nutr* **87**, 1039–1044.
108. Davies PS, Bates CJ, Cole TJ, *et al.* (1999) Vitamin D: seasonal and regional differences in preschool children in Great Britain. *Eur J Clin Nutr* **53**, 195–198.
109. Elia M & Stratton RJ (2005) Geographical inequalities in nutrient status and risk of malnutrition among English people aged 65 y and older. *Nutrition* **21**, 1100–1106.
110. Forouhi NG, Luan J, Cooper A, *et al.* (2008) Baseline serum 25-hydroxy vitamin D is predictive of future glycemic status and insulin resistance: the Medical Research Council Ely Prospective Study 1990–2000. *Diabetes* **57**, 2619–2625.
111. Hegarty V, Woodhouse P & Khaw KT (1994) Seasonal variation in 25-hydroxyvitamin D and parathyroid hormone concentrations in healthy elderly people. *Age Ageing* **23**, 478–482.
112. Hill TR, Cotter AA, Mitchell S, *et al.* (2008) Vitamin D status and its determinants in adolescents from the Northern Ireland Young Hearts 2000 cohort. *Br J Nutr* **99**, 1061–1067.
113. Hirani V & Primatesta P (2005) Vitamin D concentrations among people aged 65 years and over living in private households and institutions in England: population survey. *Age Ageing* **34**, 485–491.

114. Hypponen E & Power C (2007) Hypovitaminosis D in British adults at age 45 y: nationwide cohort study of dietary and lifestyle predictors. *Am J Clin Nutr* **85**, 860–868.
115. Macdonald HM, McGuigan FE, Stewart A, *et al.* (2006) Large-scale population-based study shows no evidence of association between common polymorphism of the VDR gene and BMD in British women. *J Bone Miner Res* **21**, 151–162.
116. Mavroiedi A, O'Neill F, Lee PA, *et al.* (2010) Seasonal 25-hydroxyvitamin D changes in British postmenopausal women at 57 degrees N and 51 degrees N: a longitudinal study. *J Steroid Biochem Mol Biol* **121**, 459–461.
117. Wareham NJ, Byrne CD, Carr C, *et al.* (1997) Glucose intolerance is associated with altered calcium homeostasis: a possible link between increased serum calcium concentration and cardiovascular disease mortality. *Metabolism* **46**, 1171–1177.
118. Barake R, Weiler H, Payette H, *et al.* (2010) Vitamin D supplement consumption is required to achieve a minimal target 25-hydroxyvitamin D concentration of > or =75 nmol/l in older people. *J Nutr* **140**, 551–556.
119. El Hayek J, Egeland G & Weiler H (2010) Vitamin D status of Inuit preschoolers reflects season and vitamin D intake. *J Nutr* **140**, 1839–1845.
120. Langlois K, Greene-Finestone L, Little J, *et al.* (2010) Vitamin D status of Canadians as measured in the 2007 to 2009 Canadian Health Measures Survey. *Health Rep* **21**, 47–55.
121. Lebrun JB, Moffatt ME, Mundy RJ, *et al.* (1993) Vitamin D deficiency in a Manitoba community. *Can J Public Health* **84**, 394–396.
122. Liu BA, Gordon M, Labranche JM, *et al.* (1997) Seasonal prevalence of vitamin D deficiency in institutionalized older adults. *J Am Geriatr Soc* **45**, 598–603.
123. Mark S, Gray-Donald K, Delvin EE, *et al.* (2008) Low vitamin D status in a representative sample of youth from Quebec, Canada. *Clin Chem* **54**, 1283–1289.
124. Newhook LA, Sloka S, Grant M, *et al.* (2009) Vitamin D insufficiency common in newborns, children and pregnant women living in Newfoundland and Labrador, Canada. *Matern Child Nutr* **5**, 186–191.
125. Overton TR & Basu TK (1999) Longitudinal changes in radial bone density in older men. *Eur J Clin Nutr* **53**, 211–215.
126. Rucker D, Allan JA, Fick GH, *et al.* (2002) Vitamin D insufficiency in a population of healthy western Canadians. *Can Med Assoc J* **166**, 1517–1524.
127. Sinotte M, Diorio C, Berube S, *et al.* (2009) Genetic polymorphisms of the vitamin D binding protein and plasma concentrations of 25-hydroxyvitamin D in premenopausal women. *Am J Clin Nutr* **89**, 634–640.
128. Alvarez JA, Ashraf AP, Hunter GR, *et al.* (2010) Serum 25-hydroxyvitamin D and parathyroid hormone are independent determinants of whole-body insulin sensitivity in women and may contribute to lower insulin sensitivity in African Americans. *Am J Clin Nutr* **92**, 1344–1349.
129. Arunabh S, Pollack S, Yeh J, *et al.* (2003) Body fat content and 25-hydroxyvitamin D levels in healthy women. *J Clin Endocrinol Metab* **88**, 157–161.
130. Avery E, Kleppinger A, Feinn R, *et al.* (2010) Determinants of living situation in a population of community-dwelling and assisted living-dwelling elders. *J Am Med Dir Assoc* **11**, 140–144.
131. Chai W, Maskarinec G & Cooney RV (2010) Serum 25-hydroxyvitamin D levels and mammographic density among premenopausal women in a multiethnic population. *Eur J Clin Nutr* **64**, 652–654.
132. Cheng S, Massaro JM, Fox CS, *et al.* (2010) Adiposity, cardiometabolic risk, and vitamin D status: the Framingham Heart Study. *Diabetes* **59**, 242–248.
133. Dawson-Hughes B, Harris SS & Dallal GE (1997) Plasma calcidiol, season, and serum parathyroid hormone concentrations in healthy elderly men and women. *Am J Clin Nutr* **65**, 67–71.
134. Dror DK, King JC, Durand DJ, *et al.* (2011) Association of modifiable and nonmodifiable factors with vitamin D status in pregnant women and neonates in Oakland, CA. *J Am Diet Assoc* **111**, 111–116.
135. Looker AC, Dawson-Hughes B, Calvo MS, *et al.* (2002) Serum 25-hydroxyvitamin D status of adolescents and adults in two seasonal subpopulations from NHANES III. *Bone* **30**, 771–777.
136. Hannan MT, Felson DT, Dawson-Hughes B, *et al.* (2000) Risk factors for longitudinal bone loss in elderly men and women: the Framingham Osteoporosis Study. *J Bone Miner Res* **15**, 710–720.
137. Hill KM, McCabe GP, McCabe LD, *et al.* (2010) An inflection point of serum 25-hydroxyvitamin D for maximal suppression of parathyroid hormone is not evident from multi-site pooled data in children and adolescents. *J Nutr* **140**, 1983–1988.
138. Iannuzzi-Sucich M, Prestwood KM & Kenny AM (2002) Prevalence of sarcopenia and predictors of skeletal muscle mass in healthy, older men and women. *J Gerontol A Biol Sci Med Sci* **57**, 772–777.
139. Ilich JZ, Brownbill RA & Tamborini L (2003) Bone and nutrition in elderly women: protein, energy, and calcium as main determinants of bone mineral density. *Eur J Clin Nutr* **57**, 554–565.
140. Jacques PF, Felson DT, Tucker KL, *et al.* (1997) Plasma 25-hydroxyvitamin D and its determinants in an elderly population sample. *Am J Clin Nutr* **66**, 929–936.
141. Johnson MA, Davey A, Park S, *et al.* (2008) Age, race and season predict vitamin status in African American and white octogenarians and centenarians. *J Nutr Health Aging* **12**, 690–695.
142. Khosla S, Atkinson EJ, Melton IJ, *et al.* (1997) Effects of age and estrogen status on serum parathyroid hormone levels and biochemical markers of bone turnover in women: a population-based study. *J Clin Endocrinol Metab* **82**, 1522–1527.
143. Kim DH, Sabour S, Sagar UN, *et al.* (2008) Prevalence of hypovitaminosis D in cardiovascular diseases (from the National Health and Nutrition Examination Survey 2001 to 2004). *Am J Cardiol* **102**, 1540–1544.
144. Kremer R, Campbell PP, Reinhardt T, *et al.* (2009) Vitamin D status and its relationship to body fat, final height, and peak bone mass in young women. *J Clin Endocrinol Metab* **94**, 67–73.
145. Lappe JM, Davies KM, Travers-Gustafson D, *et al.* (2006) Vitamin D status in a rural postmenopausal female population. *J Am Coll Nutr* **25**, 395–402.
146. Mansbach JM, Ginde AA, Camargo CA, *et al.* (2009) Serum 25-hydroxyvitamin D levels among US children aged 1 to 11 years: do children need more vitamin D? *Pediatrics* **124**, 1404–1410.
147. Mirza FS, Padhi ID, Raisz LG, *et al.* (2010) Serum sclerostin levels negatively correlate with parathyroid hormone levels and free estrogen index in postmenopausal women. *J Clin Endocrinol Metab* **95**, 1991–1997.
148. Reis JP, von Muhlen D, Michos ED, *et al.* (2009) Serum vitamin D, parathyroid hormone levels, and carotid atherosclerosis. *Atherosclerosis* **207**, 585–590.
149. Rock CL, Thornquist MD, Kristal AR, *et al.* (1999) Demographic, dietary and lifestyle factors differentially explain variability in serum carotenoids and fat-soluble vitamins:

- baseline results from the sentinel site of the Olestra Post-Marketing Surveillance Study. *J Nutr* **129**, 855–864.
150. Sabetta JR, DePetrillo P, Cipriani RJ, *et al.* (2010) Serum 25-hydroxyvitamin D and the incidence of acute viral respiratory tract infections in healthy adults. *PLoS One* **5**, 11088.
 151. Shea MK, Booth SL, Massaro JM, *et al.* (2008) Vitamin K and vitamin D status: associations with inflammatory markers in the Framingham Offspring Study. *Am J Epidemiol* **167**, 313–320.
 152. Stein EM, Laing EM, Hall DB, *et al.* (2006) Serum 25-hydroxyvitamin D concentrations in girls aged 4–8 y living in the southeastern United States. *Am J Clin Nutr* **83**, 75–81.
 153. Sullivan SS, Rosen CJ, Halteman WA, *et al.* (2005) Adolescent girls in Maine are at risk for vitamin D insufficiency. *J Am Diet Assoc* **105**, 971–974.
 154. Weng FL, Shults J, Leonard MB, *et al.* (2007) Risk factors for low serum 25-hydroxyvitamin D concentrations in otherwise healthy children and adolescents. *Am J Clin Nutr* **86**, 150–158.
 155. Bowyer L, Catling-Paull C, Diamond T, *et al.* (2009) Vitamin D, PTH and calcium levels in pregnant women and their neonates. *Clin Endocrinol (Oxf)* **70**, 372–377.
 156. Brock K, Wilkinson M, Cook R, *et al.* (2004) Associations with vitamin D deficiency in “at risk” Australians. *J Steroid Biochem Mol Biol* **89–90**, 581–588.
 157. Center JR, Nguyen TV, Sambrook PN, *et al.* (1999) Hormonal and biochemical parameters in the determination of osteoporosis in elderly men. *J Clin Endocrinol Metab* **84**, 3626–3635.
 158. Ding C, Cicuttini F, Parameswaran V, *et al.* (2009) Serum levels of vitamin D, sunlight exposure, and knee cartilage loss in older adults: the Tasmanian older adult cohort study. *Arthritis Rheum* **60**, 1381–1389.
 159. Ngo DT, Sverdlow AL, McNeil JJ, *et al.* (2010) Does vitamin D modulate asymmetric dimethylarginine and C-reactive protein concentrations? *Am J Med* **123**, 335–341.
 160. Pasco JA, Henry MJ, Nicholson GC, *et al.* (2001) Vitamin D status of women in the Geelong Osteoporosis Study: association with diet and casual exposure to sunlight. *Med J Aust* **175**, 401–405.
 161. Stein MS, Scherer SC, Walton SL, *et al.* (1996) Risk factors for secondary hyperparathyroidism in a nursing home population. *Clin Endocrinol (Oxf)* **44**, 375–383.
 162. Zochling J, Sitoh YY, Lau TC, *et al.* (2002) Quantitative ultrasound of the calcaneus and falls risk in the institutionalized elderly: sex differences and relationship to vitamin D status. *Osteoporos Int* **13**, 882–887.
 163. Abnet CC, Chen W, Dawsey SM, *et al.* (2007) Serum 25(OH)-vitamin D concentration and risk of esophageal squamous dysplasia. *Cancer Epidemiol Biomarkers Prev* **16**, 1889–1893.
 164. Chan EL, Lau E, Shek CC, *et al.* (1992) Age-related changes in bone density, serum parathyroid hormone, calcium absorption and other indices of bone metabolism in Chinese women. *Clin Endocrinol (Oxf)* **36**, 375–381.
 165. Chen W, Dawsey SM, Qiao YL, *et al.* (2007) Prospective study of serum 25(OH)-vitamin D concentration and risk of oesophageal and gastric cancers. *Br J Cancer* **97**, 123–128.
 166. Du X, Greenfield H, Fraser DR, *et al.* (2001) Vitamin D deficiency and associated factors in adolescent girls in Beijing. *Am J Clin Nutr* **74**, 494–500.
 167. Strand MA, Perry J, Zhao J, *et al.* (2009) Severe vitamin D-deficiency and the health of North China children. *Matern Child Health J* **13**, 144–150.
 168. Tsai KS, Hsu SH, Cheng JP, *et al.* (1997) Vitamin D stores of urban women in Taipei: effect on bone density and bone turnover, and seasonal variation. *Bone* **20**, 371–374.
 169. Heere C, Skeaff CM, Waqatakiwewa L, *et al.* (2010) Serum 25-hydroxyvitamin D concentration of Indigenous-Fijian and Fijian-Indian women. *Asia Pac J Clin Nutr* **19**, 43–48.
 170. Goswami R, Kochupillai N, Gupta N, *et al.* (2008) Presence of 25(OH)D deficiency in a rural North Indian village despite abundant sunshine. *J Assoc Physicians India* **56**, 755–757.
 171. Harinarayan CV, Ramalakshmi T, Prasad UV, *et al.* (2007) High prevalence of low dietary calcium, high phytate consumption, and vitamin D deficiency in healthy south Indians. *Am J Clin Nutr* **85**, 1062–1067.
 172. Sachan A, Gupta R, Das V, *et al.* (2005) High prevalence of vitamin D deficiency among pregnant women and their newborns in northern India. *Am J Clin Nutr* **81**, 1060–1064.
 173. Rinaldi I, Setiati S, Oemardi M, *et al.* (2007) Correlation between serum vitamin D (25(OH)D) concentration and quadriceps femoris muscle strength in Indonesian elderly women living in three nursing homes. *Acta Med Indones* **39**, 107–111.
 174. Setiati S (2008) Vitamin D status among Indonesian elderly women living in institutionalized care units. *Acta Med Indones* **40**, 78–83.
 175. Kuwabara A, Himeno M, Tsugawa N, *et al.* (2010) Hypovitaminosis D and K are highly prevalent and independent of overall malnutrition in the institutionalized elderly. *Asia Pac J Clin Nutr* **19**, 49–56.
 176. Kwon J, Suzuki T, Yoshida H, *et al.* (2007) Concomitant lower serum albumin and vitamin D levels are associated with decreased objective physical performance among Japanese community-dwelling elderly. *Gerontology* **53**, 322–328.
 177. Nakamura K, Nashimoto M, Hori Y, *et al.* (1999) Serum 25-hydroxyvitamin D levels in active women of middle and advanced age in a rural community in Japan. *Nutrition* **15**, 870–873.
 178. Nakamura K, Nashimoto M & Yamamoto M (2001) Are the serum 25-hydroxyvitamin D concentrations in winter associated with forearm bone mineral density in healthy elderly Japanese women? *Int J Vitam Nutr Res* **71**, 25–29.
 179. Suzuki T, Kwon J, Kim H, *et al.* (2008) Low serum 25-hydroxyvitamin D levels associated with falls among Japanese community-dwelling elderly. *J Bone Miner Res* **23**, 1309–1317.
 180. Rahman SA, Chee WS, Yassin Z, *et al.* (2004) Vitamin D status among postmenopausal Malaysian women. *Asia Pac J Clin Nutr* **13**, 255–260.
 181. Lander RL, Enkhjargal T, Batjargal J, *et al.* (2008) Multiple micronutrient deficiencies persist during early childhood in Mongolia. *Asia Pac J Clin Nutr* **17**, 429–440.
 182. Bolland MJ, Grey AB, Ames RW, *et al.* (2006) Determinants of vitamin D status in older men living in a subtropical climate. *Osteoporos Int* **17**, 1742–1748.
 183. Bolland MJ, Grey AB, Ames RW, *et al.* (2006) Fat mass is an important predictor of parathyroid hormone levels in postmenopausal women. *Bone* **38**, 317–321.
 184. Bolland MJ, Grey AB, Ames RW, *et al.* (2007) Age-, gender-, and weight-related effects on levels of 25-hydroxyvitamin D are not mediated by vitamin D binding protein. *Clin Endocrinol (Oxf)* **67**, 259–264.
 185. Camargo CA Jr, Ingham T, Wickens K, *et al.* (2010) Vitamin D status of newborns in New Zealand. *Br J Nutr* **104**, 1051–1057.



186. Grant CC, Wall CR, Crengle S, *et al.* (2009) Vitamin D deficiency in early childhood: prevalent in the sunny South Pacific. *Public Health Nutr* **12**, 1893–1901.
187. Houghton LA, Szymlek-Gay EA, Gray AR, *et al.* (2010) Predictors of vitamin D status and its association with parathyroid hormone in young New Zealand children. *Am J Clin Nutr* **92**, 69–76.
188. Ley SJ, Horwath CC & Stewart JM (1999) Attention is needed to the high prevalence of vitamin D deficiency in our older population. *N Z Med J* **112**, 471–472.
189. Lucas JA, Bolland MJ, Grey AB, *et al.* (2005) Determinants of vitamin D status in older women living in a subtropical climate. *Osteoporos Int* **16**, 1641–1648.
190. Rockell JE, Green TJ, Skeaff CM, *et al.* (2005) Season and ethnicity are determinants of serum 25-hydroxyvitamin D concentrations in New Zealand children aged 5–14 y. *J Nutr* **135**, 2602–2608.
191. Rockell JE, Skeaff CM, Williams SM, *et al.* (2008) Association between quantitative measures of skin color and plasma 25-hydroxyvitamin D. *Osteoporos Int* **19**, 1639–1642.
192. Scragg R, Holdaway I, Jackson R, *et al.* (1992) Plasma 25-hydroxyvitamin D₃ and its relation to physical activity and other heart disease risk factors in the general population. *Ann Epidemiol* **2**, 697–703.
193. Kim MK, Il Kang M, Won Oh K, *et al.* (2010) The association of serum vitamin D level with presence of metabolic syndrome and hypertension in middle-aged Korean subjects. *Clin Endocrinol* **73**, 330–338.
194. Namgung R, Tsang RC, Lee C, *et al.* (1998) Low total body bone mineral content and high bone resorption in Korean winter-born versus summer-born newborn infants. *J Pediatr* **132**, 421–425.
195. Chailurkit LO, Rajatanavin R, Teerarungsikul K, *et al.* (1996) Serum vitamin D, parathyroid hormone and biochemical markers of bone turnover in normal Thai subjects. *J Med Assoc Thai* **79**, 499–504.
196. Chailurkit LO, Pongchaiyakul C, Charoenkiatkul S, *et al.* (2001) Different mechanism of bone loss in ageing women and men in Khon Kaen Province. *J Med Assoc Thai* **84**, 1175–1182.
197. Chailurkit LO, Piaseu N & Rajatanavin R (2002) Influence of normal ageing on mechanism of bone loss in women and men in Bangkok. *J Med Assoc Thai* **85**, 915–921.
198. Soontrapa S, Boonsiri P & Khampitak T (2009) The prevalence of hypovitaminosis D in the elderly women living in the rural area of Khon Kaen Province, Thailand. *J Med Assoc Thai* **92**, S21–S25.
199. Ho-Pham LT, Nguyen ND, Lai TQ, *et al.* (2011) Vitamin D status and parathyroid hormone in a urban population in Vietnam. *Osteoporos Int* **22**, 241–248.
200. Njemini R, Meyers I, Demanet C, *et al.* (2002) The prevalence of autoantibodies in an elderly sub-Saharan African population. *Clin Exp Immunol* **127**, 99–106.
201. Bassir M, Laborie S, Lapillonne A, *et al.* (2001) Vitamin D deficiency in Iranian mothers and their neonates: a pilot study. *Acta Paediatr* **90**, 577–579.
202. Dahifan H, Faraji A, Yassobi S, *et al.* (2007) Asymptomatic rickets in adolescent girls. *Indian J Pediatr* **74**, 571–575.
203. Hashemipour S, Larijani B, Adibi H, *et al.* (2004) Vitamin D deficiency and causative factors in the population of Tehran. *BMC Public Health* **4**, 38.
204. Hossein-Nezhad A, Khoshniat Nikoo M, Maghbooli Z, *et al.* (2009) Relationship between serum vitamin D concentration and metabolic syndrome among Iranian adults population. *DARU* **17**, 1–5.
205. Hosseinpanah F, Rambod M, Hossein-nejad A, *et al.* (2008) Association between vitamin D and bone mineral density in Iranian postmenopausal women. *J Bone Miner Metab* **26**, 86–92.
206. Kazemi A, Sharifi F, Jafari N, *et al.* (2009) High prevalence of vitamin D deficiency among pregnant women and their newborns in an Iranian population. *J Womens Health (Larchmt)* **18**, 835–839.
207. Masoompour SM, Sadegholvaad A, Larijani B, *et al.* (2008) Effects of age and renal function on vitamin D status in men. *Arch Iran Med* **11**, 377–381.
208. Mirsaeid Ghazi AA, Rais Zadeh F, Pezeshk P, *et al.* (2004) Seasonal variation of serum 25 hydroxy D₃ in residents of Tehran. *J Endocrinol Invest* **27**, 676–679.
209. Mousavi M, Heidarpour R, Aminorroaya A, *et al.* (2005) Prevalence of vitamin D deficiency in Isfahani high school students in 2004. *Horm Res* **64**, 144–148.
210. Niafar M, Bahrami A, Aliasgharzadeh A, *et al.* (2009) Vitamin D status in healthy postmenopausal Iranian women. *J Res Med Sci* **14**, 171–177.
211. Rabbani A, Alavian SM, Motlagh ME, *et al.* (2009) Vitamin D insufficiency among children and adolescents living in Tehran, Iran. *J Trop Pediatr* **55**, 189–191.
212. Salek M, Hashemipour M, Aminorroaya A, *et al.* (2008) Vitamin D deficiency among pregnant women and their newborns in Isfahan, Iran. *Exp Clin Endocrinol Diabetes* **116**, 352–356.
213. Arabi A, Baddoura R, El-Rassi R, *et al.* (2010) Age but not gender modulates the relationship between PTH and vitamin D. *Bone* **47**, 408–412.
214. Gannage-Yared MH, Chemali R, Yaacoub N, *et al.* (2000) Hypovitaminosis D in a sunny country: relation to lifestyle and bone markers. *J Bone Miner Res* **15**, 1856–1862.
215. Pfitzner MA, Thacher TD, Pettifor JM, *et al.* (1998) Absence of vitamin D deficiency in young Nigerian children. *J Pediatr* **133**, 740–744.
216. Charlton KE, Labadarios D, Lombard CJ, *et al.* (1996) Vitamin D status of older South Africans. *S Afr Med J* **86**, 1406–1410.
217. Aspray TJ, Yan L & Prentice A (2005) Parathyroid hormone and rates of bone formation are raised in perimenopausal rural Gambian women. *Bone* **36**, 710–720.
218. Oliveri MB, Ladizesky M, Mautalen CA, *et al.* (1993) Seasonal variations of 25 hydroxyvitamin D and parathyroid hormone in Ushuaia (Argentina), the southernmost city of the world. *Bone Miner* **20**, 99–108.
219. Canto-Costa MH, Kunii I & Hauache OM (2006) Body fat and cholecalciferol supplementation in elderly homebound individuals. *Braz J Med Biol Res* **39**, 91–98.
220. Saraiva GL, Cendoroglo MS, Ramos LR, *et al.* (2005) Influence of ultraviolet radiation on the production of 25 hydroxyvitamin D in the elderly population in the city of Sao Paulo (23 degrees 34'S), Brazil. *Osteoporos Int* **16**, 1649–1654.
221. Breen ME, Laing EM, Hall DB, *et al.* (2011) 25-Hydroxyvitamin D, insulin-like growth factor-I, and bone mineral accrual during growth. *J Clin Endocrinol Metab* **96**, 89–98.
222. Rolland YM, Perry HM 3rd, Patrick P, *et al.* (2007) Loss of appendicular muscle mass and loss of muscle strength in young postmenopausal women. *J Gerontol A Biol Sci Med Sci* **62**, 330–335.
223. Sadideen H & Swaminathan R (2004) Effect of acute oral calcium load on serum PTH and bone resorption in young healthy subjects: an overnight study. *Eur J Clin Nutr* **58**, 1661–1665.

224. Boonen S, Cheng XG, Nijs J, *et al.* (1997) Factors associated with cortical and trabecular bone loss as quantified by peripheral computed tomography (pQCT) at the ultradistal radius in aging women. *Calcif Tissue Int* **60**, 164–170.
225. Boonen S, Lesaffre E, Dequeker J, *et al.* (1996) Relationship between baseline insulin-like growth factor-I (IGF-I) and femoral bone density in women aged over 70 years: potential implications for the prevention of age-related bone loss. *J Am Geriatr Soc* **44**, 1301–1306.
226. Kilkkinen A, Knekt P, Aro A, *et al.* (2009) Vitamin D status and the risk of cardiovascular disease death. *Am J Epidemiol* **170**, 1032–1039.
227. Kilkkinen A, Knekt P, Heliövaara M, *et al.* (2008) Vitamin D status and the risk of lung cancer: a cohort study in Finland. *Cancer Epidemiol Biomarkers Prev* **17**, 3274–3278.
228. Woitge HW, Scheidt-Nave C, Kissling C, *et al.* (1998) Seasonal variation of biochemical indexes of bone turnover: results of a population-based study. *J Clin Endocrinol Metab* **83**, 68–75.
229. Hill TR, McCarthy D, Jakobsen J, *et al.* (2007) Seasonal changes in vitamin D status and bone turnover in healthy Irish postmenopausal women. *Int J Vitam Nutr Res* **77**, 320–325.
230. Hill TR, O'Brien MM, Lamberg-Allardt C, *et al.* (2006) Vitamin D status of 51–75-year-old Irish women: its determinants and impact on biochemical indices of bone turnover. *Public Health Nutr* **9**, 225–233.
231. McCarthy D, Collins A, O'Brien M, *et al.* (2006) Vitamin D intake and status in Irish elderly women and adolescent girls. *Ir J Med Sci* **175**, 14–20.
232. Atherton K, Berry DJ, Parsons T, *et al.* (2009) Vitamin D and chronic widespread pain in a white middle-aged British population: evidence from a cross-sectional population survey. *Ann Rheum Dis* **68**, 817–822.
233. Hyppönen E, Berry D, Cortina-Borja M, *et al.* (2010) 25-Hydroxyvitamin D and pre-clinical alterations in inflammatory and hemostatic markers: a cross sectional analysis in the 1958 British Birth Cohort. *PLoS One* **5**, 10801.
234. Hyppönen E, Boucher BJ, Berry DJ, *et al.* (2008) 25-Hydroxyvitamin D, IGF-1, and metabolic syndrome at 45 years of age: a cross-sectional study in the 1958 British Birth Cohort. *Diabetes* **57**, 298–305.
235. Hirani V, Tull K, Ali A, *et al.* (2010) Urgent action needed to improve vitamin D status among older people in England! *Age Ageing* **39**, 62–68.
236. Macdonald HM, Mavroeidi A, Barr RJ, *et al.* (2008) Vitamin D status in postmenopausal women living at higher latitudes in the UK in relation to bone health, overweight, sunlight exposure and dietary vitamin D. *Bone* **42**, 996–1003.
237. Barake R, Weiler H, Payette H, *et al.* (2010) Vitamin D status in healthy free-living elderly men and women living in Quebec, Canada. *J Am Coll Nutr* **29**, 25–30.
238. Kiel DP, Myers RH, Cupples LA, *et al.* (1997) The Bsm1 vitamin D receptor restriction fragment length polymorphism (bb) influences the effect of calcium intake on bone mineral density. *J Bone Miner Res* **12**, 1049–1057.
239. Camargo CA Jr, Ingham T, Wickens K, *et al.* (2011) Cord-blood 25-hydroxyvitamin D levels and risk of respiratory infection, wheezing, and asthma. *Pediatrics* **127**, 180–187.
240. Bolland MJ, Grey AB, Ames RW, *et al.* (2007) The effects of seasonal variation of 25-hydroxyvitamin D and fat mass on a diagnosis of vitamin D sufficiency. *Am J Clin Nutr* **86**, 959–964.
241. Harinarayan CV, Ramalakshmi T, Prasad UV, *et al.* (2008) Vitamin D status in Andhra Pradesh: a population based study. *Indian J Med Res* **127**, 211–218.
242. von Muhlen DG, Greendale GA, Garland CF, *et al.* (2005) Vitamin D, parathyroid hormone levels and bone mineral density in community-dwelling older women: the Rancho Bernardo Study. *Osteoporos Int* **16**, 1721–1726.
243. Badalian SS & Rosenbaum PF (2010) Vitamin D and pelvic floor disorders in women: results from the national health and nutrition examination survey. *Obstet Gynecol Surv* **115**, 795–803.
244. Forrest KYZ & Stuhldreher WL (2011) Prevalence and correlates of vitamin D deficiency in US adults. *Nutr Res* **31**, 48–54.
245. Skinner HG & Schwartz GG (2009) The relation of serum parathyroid hormone and serum calcium to serum levels of prostate-specific antigen: a population-based study. *Cancer Epidemiol Biomarkers Prev* **18**, 2869–2873.
246. Harkness LS & Cromer BA (2005) Vitamin D deficiency in adolescent females. *J Adolesc Health* **37**, 75.
247. Looker AC, Pfeiffer CM, Lacher DA, *et al.* (2008) Serum 25-hydroxyvitamin D status of the US population: 1988–1994 compared with 2000–2004. *Am J Clin Nutr* **88**, 1519–1527.
248. Reis JP, von Muhlen D, Miller ER, *et al.* (2008) Relation of 25-hydroxyvitamin D and parathyroid hormone levels with metabolic syndrome among US adults. *Eur J Endocrinol* **159**, 41–48.
249. Reis JP, von Muhlen D, Miller ER, *et al.* (2009) Vitamin D status and cardiometabolic risk factors in the United States adolescent population. *Pediatrics* **124**, 371–379.
250. Gilsanz V, Kremer A, Mo AO, *et al.* (2010) Vitamin D status and its relation to muscle mass and muscle fat in young women. *J Clin Endocrinol Metab* **95**, 1595–1601.
251. Melhus H, Snellman G, Gedeberg R, *et al.* (2010) Plasma 25-hydroxyvitamin D levels and fracture risk in a community-based cohort of elderly men in Sweden. *J Clin Endocrinol Metab* **95**, 2637–2645.
252. Theiler R, Stahelin HB, Kranzlin M, *et al.* (1999) High bone turnover in the elderly. *Arch Phys Med Rehabil* **80**, 485–489.
253. Grimnes G, Almaas B, Eggen AE, *et al.* (2010) Effect of smoking on the serum levels of 25-hydroxyvitamin D depends on the assay employed. *Eur J Endocrinol* **163**, 339–348.
254. Jorde R, Figenschau Y, Emaus N, *et al.* (2010) Serum 25-hydroxyvitamin D levels are strongly related to systolic blood pressure but do not predict future hypertension. *Hypertension* **55**, 792–798.
255. Jorde R, Sneve M, Hutchinson M, *et al.* (2010) Tracking of serum 25-hydroxyvitamin D levels during 14 years in a population-based study and during 12 months in an intervention study. *Am J Epidemiol* **171**, 903–908.
256. Buizert PJ, van Schoor NM, Lips P, *et al.* (2009) Lipid levels: a link between cardiovascular disease and osteoporosis? *J Bone Miner Res* **24**, 1103–1109.
257. de Jongh RT, Lips P, Rijs KJ, *et al.* (2011) Associations between vitamin D receptor genotypes and mortality in a cohort of older Dutch individuals. *Eur J Endocrinol* **164**, 75–82.
258. Hoogendijk WJ, Lips P, Dik MG, *et al.* (2008) Depression is associated with decreased 25-hydroxyvitamin D and increased parathyroid hormone levels in older adults. *Arch Gen Psychiatry* **65**, 508–512.
259. van Schoor NM, Visser M, Pluijm SM, *et al.* (2008) Vitamin D deficiency as a risk factor for osteoporotic fractures. *Bone* **42**, 260–266.
260. Wicherts IS, van Schoor NM, Boeke AJ, *et al.* (2007) Vitamin D status predicts physical performance and its decline in older persons. *J Clin Endocrinol Metab* **92**, 2058–2065.
261. Hicks GE, Shardell M, Miller RR, *et al.* (2008) Associations between vitamin D status and pain in older adults: the Invecchiare in Chianti study. *J Am Geriatr Soc* **56**, 785–791.
262. Houston DK, Cesari M, Ferrucci L, *et al.* (2007) Association between vitamin D status and physical performance: the InCHIANTI study. *J Gerontol A Biol Sci Med Sci* **62**, 440–446.



263. Lauretani F, Bandinelli S, Russo CR, *et al.* (2006) Correlates of bone quality in older persons. *Bone* **39**, 915–921.
264. Semba RD, Houston DK, Bandinelli S, *et al.* (2010) Relationship of 25-hydroxyvitamin D with all-cause and cardiovascular disease mortality in older community-dwelling adults. *Eur J Clin Nutr* **64**, 203–209.
265. Bischoff-Ferrari HA, Kiel DP, Dawson-Hughes B, *et al.* (2009) Dietary calcium and serum 25-hydroxyvitamin D status in relation to BMD among U.S. adults. *J Bone Miner Res* **24**, 935–942.
266. Black PN & Scragg R (2005) Relationship between serum 25-hydroxyvitamin D and pulmonary function in the Third National Health and Nutrition Examination Survey. *Chest* **128**, 3792–3798.
267. Chonchol M & Scragg R (2007) 25-Hydroxyvitamin D, insulin resistance, and kidney function in the Third National Health and Nutrition Examination Survey. *Kidney Int* **71**, 134–139.
268. de Boer IH, Ioannou GN, Kestenbaum B, *et al.* (2007) 25-Hydroxyvitamin D levels and albuminuria in the Third National Health and Nutrition Examination Survey (NHANES III). *Am J Kidney Dis* **50**, 69–77.
269. Dietrich T, Joshipura KJ, Dawson-Hughes B, *et al.* (2004) Association between serum concentrations of 25-hydroxyvitamin D₃ and periodontal disease in the US population. *Am J Clin Nutr* **80**, 108–113.
270. Ford ES, Ajani UA, McGuire LC, *et al.* (2005) Concentrations of serum vitamin D and the metabolic syndrome among U.S. adults. *Diabetes Care* **28**, 1228–1230.
271. Freedman DM, Looker AC, Abnet CC, *et al.* (2010) Serum 25-hydroxyvitamin D and cancer mortality in the NHANES III study (1988–2006). *Cancer Res* **70**, 8587–8597.
272. Ganji V, Milone C, Cody MM, *et al.* (2010) Serum vitamin D concentrations are related to depression in young adult US population: the Third National Health and Nutrition Examination Survey. *Int Arch Med* **3**, 29.
273. Kant AK & Graubard BI (2008) Ethnic and socioeconomic differences in variability in nutritional biomarkers. *Am J Clin Nutr* **87**, 1464–1471.
274. Kendrick J, Targher G, Smits G, *et al.* (2009) 25-Hydroxyvitamin D deficiency is independently associated with cardiovascular disease in the Third National Health and Nutrition Examination Survey. *Atherosclerosis* **205**, 255–260.
275. Looker AC & Mussolino ME (2008) Serum 25-hydroxyvitamin D and hip fracture risk in older U.S. white adults. *J Bone Miner Res* **23**, 143–150.
276. Martins D, Wolf M, Pan D, *et al.* (2007) Prevalence of cardiovascular risk factors and the serum levels of 25-hydroxyvitamin D in the United States: data from the Third National Health and Nutrition Examination Survey. *Arch Intern Med* **167**, 1159–1165.
277. Saintonge S, Bang H & Gerber LM (2009) Implications of a new definition of vitamin D deficiency in a multiracial US adolescent population: the National Health and Nutrition Examination Survey III. *Pediatrics* **123**, 797–803.
278. Scragg R & Camargo CA Jr (2008) Frequency of leisure-time physical activity and serum 25-hydroxyvitamin D levels in the US population: results from the Third National Health and Nutrition Examination Survey. *Am J Epidemiol* **168**, 577–591.
279. Scragg R, Sowers M & Bell C (2004) Serum 25-hydroxyvitamin D, diabetes, and ethnicity in the Third National Health and Nutrition Examination Survey. *Diabetes Care* **27**, 2813–2818.
280. Scragg R, Sowers M & Bell C (2007) Serum 25-hydroxyvitamin D, ethnicity, and blood pressure in the Third National Health and Nutrition Examination Survey. *Am J Hypertens* **20**, 713–719.
281. Tolppanen AM, Williams D & Lawlor DA (2011) The association of circulating 25-hydroxyvitamin D and calcium with cognitive performance in adolescents: cross-sectional study using data from the third National Health and Nutrition Examination Survey. *Paediatr Perinat Epidemiol* **25**, 67–74.
282. Tolppanen AM, Williams DM & Lawlor DA (2011) The association of serum ionized calcium and vitamin D with adult cognitive performance. *Epidemiology* **22**, 113–117.
283. Zadshir A, Tareen N, Pan D, *et al.* (2005) The prevalence of hypovitaminosis D among US adults: data from the NHANES III. *Ethn Dis* **15**, 5–101.
284. Hashemipour S, Larijani B, Adibi H, *et al.* (2006) The status of biochemical parameters in varying degrees of vitamin D deficiency. *J Bone Miner Metab* **24**, 213–218.
285. Omrani GR, Masoompour SM, Sadegholvaad A, *et al.* (2006) Effect of menopause and renal function on vitamin D status in Iranian women. *East Mediterr Health J* **12**, 188–195.
286. Rockell JE, Skeaff CM, Venn BJ, *et al.* (2008) Vitamin D insufficiency in New Zealanders during the winter is associated with higher parathyroid hormone concentrations: implications for bone health? *N Z Med J* **121**, 75–84.
287. Holvik K, Meyer HE, Sogaard A, *et al.* (2007) Pakistanis living in Oslo have lower serum 1,25-dihydroxyvitamin D levels but higher serum ionized calcium levels compared with ethnic Norwegians. The Oslo Health Study. *BMC Endocr Disord* **7**, 9.
288. Holvik K, Meyer HE, Sogaard AJ, *et al.* (2006) Biochemical markers of bone turnover and their relation to forearm bone mineral density in persons of Pakistani and Norwegian background living in Oslo, Norway: The Oslo Health Study. *Eur J Endocrinol* **155**, 693–699.
289. Liu E, Meigs JB, Pittas AG, *et al.* (2009) Plasma 25-hydroxyvitamin D is associated with markers of the insulin resistant phenotype in nondiabetic adults. *J Nutr* **139**, 329–334.
290. Shea MK, Benjamin EJ, Dupuis J, *et al.* (2009) Genetic and non-genetic correlates of vitamins K and D. *Eur J Clin Nutr* **63**, 458–464.
291. Soontrapa S & Chailurkit LO (2005) Difference in serum calcidiol and parathyroid hormone levels between elderly urban vs suburban women. *J Med Assoc Thai* **88**, 17–20.
292. Ginde AA, Scragg R, Schwartz RS, *et al.* (2009) Prospective study of serum 25-hydroxyvitamin D level, cardiovascular disease mortality, and all-cause mortality in older U.S. adults. *J Am Geriatr Soc* **57**, 1595–1603.
293. Jassal SK, Chonchol M, von Muhlen D, *et al.* (2010) Vitamin D, parathyroid hormone, and cardiovascular mortality in older adults: the Rancho Bernardo study. *Am J Med* **123**, 1114–1120.
294. Delvin EE, Lambert M, Levy E, *et al.* (2010) Vitamin D status is modestly associated with glycemia and indicators of lipid metabolism in French-Canadian children and adolescents. *J Nutr* **140**, 987–991.
295. Ginde AA, Mansbach JM, Camargo CA, *et al.* (2009) Association between serum 25-hydroxyvitamin D level and upper respiratory tract infection in the Third National Health and Nutrition Examination Survey. *Arch Intern Med* **169**, 384–390.
296. Maggio D, Cherubini A, Lauretani F, *et al.* (2005) 25(OH)D Serum levels decline with age earlier in women than in men and less efficiently prevent compensatory hyperparathyroidism in older adults. *J Gerontol A Biol Sci Med Sci* **60**, 1414–1419.
297. Visser M, Deeg DJ, Puts MT, *et al.* (2006) Low serum concentrations of 25-hydroxyvitamin D in older persons and the risk of nursing home admission. *Am J Clin Nutr* **84**, 616–622.