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Abstract: Background: The vitamin D status of African populations remains inadequately characterized. Our objective was to estimate the prevalence of vitamin D deficiency in children and adults living in Africa.

Methods: We searched PubMed/MEDLINE, Web of Science, Embase, African Journals Online and African Index Medicus for published vitamin D prevalence studies without language restriction. We included all studies with measured serum 25-hydroxyvitamin D (25(OH)D) concentrations from healthy participants residing in Africa. We conducted meta-analyses to derive the pooled prevalence of vitamin D deficiency using established cut-offs and mean 25(OH)D concentrations. We stratified by participant age group (adults vs. children) and area of residence (urban vs. rural). The study protocol was registered with PROSPERO (number CRD42018112030).

Findings: One hundred and thirteen studies with 19,380 participants from 21 African countries were included in the meta-analysis. The pooled prevalence of low vitamin D status was 57·6% (95% CI 48·4, 66·6), 39·3% (95% CI 30·8, 48·3) and 25·1% (95% CI 15·9, 35·6) for cut-offs of <75 nmol/L, <50 nmol/L, and <30 nmol/L respectively. The overall mean 25(OH)D concentration was 69·1 nmol/L (95% CI 65·4, 72·8). Vitamin D levels were relatively lower in populations living further from the equator, in women, children, and in urban areas.

Interpretation: The prevalence of vitamin D deficiency is high in African populations. Public health strategies should include efforts to prevent, detect and treat vitamin D deficiency, especially in vulnerable populations.

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Prevalence of Vitamin D deficiency in Africa - a systematic review and meta-analysis

Vitamin D deficiency in Africa

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Research in context

Evidence before this study

Low vitamin D status has been linked to disease. Although Africa has a high burden of disease, the prevalence of vitamin D deficiency in Africa and its association with disease has been inadequately characterised. Previous reviews of vitamin D status globally have reported that vitamin D deficiency exists in African populations, but these reviews had few studies from Africa and none quantified the overall prevalence. Between 1st September 2018 and 8th April 2019, we searched PubMed, Embase, Web of Science, African Journals Online and African Index Medicus, without restriction on language or date of publication, to identify epidemiological studies that measured 25-hydroxyvitamin D (25(OH)D) levels in African populations.

Added value of this study

Through this study, we estimate that approximately a quarter of African residents have inadequate 25(OH)D levels (<30 nmol/L). The prevalence of low 25(OH)D levels appears to be higher in infants, urban populations, and in north African countries and South Africa. To our knowledge, this is the first systematic review and meta-analysis that has yet been conducted to quantify the prevalence of vitamin D deficiency in African populations.

Implication of all the available evidence

Health professionals, policy-makers and the general public in Africa should be aware of the high prevalence of vitamin D deficiency and the associated health risks. Efforts to reduce the burden of diseases in Africa should also incorporate strategies to prevent, detect and treat vitamin D deficiency.

Abstract

Background: The vitamin D status of African populations remains inadequately characterized. Our objective was to estimate the prevalence of vitamin D deficiency in children and adults living in Africa.

Methods: We searched PubMed/MEDLINE, Web of Science, Embase, African Journals Online and African Index Medicus for published vitamin D prevalence studies without language restriction. We included all studies with measured serum 25-hydroxyvitamin D (25(OH)D) concentrations from healthy participants residing in Africa. We conducted meta-analyses to derive the pooled prevalence of vitamin D deficiency using established cut-offs and mean 25(OH)D concentrations. We stratified by participant age group (adults vs. children) and area of residence (urban vs. rural). The study protocol was registered with PROSPERO (number CRD42018112030).

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Introduction

Vitamin D deficiency is reported worldwide,[1] and has been associated with non-communicable and infectious diseases.[2] Africa has a high burden of infectious diseases, and the prevalence of non-communicable diseases is rising. A recent report by WHO estimates that the increasing burden of non-communicable diseases will overtake non-communicable diseases in Africa by 2030, trends that have been attributed to lifestyle changes due to rapid urbanisation.[3] Individuals of African ancestry living in temperate regions have lower vitamin D status compared to other ethnicities, and this has been associated with higher prevalences of cardiovascular disease, diabetes, and some cancers observed among African Americans.[4] The presence of vitamin D receptors in most tissues and cells[5] and the regulation of more than 200 human genes by vitamin D[6] indicate that vitamin D may have diverse roles in maintaining health.

Measurement of serum 25-hydroxyvitamin D (25(OH)D) is widely accepted as a proxy for vitamin D status.[7] However, no consensus has been reached on the definition of low vitamin D status. Rickets and osteomalacia are associated with severe vitamin D deficiency, characterized by very low levels of 25(OH)D, whereas extraskeletal diseases have been associated with more modest vitamin D insufficiency (i.e. lower than normal 25(OH)D levels).[8] Rickets and osteomalacia due to vitamin D deficiency are considered unlikely at levels above 30 nmol/L,[9] while the Institute of Medicine of the United States National Academy of Sciences recommends 25(OH)D concentrations above 50 nmol/L for optimum bone health.[10] The Endocrine Society of the United States of America recommends levels above 75 nmol/L to reduce the risk of various non-communicable, and communicable diseases.[8]

The prevalence of vitamin D deficiency has been estimated in temperate regions, but there are few prevalence studies from Africa.[11-14] We conducted a systematic review and meta-analysis of the prevalence of vitamin D deficiency in populations living in Africa to guide prevention, detection and control strategies.

Methods

Search strategy and selection criteria

This systematic review and meta-analysis is reported as per the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) standards.[15] The protocol was written *a priori* and registered in PROSPERO (number CRD42018112030).

We searched PubMed/MEDLINE, Embase, Web of Science and African Journals Online for relevant articles without restrictions on the date or language of publication. All the search terms were Medical Subject Heading (MeSH) terms, this included vitamin D terms ("vitamin D", "vitamin D deficiency" and "cholecalciferol") and terms for Africans and African countries ("African Continental Ancestry Group" and "names of all the 54 African countries"). The search strategy used in PubMed was modified to suit other databases. The full search strategy is outlined in Supplementary Table 1. We included all studies that met the inclusion criteria and that had data available before 8th April 2019 without language restrictions. When the required information was not readily available from published reports, we requested the raw data from the authors. We also manually screened citations of relevant articles to identify additional studies.

For studies to be included, they had to fulfil the following criteria: (1) an original article published or accepted in a peer reviewed journal; (2) have study subjects residing in Africa; (3) have a cross-sectional or longitudinal design with baseline data; and (4) measured 25(OH)D in blood. We excluded studies that: (1) were conducted outside Africa; (2) were case reports and case series; (3) measured 25(OH)D only after a clinical intervention; or (4) only had meeting abstract or unpublished material available. For case-control studies, only data from healthy population subgroups were considered in the meta-analysis.

We began the study selection by screening titles and abstracts of articles retrieved from the database's search. We considered the full text of articles identified to be potentially relevant or if a decision could not be made from reading the title and abstract alone. Two investigators independently screened the titles and abstracts of retrieved articles and disagreements in the study selection were resolved by consensus. Figure 1 illustrates study selection. We quantified the inter-rater agreement for study selection using Cohen's kappa coefficient (k).[16] Where multiple studies used the same dataset or cohort, we considered the most comprehensive one with the largest number of participants.

Data extraction

Data extraction was conducted by two observers independently and then compared. Disagreements were resolved by discussion. We used a predefined and standardised data extraction form to collect information from all the eligible studies. All non-English-language studies were translated into English before data extraction. The information extracted from each eligible study included: year of publication, first author's name, sample size, method of recruitment, study design, dates or season of blood sample collection, ethnicity, proportion of males, study country, method of 25(OH)D measurement, mean 25(OH)D concentrations, prevalence of vitamin D deficiency, and risk factors for low vitamin D status. In cases where a study only reported 25(OH)D means for population subgroups or means for different time points, we computed the overall mean for the cohort where appropriate. In case-control studies, only the baseline 25(OH)D levels of healthy controls were used in the meta-analysis.

Statistical analysis

The quality of the studies included in the meta-analysis was evaluated by a tool developed by Hoy et al.[17] Each study was assessed on 10 items and a score of 1 (yes) or 0 (no) was assigned for each item. The studies were classified into low (>8), moderate (6-8) or high (≤5) risk of bias based on the overall score, which ranged from 0 to 10.

All data analyses were performed using R version 3·5·1. We carried out meta-analyses of established cut-offs for vitamin D status (<75 nmol/L, <50 nmol/L and <30 nmol/L),[8-10] as well as a meta-analysis of mean 25(OH)D levels using the "*metaprop*" and "*metamean*" packages, respectively. Studies that only reported median 25(OH)D values were excluded from the meta-analyses. A random effects model was used due to high levels of heterogeneity between populations.[18] Heterogeneity between studies was assessed using the Cochran's Q, I^2 and H statistics, with an I^2 >75% indicating substantial heterogeneity.[19] We explored sources of heterogeneity by carrying out subgroup analyses by age group (children [0-17 years] vs. adults [≥18 years]), WHO African regions (Northern and Southern African regions vs Western, Central and Eastern African regions) and area of residence (urban vs. rural). The overall mean 25(OH)D concentration for each country was computed from all the eligible studies in the country, and the results illustrated in a map of Africa using ArcGIS 10·6 (ESRI, California). To assess for publication bias, we used the Egger test of bias[20] with P <0·05 indicating significant bias.

Role of the funding source
The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

Our search yielded 1570 articles and conference abstracts (Figure 1). After screening abstracts and titles, we excluded 1320 studies that did not appear to be relevant for the purposes of our meta-analysis. Based on the full texts, we excluded an additional 126 studies that did not have prevalence of vitamin D deficiency or 25(OH)D measurements for healthy participants residing in Africa. The inter-rater agreement for study selection was high (κ=0·85, 92% agreement). Two (2%), 72 (63%) and 39 (35%) studies were classified as having a high, moderate, and low risk of bias, respectively.The I^2 ranged from 98% to 100%, indicating substantial heterogeneity between populations.

We included 113 studies with 19,380 participants from 21 African countries in our meta-analyses. The studies were published between 1978 and 2019. Study characteristics and their corresponding mean 25(OH)D levels are presented in Supplementary Table 2. Figure 2 shows a map of Africa with average 25(OH)D levels by country. Egypt had the highest number of eligible studies (29) followed by Nigeria (19) and South Africa (17). The age of the study participants ranged from birth to 90 years and age was associated with 25(OH)D levels in 14 out of 30 studies that assessed for an association (Supplementary Figure 1). Sixty eight studies had adult participants only, 38 had children only and seven included both.

Sixty five studies reported data on pre-specified cut-offs for vitamin D status and were included in the meta-analysis of prevalence of low vitamin D status, with 23, 58 and 42 studies reporting cut-offs of <30 nmol/L, <50 nmol/L and <75 nmol/L respectively. The overall prevalence of low vitamin D status was 57·6% (95% CI 48·4, 66·6), 39·3% (95% CI 30·7, 48·3), and 25·1% (95% CI 15·9, 35·6) using the 75 nmol/L, 50 nmol/L, and 30 nmol/L thresholds, respectively (Supplementary Figure 2, Figures 3 and 4). We found no evidence of publication bias using significance of $p < 0.05$ (Supplementary Figure 3). Overall pooled mean 25(OH)D level was 69·1 (95% 65·4, 72·8) nmol/L, while the pooled mean was 71·7 (95% 65·7, 77·7) nmol/L for adults and 65·3 (95% 60·4, 70·3) nmol/L for children (Supplementary Figure 4).

Most studies that reported low 25(OH)D levels were from northern African countries and South Africa (Figure 2 and Supplementary Figure 5). Populations in urban areas had lower vitamin D status than those in rural areas (Supplementary Figure 6). Men had higher 25(OH)D levels than women in six out of nine studies where a break-down by gender was given, whilst mothers had higher 25(OH)D levels than their infants in all studies (Supplementary Figure 7). Case-control studies reported that children with rickets had significantly lower 25(OH)D levels compared to healthy community controls and lower vitamin D status was also observed in most of the investigated clinical conditions (Supplementary Table 3).

Discussion

In this systematic review and meta-analysis, we found that vitamin D deficiency, as defined by three different thresholds, is common among African populations. The findings indicate that one in every five adults and children living in Africa have low 25(OH)D levels using the <30 nmol/L cut-off, two in every five using the 50 nmol/L cut-off, and three in every five using the 75 nmol/L cut-off . Prevalence of vitamin D deficiency varied by region with the highest prevalences reported in South Africa and in northern African countries. Population subgroups with the lowest 25(OH)D concentrations included women, children, and urban populations. We observed substantial heterogeneity in the meta-analyses estimates which was not fully explained by region, and speculate that there are substantial within-population variations induced by other factors such as socioeconomic conditions, diet and custom as previously described.[12]

The prevalence of low 25(OH)D concentrations in Africa was higher than might have been expected and challenges the misconception that vitamin D deficiency, as defined by 25(OH)D levels of <30 nmol/L, is rare in Africa. Rapid urbanization and associated lifestyle changes in Africa[3,21] could explain why 25(OH)D concentrations were lower than expected. We observed that populations living in urban areas had lower 25(OH)D concentrations than rural populations, perhaps due to lifestyles that limit the duration of sunlight exposure or reduce the dietary intake of vitamin D.[22] The United Nations report on World Population Prospects estimates that more than 50% of Africans will live in urban areas by 2035,[21] suggesting that the prevalence of vitamin D deficiency is likely to rise.

Surprisingly, we found that the prevalence of low vitamin D status (using the <50 nmol/L cut-off) in Africa was comparable to that in Europe and America. Nationally representative surveys in Europe and America revealed that approximately 40% of these populations have 25(OH)D levels below 50 nmol/l,[23,24] compared to the 39% that we found in Africa. Additionally, a study by Durazo-Arvizu and colleagues observed that Africans residing in Africa had comparable 25(OH)D levels to Caucasians residing in the United States.[25] However, the determinants of vitamin D status may differ between these populations. For instance, supplementation and fortification of foods with vitamin D is a common source of vitamin D in North American countries and some parts of Europe[26,27] but is rare in Africa. It is likely that vitamin D is largely obtained from the sun in Africa since many of the determinants of vitamin D status in the prevalence studies included in this review were associated with sun exposure.

People of African ancestry living in temperate regions have consistently been reported to have lower vitamin D levels compared to other ethnicities in the same setting[28] and compared to Africans living in sub-Saharan Africa.[25,29] This has been attributed to their skin colour being less well-adapted to maximize vitamin D synthesis in temperate climates which have less sunshine.[30] For instance, the prevalence of vitamin D deficiency (<50 nmol/L) in African Americans was reported to be 82·1% compared to the US national average of 41·9%.[24] Recent studies have also reported a decrease in 25(OH)D levels in Africans with increasing distance from the Equator[25] and duration of time since migrating from Africa.[31] We similarly found that 25(OH)D concentrations varied by region with the lowest concentrations observed in South Africa and northern African countries.

There are several other factors that could be influencing vitamin D status in Africa. In sub-group analyses we found that vitamin D status varied by age in African populations with lower levels of 25(OH)D observed in children and infants. A recent systematic review reported that 25(OH)D concentrations were lower in infants than their mothers and that the concentrations were highly correlated.[32] In the three studies that included populations from both urban and rural areas in Africa, participants from urban areas had significantly lower 25(OH)D levels than those in rural areas[29,33,34]. In agreement with studies from other populations,[35,36] we observed that women living in Africa had generally lower 25(OH)D concentrations than men in most studies.

The prevalence of rickets is high in Africa, although this may in some populations be due to calcium rather than vitamin D deficiency.[37,38] The case-control studies included in this review reported that children with rickets had significantly lower 25(OH)D levels compared to healthy community controls. Other clinical conditions have also been associated with lower vitamin D status in case-control studies (Supplementary Table 3). Many pathways have been suggested by which vitamin D could influence susceptibility to disease.[39] However, the studies included in this review were observational studies and therefore could not provide evidence of causality.

Strengths and limitations

To our knowledge, this is the first meta-analysis of the prevalence of vitamin D deficiency and mean 25(OH)D levels in the general population in Africa and includes the largest number of studies from Africa. However, a few of the included studies were published more than ten years ago and may be less representative of current vitamin D status. In addition, many African countries did not have any studies of vitamin D status and more studies are needed to better reflect heterogeneity in African populations. A more detailed analysis of the factors associated with vitamin D status could have been conducted with access to the individual-level datasets rather than relying on published summary measures.

Conclusions

We report that vitamin D deficiency, as defined by three different thresholds, is prevalent in Africa, especially in vulnerable populations. There is a need to incorporate strategies to prevent, detect and treat vitamin D deficiency as part of public health and primary care in Africa.

Contributors

RMM, SHA, AA and TNW conceived the idea of the study and developed the protocol. RMM, WK and AM did the literature search, selected the studies and extracted the relevant information. RMM, SHA, AA, and TNW synthesized the data and wrote the first draft of the manuscript. RMM, SHA, AA, PB, TNW, JMP, AM, and WK revised successive drafts of the paper and approved the final version. SHA supervised the overall work and is the guarantor of the review.

Declaration of interests

We declare no competing interests.

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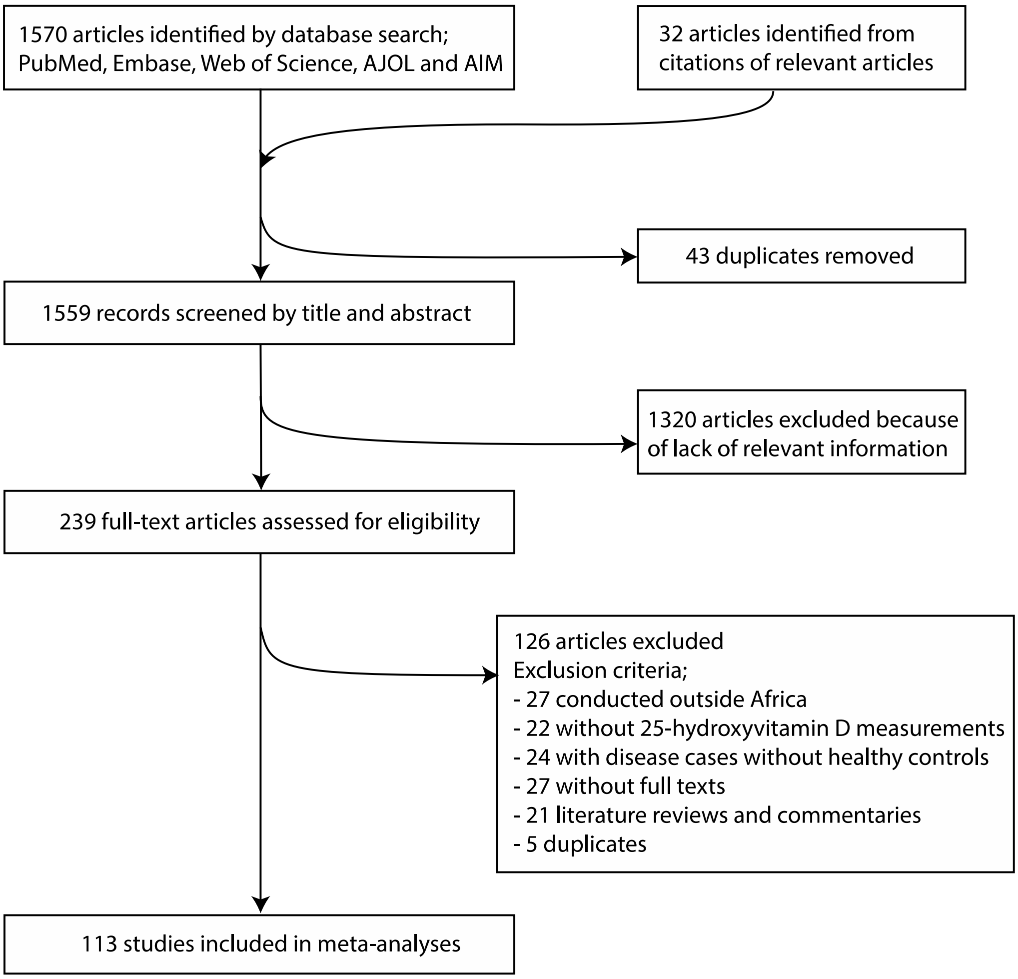


Figure 1. Flowchart summary of the systematic review

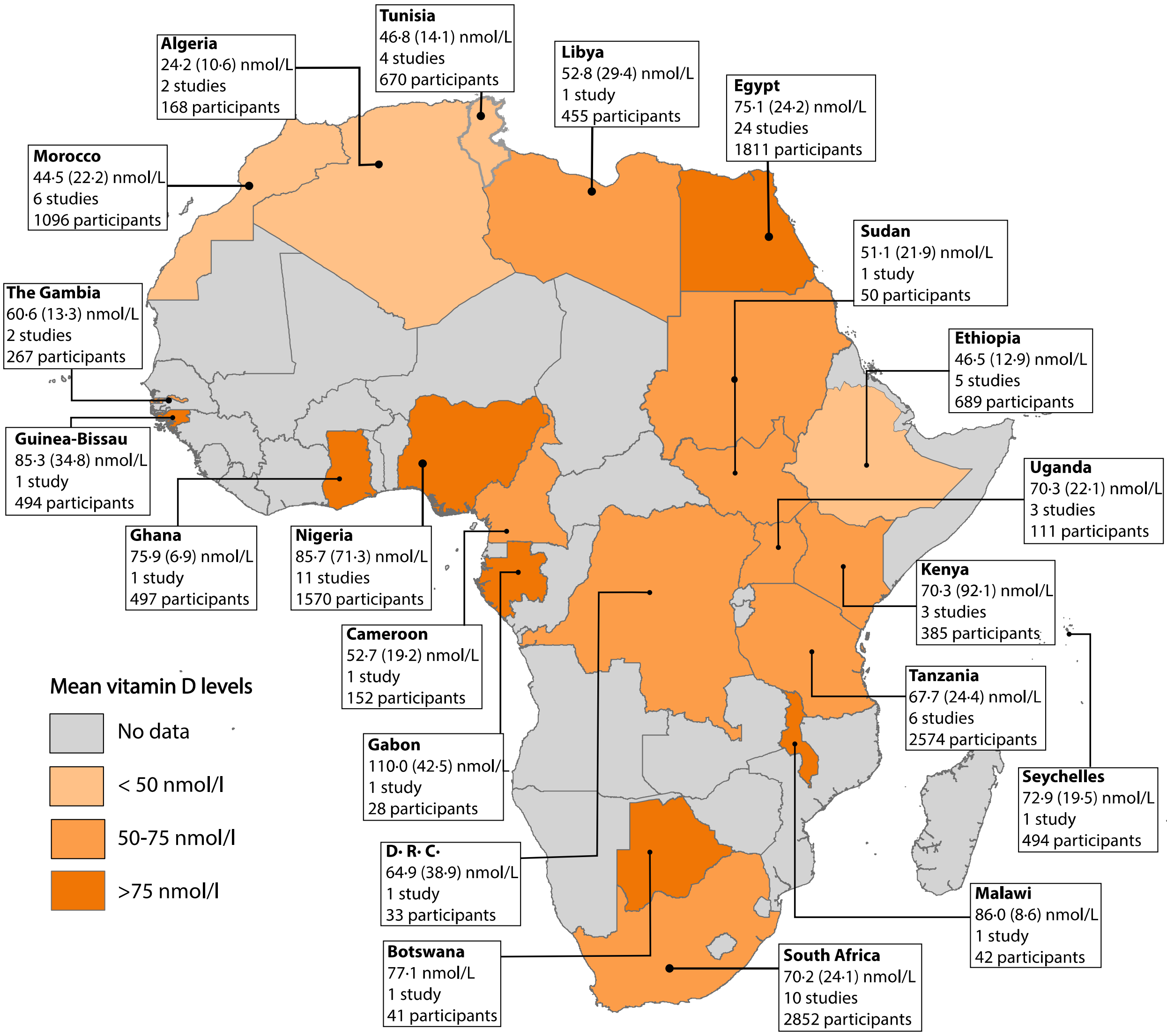
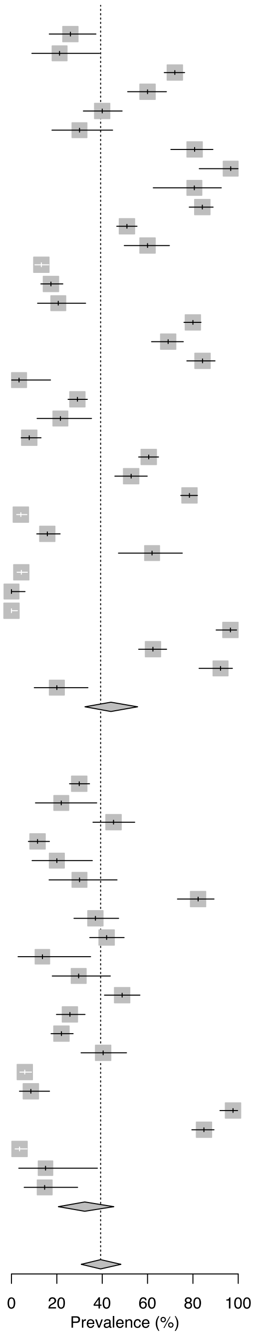


Figure 2. Mean (SD) 25(OH)D levels of studies conducted in African countries. The pooled mean (SD) is reported if a country had more than one study, this was computed from studies that stated 25(OH)D mean (SD) levels only. Studies that only reported medians are not included in this map, with the exception of Botswana which had a single study that only reported the median.



Study	Events	Total	Prevalence (%)	95% CI	Weight (%)
Adults					
Egypt - Aboelnaga 2016	20	77	25·97	[16·64; 37·23]	1·8
Egypt - Ali 2017	7	33	21·21	[8·98; 38·91]	1·7
Egypt - Botros 2015	291	404	72·03	[67·38; 76·35]	1·8
Egypt - El Rifai 2014 (infants)	81	135	60·00	[51·22; 68·33]	1·8
Egypt - El Rifai 2014 (mothers)	54	135	40·00	[31·67; 48·78]	1·8
Egypt - Olama 2013	15	50	30·00	[17·86; 44·61]	1·7
Ethiopia - Ashenafi 2018	63	78	80·77	[70·27; 88·82]	1·8
Ethiopia - Feleke 1999 (non-pregnant adults)	29	30	96·67	[82·78; 99·92]	1·7
Ethiopia - Feleke 1999 (pregnant women)	25	31	80·65	[62·53; 92·55]	1·7
Ethiopia - Gebreegziabher 2013	170	202	84·16	[78·38; 88·90]	1·8
Ghana - Durazo-Arvizu 2014	253	497	50·91	[46·42; 55·38]	1·8
Ghana - Fondjo 2017	60	100	60·00	[49·72; 69·67]	1·8
Guinea Bissau - Wejse 2007	65	494	13·16	[10·30; 16·46]	1·8
Kenya - Kagotho 2018	44	253	17·39	[12·93; 22·63]	1·8
Kenya - Toko 2016 (mothers)	13	63	20·63	[11·47; 32·70]	1·7
Libya - Faid 2018	364	455	80·00	[76·02; 83·58]	1·8
Morocco - El Maghraoui 2012	123	178	69·10	[61·75; 75·80]	1·8
Morocco - Skalli 2018	123	146	84·25	[77·31; 89·74]	1·8
Nigeria - Akinlade 2017	1	30	3·33	[0·08; 17·22]	1·7
Nigeria - Gbadegesin 2017	134	461	29·07	[24·96; 33·45]	1·8
Nigeria - Glew 2010	11	51	21·57	[11·29; 35·32]	1·7
Nigeria - Owie 2018 (mothers)	13	166	7·83	[4·24; 13·02]	1·8
Seychelles - Durazo-Arvizu 2014	299	494	60·53	[56·06; 64·86]	1·8
South Africa - Basson 2015	105	199	52·76	[45·58; 59·86]	1·8
South Africa - Durazo-Arvizu 2014	394	502	78·49	[74·63; 82·00]	1·8
South Africa - Lategan 2016	14	339	4·13	[2·28; 6·83]	1·8
South Africa - Sotunde 2017	33	209	15·79	[11·12; 21·45]	1·8
South Africa - Van der Walt 2016	31	50	62·00	[47·17; 75·35]	1·7
Tanzania - Friis 2013	15	347	4·32	[2·44; 7·03]	1·8
Tanzania - Luxwolda 2013 (adults)	0	60	0·00	[0·00; 5·96]	1·7
Tanzania - Luxwolda 2013 (pregnant women)	0	138	0·00	[0·00; 2·64]	1·8
Tunisia - Ayadi 2016 (mothers)	84	87	96·55	[90·25; 99·28]	1·8
Tunisia - Ben Fradj 2016	156	250	62·40	[56·08; 68·43]	1·8
Tunisia - Nasri 2016	59	64	92·19	[82·70; 97·41]	1·7
Uganda - Nansera 2011	10	50	20·00	[10·03; 33·72]	1·7
Random effects meta-analyis		**6858**	**43·84**	**[32·39; 55·62]**	**61·6**
Heterogeneity: $I^2 = 99\%$, $\tau^2 = 0{\cdot}12$, $p = 0$					
Children					
Algeria - Djennane 2014	130	435	29·89	[25·62; 34·43]	1·8
Botwsana - Ludmir 2016	9	41	21·95	[10·56; 37·61]	1·7
Egypt - Abd-Allah 2014	54	120	45·00	[35·91; 54·35]	1·8
Egypt - Abu Shady 2015	23	200	11·50	[7·43; 16·75]	1·8
Egypt - Albanna 2010	8	40	20·00	[9·05; 35·65]	1·7
Egypt - Azab 2013	12	40	30·00	[16·56; 46·53]	1·7
Egypt - El Sakka 2014	79	96	82·29	[73·17; 89·33]	1·8
Egypt - Fahim 2013	37	100	37·00	[27·56; 47·24]	1·8
Ethiopia - Wakayo 2015	73	174	41·95	[34·53; 49·66]	1·8
Kenya - Jones 2016	3	22	13·64	[2·91; 34·91]	1·6
Kenya - Toko 2016 (infants)	16	54	29·63	[17·98; 43·61]	1·7
Nigeria - Owie 2019 (infants)	81	166	48·80	[40·97; 56·66]	1·8
Nigeria - Pfitzner 1998	51	198	25·76	[19·82; 32·44]	1·8
South Africa - Poopedi 2011	65	295	22·03	[17·44; 27·20]	1·8
South Africa - Poopedi 2015	40	99	40·40	[30·66; 50·74]	1·8
Tanzania - Boillat-Blanco 2016	21	358	5·87	[3·67; 8·83]	1·8
Tanzania - Luxwolda 2013 (infants)	7	82	8·54	[3·50; 16·80]	1·8
Tunisia - Ayadi 2016 (infants)	85	87	97·70	[91·94; 99·72]	1·8
Tunisia - Bezrati 2016	191	225	84·89	[79·53; 89·30]	1·8
Tunisia - Maalmi 2013	8	225	3·56	[1·55; 6·89]	1·8
Uganda - Cusick 2014	3	20	15·00	[3·21; 37·89]	1·6
Uganda - Nabeta 2015	6	41	14·63	[5·57; 29·17]	1·7
Random effects meta-analyis		**3118**	**32·31**	**[20·68; 45·14]**	**38·4**
Heterogeneity: $I^2 = 98\%$, $\tau^2 = 0{\cdot}09$, $p < 0{\cdot}01$					
Random effects meta-analyis		**9976**	**39·33**	**[30·74; 48·25]**	**100·0**
Heterogeneity: $I^2 = 99\%$, $\tau^2 = 0{\cdot}11$, $p = 0$					
Residual heterogeneity: $I^2 = 99\%$, $p = 0$					
Test for subgroup differences: $\chi^2_1 = 1{\cdot}72$, df = 1 ($p = 0{\cdot}19$)					

Figure 3. Pooled prevalence of vitamin D deficiency in the general population in Africa using the <50 nmol/L cut-off. Events were defined as number of participants in a study with 25(OH)D levels <50 nmol/L; total, the total number of participants in the study

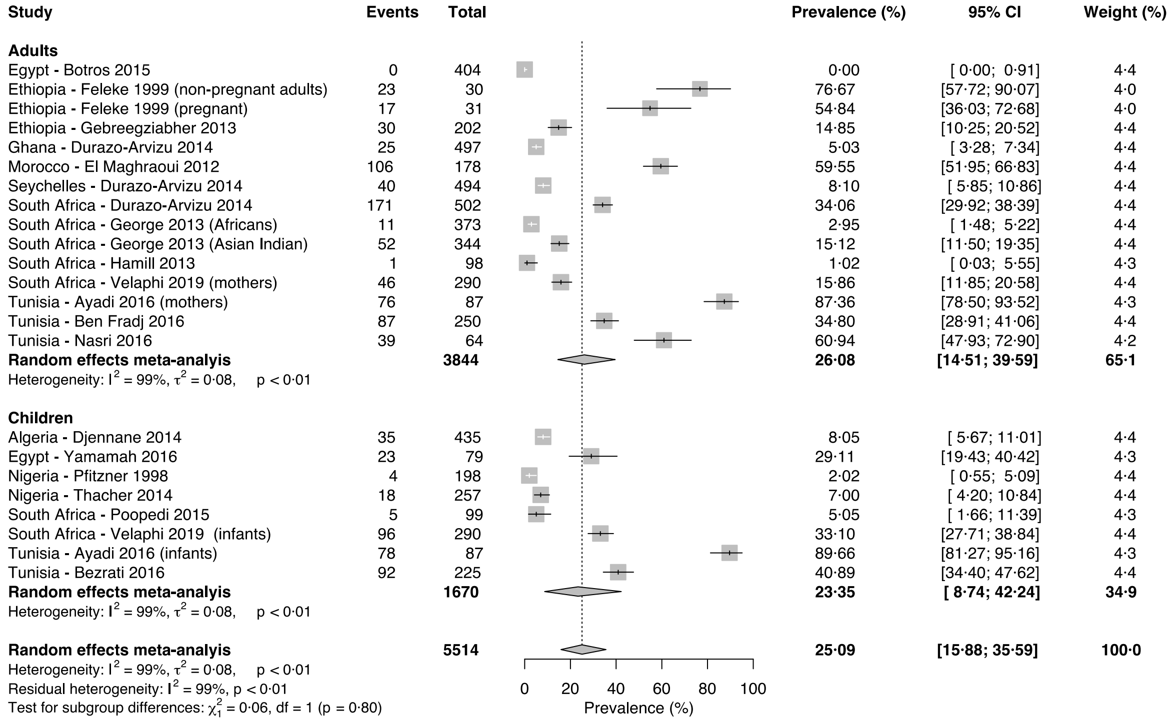


Figure 4. Pooled prevalence of vitamin D deficiency in the general population in Africa using the <30 nmol/L cut-off. Events were defined as number of participants in a study with 25(OH)D levels <30 nmol/L; total, the total number of participants in the study.

Supplementary Materials

Supplementary Table 1. Keywords used to search databases.

Database	Search terms
PubMed/ MEDLINE*	("Vitamin D"[Mesh] OR "Vitamin D Deficiency"[Mesh] OR "Cholecalciferol"[Mesh]) AND ("African Continental Ancestry Group"[Mesh] OR “Algeria”[Mesh] OR “Egypt”[Mesh] OR “Libya”[Mesh] OR “Morocco”[Mesh] OR “South Sudan”[Mesh] OR “Sudan”[Mesh] OR “Tunisia”[Mesh] OR “Burundi”[Mesh] OR “Comoros”[Mesh] OR “Djibouti”[Mesh] OR “Eritrea”[Mesh] OR “Ethiopia”[Mesh] OR “Kenya”[Mesh] OR “Madagascar”[Mesh] OR “Malawi”[Mesh] OR “Mauritius”[Mesh] OR “Mayotte”[Mesh] OR “Mozambique”[Mesh] OR “Reunion”[Mesh] OR “Rwanda”[Mesh] OR “Seychelles”[Mesh] OR “Somalia”[Mesh] OR “Tanzania”[Mesh] OR “Uganda”[Mesh] OR “Zambia”[Mesh] OR “Zimbabwe”[Mesh] OR “Benin”[Mesh] OR “Burkina Faso”[Mesh] OR “Cape Verde”[Mesh] OR “Cote d'Ivoire”[Mesh] OR “Ivory Coast”[Mesh] OR “Gambia”[Mesh] OR “Ghana”[Mesh] OR “Guinea”[Mesh] OR “Guinea-Bissau”[Mesh] OR “Liberia”[Mesh] OR “Mali”[Mesh] OR “Mauritania”[Mesh] OR “Niger”[Mesh] OR “Nigeria”[Mesh] OR “Saint Helena”[Mesh] OR “Senegal”[Mesh] OR “Sierra Leone”[Mesh] OR “Togo”[Mesh] OR “Angola”[Mesh] OR “Cameroon”[Mesh] OR “Central African Republic”[Mesh] OR “Chad”[Mesh] OR “Congo”[Mesh] OR “Democratic Republic of the Congo”[Mesh] OR “Equatorial Guinea”[Mesh] OR “Gabon”[Mesh] OR “Sao Tome and Principe”[Mesh] OR “Botswana”[Mesh] OR “Lesotho”[Mesh] OR “Namibia”[Mesh] OR “South Africa”[Mesh] OR “Swaziland”[Mesh])
Web of Science	ts = (" vitamin D" and ("Algeria" or " Egypt" or " Libya" or " Morocco" or " South Sudan" or " Sudan" or " Tunisia" or " Western Sahara" or " Burundi" or " Comoros" or " Djibouti" or " Eritrea" or " Ethiopia" or " Kenya" or " Madagascar" or " Malawi" or " Mauritius" or " Mayotte" or " Mozambique" or " Reunion" or " Rwanda" or " Seychelles" or " Somalia" or " Tanzania" or " Uganda" or " Zambia" or " Zimbabwe" or " Benin" or " Burkina Faso" or " Cape Verde" or " Cote d'Ivoire " or " Ivory Coast" or " Gambia" or " Ghana" or " Guinea" or " Guinea-Bissau" or " Liberia" or " Mali" or " Mauritania" or " Niger" or " Nigeria" or " Saint Helena" or " Senegal" or " Sierra Leone" or " Togo" or " Angola" or " Cameroon" or " Central African Republic" or " Chad" or " Congo" or " Democratic Republic of the Congo" or " Equatorial Guinea" or " Gabon" or " Sao Tome and Principe" or " Botswana" or " Lesotho" or " Namibia" or " South Africa" or " Swaziland")
Embase	((" vitamin D" and ("Algeria" or " Egypt" or " Libya" or " Morocco" or " South Sudan" or " Sudan" or " Tunisia" or " Western Sahara" or " Burundi" or " Comoros" or " Djibouti" or " Eritrea" or " Ethiopia" or " Kenya" or " Madagascar" or " Malawi" or " Mauritius" or " Mayotte" or " Mozambique" or " Reunion" or " Rwanda" or " Seychelles" or " Somalia" or " Tanzania" or " Uganda" or " Zambia" or " Zimbabwe" or " Benin" or " Burkina Faso" or " Cape Verde" or " Cote d'Ivoire " or " Ivory Coast" or " Gambia" or " Ghana" or " Guinea" or " Guinea-Bissau" or " Liberia" or " Mali" or " Mauritania" or " Niger" or " Nigeria" or " Saint Helena" or " Senegal" or " Sierra Leone" or " Togo" or " Angola" or " Cameroon" or " Central African Republic" or " Chad" or " Congo" or " Democratic Republic of the Congo" or " Equatorial Guinea" or " Gabon" or " Sao Tome and Principe" or " Botswana" or " Lesotho" or " Namibia" or " South Africa" or " Swaziland")) not "African American").mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]
African Journals OnLine (AJOL)	“vitamin D" and ("Algeria" or "Egypt" or "Libya" or "Morocco" or "South Sudan" or "Sudan" or "Tunisia" or "Western Sahara" or "Burundi" or "Comoros" or "Djibouti" or "Eritrea" or "Ethiopia" or "Kenya" or "Madagascar" or "Malawi" or “Mauritius" or " Mayotte" or " Mozambique" or " Reunion" or " Rwanda" or " Seychelles" or " Somalia" or " Tanzania" or " Uganda" or " Zambia" or " Zimbabwe" or " Benin" or " Burkina Faso" or " Cape Verde" or " Cote d'Ivoire " or " Ivory Coast" or " Gambia" or " Ghana" or " Guinea" or " Guinea-Bissau" or " Liberia" or " Mali" or " Mauritania" or " Niger" or " Nigeria" or " Saint Helena" or " Senegal" or " Sierra Leone" or " Togo" or " Angola" or " Cameroon" or vitamin D" and (" Central African Republic" or " Chad" or " Congo" or " Democratic Republic of the Congo" or " Equatorial Guinea" or " Gabon" or " Sao Tome and Principe" or " Botswana" or " Lesotho" or " Namibia" or " South Africa" or " Swaziland") not "African American”
African Index Medicus	“vitamin D”

*country names were also searched without the “Mesh” term.

Supplementary Table 2. Summary characteristics of eligible studies (in chronological order)

1st Author, year	City, country	Eligible subjects (n)	Male (%)	Mean age (range/SD) in years	Area	Vitamin D measurement method³	Vitamin D mean/median (nmol/L) of healthy participants*
Children (≤ 17 Years)							
Velaphi 2019[1] (infants)	Johannesburg, South Africa	290	0%	28	Urban	CLIA	57·0 (29·7)
Owie 2018[2] (infants)	Lagos, Nigeria	166	NA	0 (0)	Urban	ELISA	63·4 (1·5)
Sudfeld 2017[3]	Daresalaam, Tanzania	581	48%	0·3 (0·1–0·5)	Urban	HPLC–MS/MS	1·5 months: 36·2 (18·5) 6 months: 64·9 (21·7)
Ayadi 2016[4] (infants)	Tunis, Tunisia	87	45%	0 (0)	Rural and urban	CLIA	14·8 (10·4)
Jones 2016[5]	Nairobi, Kenya	22	64%	1·1 (0·8–1·5)	Urban	CLIA	70 (54–85)
Bezrati 2016[6]	Tunis, Tunisia	225	NA	11 (7–16)	Urban	CLIA	35·0 (12·7)
Yamamah 2016[7]	South Sinai, Egypt	79	52	8·6 (4–12)	Rural	ELISA	NA
Toko 2016[8] (infants)	Chulaimbo, Kenya	54	57%	0 (0)	Rural	EIA	64·9 (26·4)
Boillat-Blanco 2016 [9]	Kinondoni, Tanzania	358	53%	0·5	NA	CLIA	89·6 (26·9)
Ludmir 2016 [10]	Gaborone, Botwsana	41	41%	1	NA	CLIA	77·1
Eltayeb 2015 [11]	Assyout, Egypt	28	65%	9·35 (7–14)	Urban	ELISA	98·31 (3·5)
Braithwaite 2015[12]	West Kiang, Gambia	237	37%	11·9 (17–19)	Rural	CLIA	59·6 (12·9)
Sudfeld 2015[13]	Daresalaam, Tanzania	948	54%	0·1 (0·1–0·1)	Urban	HPLC–MS/MS	45·2 (23)
Poopedi 2015[14]	Johannesburg, South Africa	99	58%	15 (11–20)	Urban	CLIA	56·4 (7·2)
Wakayo 2015[15,16]	Ethiopia	174	43%	15 (11–18)	Rural and urban	CLIA	54·5 (15·9)
Abu Shady 2015 [17]	Egypt	200	49%	10 (9–11)	NR	ELISA	103·7 (33·2)
Nabeta 2015[18]	Kampala, Uganda	41	54%	1·3 (0·5–2·0)	Urban	CLIA	80·4 (27·2)
Cusick 2014[19]	Uganda	20	45%	3 (1–12)	Urban	CLIA	63·1 (21·7)
Djennane 2014[20]	Algeria	435	47%	10 (5–15)	Urban	CLIA	Summer: 71·4 (48·2–79·5) Winter: 52·9 (39·4–75·6)
El Rifai 2014[21] (infants)	Cairo, Egypt	135	53%	0 (0)	Rural and urban	ELISA	41·7 (25·0)
El Sakka 2014[22]	Egypt	96	58%	1 (0·25)	NA	RIA	NA
Abd–Allah 2014[23]	Zagazig, Egypt	120	40%	11 (7–17)	Urban	ELISA	46·6 (13·5)
Fares 2014[24]	Tunis, Tunisia	156	51%	0	Urban	RIA	29·8 (15·2)
Thacher 2014 [25]	Jos, Nigeria	257	50%	(1–10)	Urban	LC–MS/MS	49·9 (7·5–127·3)
Maalmi 2013 [26]	Ariana, Tunisia	225	56%	9·5 (2–16)	Rural	RIA	75·6 (14·9)
Azab 2013 [27]	Zagazig, Egypt	40	43%	10·8 (6–16)	Urban	ELISA	66·1 (12)
Fahim 2013[28]	Assiut, Egypt	100	NA	8 (4–15)	NA	ELISA	40·2 (12·3) pg/ml
Amukele 2012[29]	Malawi	21	NA	0 (0–1)	NA	LC–MS/MS	78·6 (10·4)
Hamza 2011 [30]	Cairo, Egypt	60	17%	13·10 (7·2–18·5)	Urban	ELISA	106·5 (23)
Poopedi 2011 [31]	Johannesburg, South Africa	295	78%	10·5	Urban	CLIA	93·4 (32·8)

Thacher 2010[32]	Jos, Nigeria	21	48%	3 (2–5)	Urban	CLIA	67
Albanna 2010[33]	Zagazig, Egypt	40	50%	3 (2–5)	Urban	EIA	87·25 (18·4)
Nguema - Asseko 2005[34]	Oyem, Gabon	28	56%	0 (0)	Urban	NA	110·0 (42·5)
Graff 2004 [35]	Jos, Nigeria	15	40%	4 (2–8)	Urban	CPBA	72·4 (11·5)
Thacher 2000[36,37]	Jos, Nigeria	123	50%	4 (2–6)	Urban	RIA	51·2 (15·5)
Thacher 1999a[38]	Jos, Nigeria	10	NA	7 (1–8)	Urban	RIA	52·2 (7·2)
Pfitzner 1998[39]	Jos, Nigeria	198	45%	2·0 (0·5–3·0)	Urban	RIA	64·9 (24)
Cornish 2000[40]	N· Province, South Africa	58	NA	12	Rural	RIA	111·4 (9·1)
Walter 1997[41]	Jos, Nigeria	27	70%	3 (1–7)	Urban	RIA	59·9 (18·7)
Oginni 1996a[42]	Ile-Ife, Nigeria	94	63%	3 (1–5)	Urban	RIA	63 (2·6)
Oginni 1996b[43]	Ile-Ife, Nigeria	20	61%	3 (1–5)	Urban	RIA	69 (22)
Okonofua 1991[44]	Ile-Ife, Nigeria	12	75%	2	Urban	RIA	41 (29–50)
Okonofua 1986[45] (infants)	Ife, Nigeria	30	NA	0	NA	CPBA	49 (12·8)
Markestad 1984[46] (infants)	Libya	14	NA	0	NA	NA	20 (10–45)
Luxwolda 2013[47] (infants)	Tanzania	82	60%	0	Rural	LC–MS/MS	79·0 (26·4)
Adults (≥18 years)							
Velaphi 2019[1] (mothers)	Johannesburg, South Africa	290	NA	0	Urban	CLIA	41·9 (21·0)
Oluwole 2019[48]	Lagos , Nigeria	206	0	31	Urban	ELISA	142·3 (112·3–164·7)
Owie 2018[2] (mothers)	Lagos, Nigeria	166	NA	31·4 (18–42)	Urban	ELISA	87·4 (2·0)
Myburgh 2018[49]	NW Province, South Africa	505	0%	NA	Rural and urban	CLIA	68·2 (median)
Kagotho 2018[50]	Nairobi, Kenya	253	75%	33 (18–65)	Urban	CLIA	69·4 (111·8)
Faid 2018[51]	Misurata, Libya	455	16%	33 (1–64)	Urban	CLIA	52·8 (29·4)
Ibrahim 2018 [52]	Qena, Egypt	20	50%	35·20 y	NA	ELISA	76·7 (10·73)
Ashenafi 2018 [53]	Addis Ababa, Ethiopia	78	54%	29 (18–68)	Urban	NA	35
Skalli 2018 [54]	Rabat, Morocco	146	NA	33·6 (18–60)	Urban	LC–MS/MS	32·4 (16·4)
Fondjo 2017 [55]	Nkawie, Ghana	100	22%	57·7	Rural	ELISA	31·3 (6·5–81·8)
Ali 2017 [56]	Cairo, Egypt	33	42%	35 (27–59)	Urban	ELISA	90·1 (26·9–189·1)
Musa 2018[57]	Khartoum, Sudan	132	0%	27·6	Rural and urban	CLIA	21·0 (18·0–27·7)
Abdel Galil 2018[58]	Zagazig, Egypt	100	0%	36·24	Urban	ELISA	114·4 (22·9)
Bakeer 2018[59]	Egypt	17	0%	26 (19–35)	NA	ELISA	48·7 (27·3)
Abdel–Mohsen 2018[45]	Alexindiria, Egypt	30	NA	NA	Urban	ELISA	164·7 (7·5)
Sotunde 2017[60]	NW Province, South Africa	209	0%	60 (43–80)	Urban	CLIA	76·4 (23·4)
Akinlade 2017[61]	Idadan, Nigeria	30	NA	35 (19–55)	NA	ELISA	28·1 (5·6)

Gbadegesin 2017[62]	Lagos, Nigeria	461	0%	31·3 (4·4)	NA	HPLC	130·3 (129·7)
Derar 2017[63]	Khartoum, Sudan	50	NA	32 (18–60)	NA	NA	51·1 (21·9)
Nielson 2016[64]	Keneba, The Gambia	17	–	29 (25–39)	Rural	EIA	20·1 (5·8) pM
Lategan 2016[65]	Mangaung, South Africa	339	22%	44 (25–63)	Urban	CLIA	96·8 (28)
Ayadi 2016[4] (mothers)	Tunis, Tunisia	87	0%	31 (19–42)	Rural and urban	CLIA	17·0 (12·8)
El Maataoui 2016[66]	Morocco	254	27%	60·5 (8·4)	NA	CLIA	50·6 (21·5)
Edem 2016[67]	Ibadan, Nigeria	20	NA	NA	Urban	HPLC	45·80 (13·30) pg/ml
Abbiyesuku 2016[68]	Ibadan, Nigeria	49	100%	54·50 (30–80)	Urban	HPLC	107·2 (25·2)
Toko 2016[8] (mothers)	Chulaimbo, Kenya	63	0%	22·5	Rural	EIA	77·0 (31·5)
Aboelnaga 2016 [69]	Dakalia, Egypt	50	36%	39·5 (18 and 65)	Rural	ELISA	60·4 (21·7)
Van der Walt 2016 [70]	Free State province, South Africa	50	33%	39	Rural and urban	ELISA	45·9
Azab 2016 [71]	Zagazig, Egypt	100	5%	11·5 (8–18)	Urban	ELISA	84·1 (3·7)
Ben Fradj 2016 [72]	Tunis, Tunisia	250	25%	63·3 (29–91)	Urban	CLIA	NA
Nasri 2016 [73]	Tunis, Tunisia	64	0%	NA	Urban	CLIA	28·3 (13·82)
Sobeih 2016 [74]	Cairo, Egypt	75	NA	31·5 (14–65)	Urban	ELISA	71·9 (26·2)
Basson 2015[75]	Cape Town, SA	199	31%	34·0 (24·0–44·3)	Rural and urban	CLIA	49·2 (42·4–59·7)
Fattah 2015[76]	Cairo, Egypt	30	60%	25·1 (19–50)	Urban	EIA	112·8 (51·2)
Botros 2015[77]	Cairo, Egypt	404	0%	31·5 (8·2)	NA	RIA	27·5 (4·0–62)
El Maataoui 2015[78]	Morocco	73	0%	59·8 (50·0–83·0)	Urban	CLIA	32·9 (23·8)
Kazem 2014[79]	Cairo, Egypt	30	0%	48	Urban	ELISA	68·3 (9·3)
Durazo–Arvizu 2014 [80]	Kumasi, Ghana Victoria, Seychelles Cape Town, South Africa	Ghana: 497 Seychelles: 494 South Africa: 502	50%	34 (25–45)	Ghana: rural Seychelles: urban South Africa: urban	LC–MS/MS	Ghana: 75·9 (6·9) Seychelles: 72·9 (19·5) South Africa: 59·2 (20·7)
George 2014[81,82]	Johannesburg, South Africa	Africans: 371 Asian–Indians: 343	48%	42 (19–65) 44 (18–65)	Urban	HPLC	Africans: 64·9 (46·4–89·4) Asian Indians: 41·2 (28·4–56·8)
Were 2014[83]	Mombasa, Kenya	15	60%	26	Urban	CLIA	76·6 (20·5)
Aly 2014[84]	Dakahlia, Egypt	176	40%	68 (60–85)	Rural	EIA	92 (17)
El Rifai 2014[21] (mothers)	Cairo, Egypt	135	0%	26·0 (5·8)	Rural and urban	ELISA	81·4 (53·4)
Durazo–Arvizu 2013[85]	Nigeria	100	0%	31 (18–59)	Rural and urban	RIA	64 (17·4)
Hamill 2013 [86]	Johannesburg, South Africa	98	0%	32 (18–49)	Urban	RIA	60 (16·5)
Luxwolda 2013[47] (adults)	Tanzania	Pregnant: 138 Other adults: 60	60%	34 (16–65)	Rural	LC–MS/MS	Pregnant: 138·5 (35·0) Other adults: 115·1 (27·0)
George 2013[87]	Johannesburg, South Africa	Africans:373 Asians:344	48%	43 (18–70)	Urban	HPLC	Africans: 70·9 (51·5–95·1) Asians: 41·8 (28·6–56·8)
Gebreegziabher 2013[88]	Rift Valley, Ethiopia	202	0%	30·8 (7·8)	Rural	ELISA	39·7 ± 9·7
El Maaty 2013[89]	Egypt	31	100%	(35–50)	Urban	HPLC	78·5 (10·5)
Olama 2013 [90]	Dakahlia, Egypt	50	0%	33·1	Rural	ELISA	46·9 (13·5)

El-Shal 2013 [91]	Zagazig, Egypt	150	0%	29·3	Urban	HPLC	67·9 (11·7)
Emerah 2013 [92]	Zagazig, Egypt	129	0%	27·14 (20 - 41)	Urban	ELISA	38·1 (15·9)
Friis 2013 [93]	Mwanza, Tanzania	347	58%	NA	Urban	CLIA	84·4 (25·6)
Ibn Yacoub 2012 [94]	Rabat, Morocco	30	0%	49·5	NA	na	57·41 (4·18)
Schaalan 2012 [95]	Cairo, Egypt	25	72%	(30–55)	Urban	RIA	99·1 (27)
Amukele 2012[29]	Malawi	21	–	23 (22–28)	NA	LC–MS/MS	93·4 (6·5)
Luxwolda 2012[96]	Tanzania	Maasai: 35 Hadzabe: 25	Maasai: 43% Hadzabe: 84%	34 (16–65)	Rural	LC–MS/MS	Maasai: 119·0 (26·0) Hadzabe: 109·0 (28·0)
Gawad 2012[97]	Mansoura, Egypt	55	27%	38 (26–54)	Rural and urban	RIA	77·1 (16·2) pmol/L
El Maghraoui 2012[98]	Rabat, Morocco	178	0%	59 (50–79)	Urban	CLIA	46·7 (31·9
Kruger 2011[99]	Johannesburg, South Africa	658	0%	50 (35–90)	Rural and urban	CLIA	71·4 (21·9)
Nansera 2011 [100]	Mbarara, Uganda	50	50%	27	NA	HPLC	64·9 (17·5)
Glew 2010[101]	Gombe, Nigeria	51	43%	52 (18–72)	Rural	LC–MS/MS	68·0 (3·7)
Allali 2009[102]	Rabat, Morocco	415	0%	50 (24–77)	Urban	RIA	45·2 (19·7)
Yan 2009[103]	Keneba, The Gambia	30	50%	67 (60–75)	Rural	RIA	68·4 (16·2)
Wejse 2007[104]	Guinea-Bissau	494	48%	37 (15–87)	Urban	LC–MS/MS	85·3 (34·8)
Alsayed 2007[105]	Cairo, Egypt	70	100%	47·1 (3·1)	Rural and urban	RIA	47·1 (3·1)
Meddeb 2005[106]	Tunis, Tunisia	261	0%	40	Urban	RIA	40
Njemini 2002[107]	Ntam, Cameroon	152	61%	66 (60–86)	Rural	RIA	52·7 (19·2)
Daniels 2000 [108]	South Africa	14	NA	NA	NA	CPBA	43·4 (19·5)
Daniels 1997[109]	South Africa	139	0%	44 (20–64)	NA	CPBA	19·3 (6·8–45·6)
Garabedian 1991[110]	Constantine, Algeria	84	NA	NA	Urban	NA	Women: 27·1 (9·4) Infants: 21·3 (11·8)
Feleke 1999[111]	Adis Ababa, Ethiopia	Pregnant: 31 Other adults: 30	0%	21 (19–40)	Urban	HPLC	Pregnant: 25 (17–46) Other adults: 23·5 (18–29)
M'Buyamba-Kabangu 1987[112]	Kinshasa, Zaire	33	100%	31	Urban	RIA	64·9 (38·9)
Okonofua 1986[45] (mothers)	Ife, Nigeria	30	NA	NA	NA	CPBA	Mothers: 77·7 (15·8)
Markestad 1984[46] (mothers)	Libya	19	0%	(26–45)	NA	NA	34 (13–75)
Pettifor 1978[113]	Johannesburg, South Africa	264	NA	7·9 (1–7)	Urban	CPBA	73·9

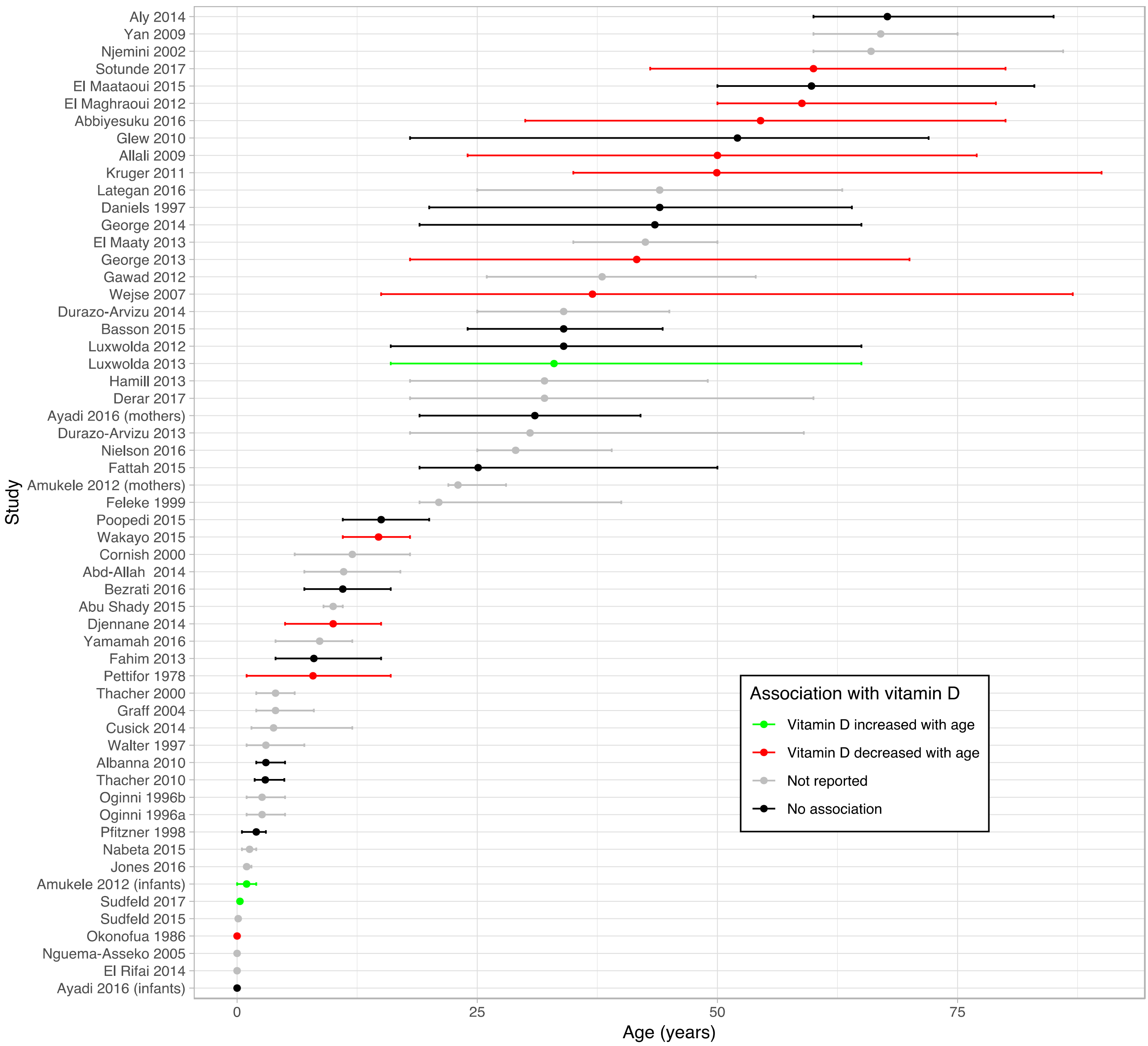
*25(OH)D levels are presented in mean (SD) or median (IQR). [a]Vitamin D measurement assays; RIA: Radioimmunoassay; CLIA: Chemiluminescence immunoassays; LC–MS/MS: liquid chromatography-tandem mass spectrometry; HPLC–MS/MS high-performance liquid chromatography-tandem mass spectrometry; HPLC: high-performance liquid chromatography; EIA: Enzyme immunoassay; CPBA: competitive protein-binding assay. Data that were not available were indicated as NA.

Supplementary Table 3. 25(OH)D levels for disease and control groups in case-control studies.

		Disease group		Healthy controls		
Disease	**Study**	**n**	**Mean (SD)/median (IQR) 25(OH)D (nmol/L)**	**n**	**Mean (SD)/median (IQR) 25(OH)D (nmol/L)**	**p**
Rickets	Graff 2004	15	37·4 (13·5)	15	72·4 (4·6)	<0·001
	Oginni 1996a	27	43 (5·5)	47	63 (2·6)	<0·001
	Oginni 1996b	22	36 (28)	20	69 (22)	<0·001
	Okonofua 1991	11	41 (22, 84)*	12	41 (29, 50)*	-
	Pfitzner 1998	20	56·4 (11·7)	198	64·9 (24·0)	0·12
	Walter 1997	16	14·1 (4·7)	27	24 (7·5)	<0·001
	Thacher 2000	123	32 (22, 40)	123	50 (42, 62)*	-
	Jones 2016	21	19 (15, 37)*	22	70 (54, 85)*	-
	Daniels 2000	41	37·7 (15·5)	14	43·4 (19·5)	<0·001
	Thacher 2014	190	34·9 (5·0, 89·9)	257	49·9 (7·5, 127·3)	-
Cardiovascular diseases	El Maaty 2013	63	60·1 (25·8)	31	78·5 (10·54)	<0·001
	Derar 2017	50	46·37 (30·74)	50	51·10 (21·91)	0·34
Vertebral fractures	El Maghraoui 2012	97	33·5 (22)	81	46·7 (31·9)	0·001
	El Maataoui 2015	134	39·1 (17·8)	73	32·9 (23·8)	0·035
HIV	Hamill 2013	74	59·2 (16·5)	98	59·7 (16·5)	0·84
	Velaphi 2019 (mothers)	137	58·8 (31·2)	152	55·5 (28·3)	0·35
	Velaphi 2019 (children)	138	40·7 (21·2)	151	42·8 (20·9)	0·40
	Were 2014	16	88·1(58·2)	23	79·9 (37·4)	0·59
	Nansera 2011 (HIV only)	50	69·9 (27·5)	50	64·9(17·5)	0·28
	Nansera 2011 (HIV+TB)	50	59·9 (27·5)	50	64·9(17·5)	0·28
Diabetes	Abd-Allah 2014	120	35·5 (12·5)	120	46·6 (13·5)	<0·001
	Abbiyesuku 2016	80	91·2 (28·2)	29	107·2 (25·2)	0·008
Type 1 diabetes	Azab 2013	80	61·7 (14·0)	40	66·1 (12·0)	0·0919
Diabetes mellitus	Fondjo 2017	18	6·1 (4·8, 22·3)	100	31·3 (6·5, 81·8)	-
Graves disease	Gawad 2012	90	53·6 (18·5)	55	77·1 (16·2)	<0·001
Hepatitis C virus	Abdel-Mohsen 2018	60	111·1 (21·1)	30	164·7 (7·5)	<0·001
	Eltayeb 2015	66	61·58 (17·05)	28	98·31 (3·50)	<0·001
	Schaalan 2012	50	37·2 (8·7)	25	99·1 (27·0)	<0·001
Malaria	Cusick 2014	40	52·9 (16)	20	63·1 (17·7)	0·001
Malnutrition	Nabeta 2015	117	81·1 (30·0)	41	80·4 (27·2)	0·90
Metabolic syndrome	Alsayed 2007	93	40 (11·3)	70	47·1 (3·1)	<0·001
Pneumonia	Albanna 2010	40	37·6 (21·1)	40	87·25 (18·4)	<0·001
Polycystic ovary syndrome	Bakeer 2018	53	31·3 (14·9)	17	48·7 (27·3)	0·0013
	El-Shal 2013	150	59·9 (13·0)	150	67·9 (11·7)	<0·001
Renal diseases	Derar 2017	50	56·2 (33·6)	50	51·1 (21·9)	0·37
Schizophrenia	Akinlade 2017	60	19·8 (5·1)	30	28·1 (5·6)	<0·001
Tuberculosis	Wejse 2007	362	78·3 (22·6)	494	85·3 (34·8)	<0·001
	Ludmir 2016	39	80·4 (53·7, 99·8)	41	77·1 (56·4, 104·6)	-
	Ashenafi 2018	78	38·5	77	35·0	-
	Friis 2013	1223	110·9 (35·7)	347	84·4 (25·6)	<0·001

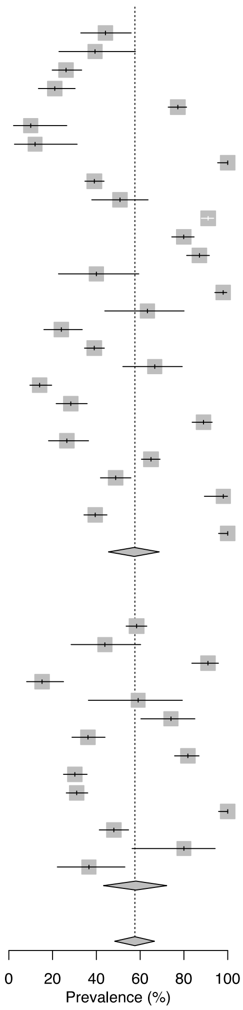
	Boillat-Blanco 2016	280	94·0 (26·9)	358	89·6 (26·9)	0·04
	Edem 2016	24	44·08 (9·5) pg/ml	20	45·80 (13·30) pg/ml	0·62
Alopecia areata	Fattah 2015	30	45·9 (8·5)	30	112·8 (51·2)	<0·001
β-thalassemia major	Fahim 2013	100	10·4 (4·6)	100	40·2 (12·3)	<0·001
Systemic lupus erythematosus	Abdel Galil 2018	123	64·6 (20·5)	100	114·4 (22·9)	<0·001
	Azab 2016	100	84·1 (3·7)	100	53·7 (3·0)	<0·001
	Emerah 2013	107	27·4 (15·4)	129	38·1 (15·9)	<0·001
	Hamza 2011	60	65·7 (30·1)	60	106·5(23·0)	<0·001
Albinism	Van der Walt 2016	50	54·4	50	45·9	-
Multiple sclerosis	Skalli 2018	113	29·2 (17·4)	146	32·4 (16·4)	0·1307
Vitiligo	Sobeih 2016	75	43·7 (20·2)	75	71·9 (26·2)	<0·001
	Ibrahim 2018	80	34·64 (3·03)	20	76·70 (10·73)	<0·001
Fibromyalgia	Olama 2013	50	37·7(15·2)	50	46·9 (13·5)	0·002
Neural tube defects	Nasri 2016	68	20·65 (10·25)	64	28·30 (13·82)	0·0004
Asthma	Maalmi 2013	155	47·1 (16·7)	225	75·6 (14·9)	<0·001
	Ali 2017	82	45·2 (8·7, 136·5)	33	90·1 (26·9, 189·1)	-
Systemic sclerosis	Ibn Yacoub 2012	30	27·2 (6·7)	30	57·41 (4·18)	<0·001
Goiter	Aboelnaga 2016	77	60·4 (21·7)	50	70·8 (27·2)	0·02

*These are median values (with IQR), the rest are means (SD). Significance between the group means was determined using the Student t-test.

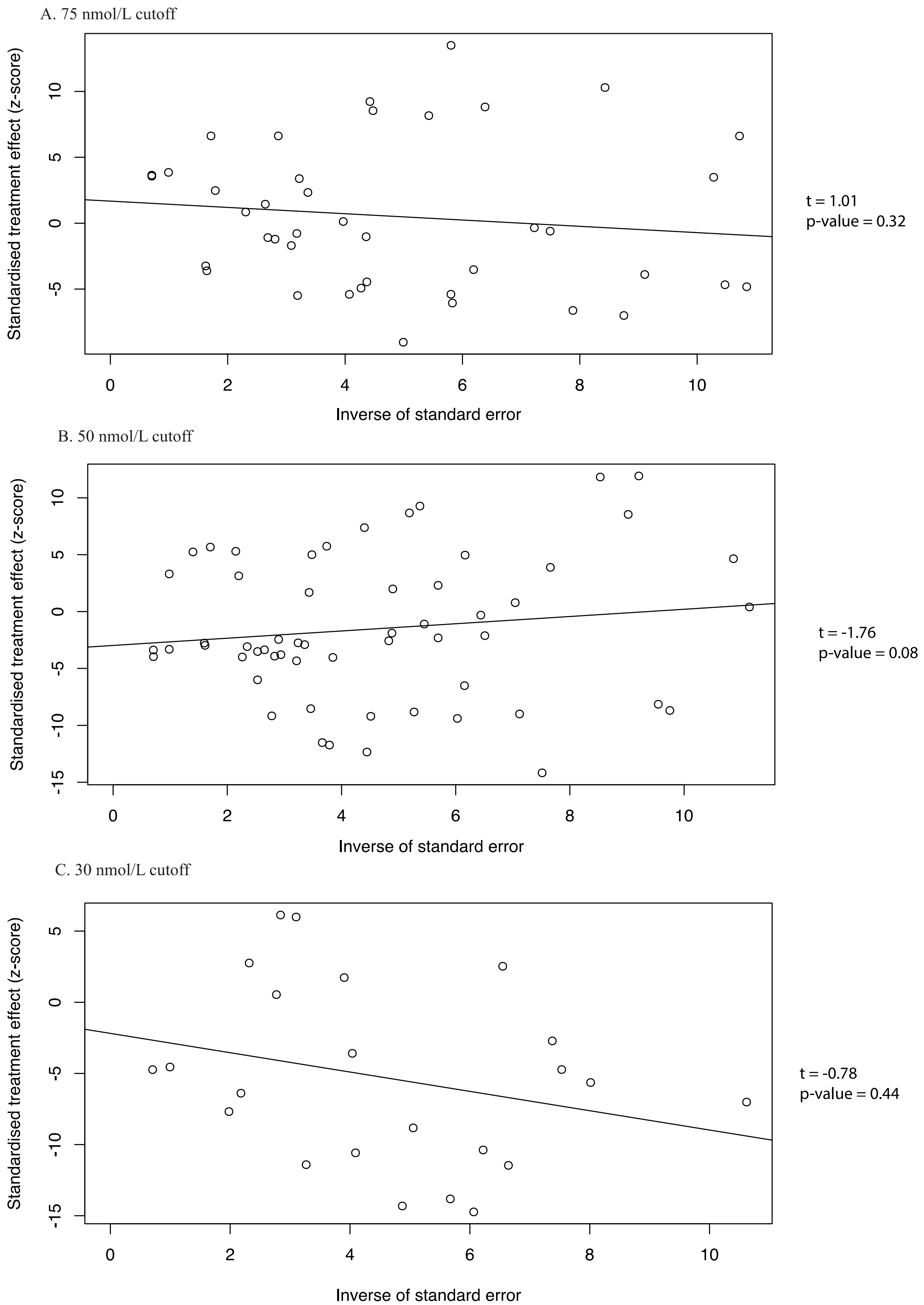


Supplementary Figure 1. Age of study participants in eligible studies and its association with 25(OH)D levels. The mean age and range are represented by the midpoints and error bars, respectively. The studies have been sorted by the participants' mean age in years. Studies that had a positive association between 25(OH)D levels and age are presented in green, negative associations are presented in red, no association in black, those that did not report any association are shown in grey.

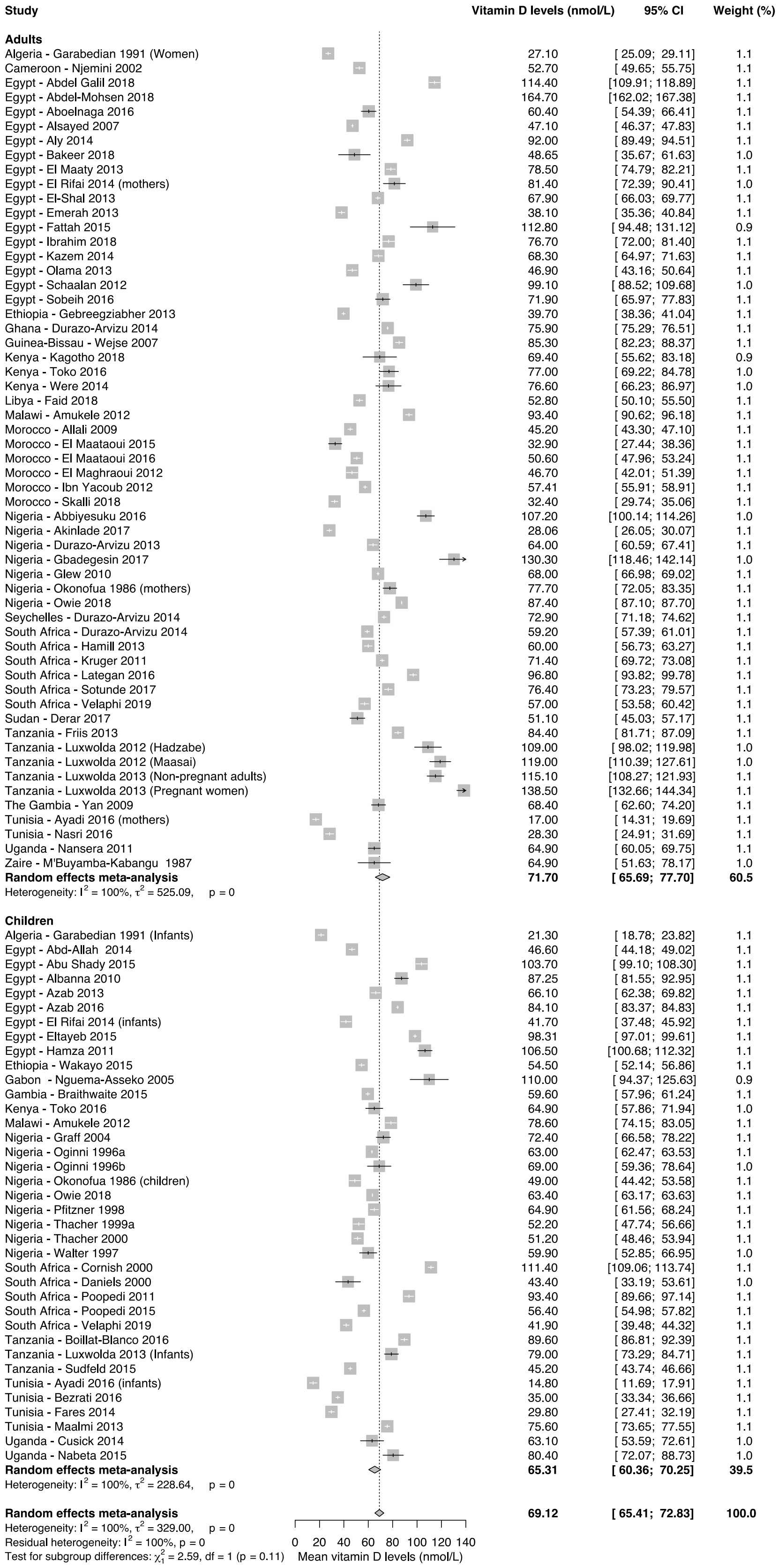
Study	Events	Total	Prevalence (%)	95% CI	Weight (%)
Adults					
Egypt - Aboelnaga 2016	34	77	44·16	[32·84; 55·93]	2·4
Egypt - Ali 2017	13	33	39·39	[22·91; 57·86]	2·3
Egypt - Aly 2014	46	176	26·14	[19·81; 33·28]	2·4
Egypt - Azab 2016	21	100	21·00	[13·49; 30·29]	2·4
Egypt - Botros 2015	312	404	77·23	[72·82; 81·23]	2·5
Egypt - Fattah 2015	3	30	10·00	[2·11; 26·53]	2·3
Egypt - Schaalan 2012	3	25	12·00	[2·55; 31·22]	2·2
Ethiopia - Ashenafi 2018	78	78	100·00	[95·38; 100·00]	2·4
Guinea Bissau - Wejse 2007	193	494	39·07	[34·74; 43·53]	2·5
Kenya - Toko 2016 (mothers)	32	63	50·79	[37·89; 63·62]	2·4
Morocco - Allali 2009	378	415	91·08	[87·92; 93·64]	2·5
Morocco - El Maataoui 2016	203	254	79·92	[74·46; 84·67]	2·4
Morocco - El Maghraoui 2012	155	178	87·08	[81·24; 91·63]	2·4
Morocco - Ibn Yacoub 2012	12	30	40·00	[22·66; 59·40]	2·3
Morocco - Skalli 2018	143	146	97·95	[94·11; 99·57]	2·4
Nigeria - Akinlade 2017	19	30	63·33	[43·86; 80·07]	2·3
Nigeria - Durazo -Arvizu 2013	24	100	24·00	[16·02; 33·57]	2·4
Nigeria - Gbadegesin 2017	180	461	39·05	[34·57; 43·67]	2·5
Nigeria - Glew 2010	34	51	66·67	[52·08; 79·24]	2·3
Nigeria - Oluwole 2019	29	206	14·08	[9·64; 19·59]	2·4
Nigeria - Owie 2018 (mothers)	47	166	28·31	[21·60; 35·82]	2·4
South Africa - Basson 2015	177	199	88·94	[83·74; 92·94]	2·4
South Africa - Hamill 2013	26	98	26·53	[18·12; 36·41]	2·4
South Africa - Myburgh 2018	328	505	64·95	[60·61; 69·11]	2·5
South Africa - Sotunde 2017	102	209	48·80	[41·85; 55·79]	2·4
South Africa - Van der Walt 2016	49	50	98·00	[89·35; 99·95]	2·3
Tanzania - Friis 2013	137	347	39·48	[34·30; 44·84]	2·4
Tunisia - Ayadi 2016 (mothers)	87	87	100·00	[95·85; 100·00]	2·4
Random effects meta-analyis		**5012**	**57·33**	**[45·53; 68·72]**	**66·8**
Heterogeneity: $I^2 = 99\%$, $\tau^2 = 0{\cdot}10$, $p = 0$					
Children					
Algeria - Djennane 2014	254	435	58·39	[53·60; 63·07]	2·5
Botwsana - Ludmir 2016	18	41	43·90	[28·47; 60·25]	2·3
Egypt - Fahim 2013	91	100	91·00	[83·60; 95·80]	2·4
Egypt - Yamamah 2016	12	79	15·19	[8·10; 25·03]	2·4
Kenya - Jones 2016	13	22	59·09	[36·35; 79·29]	2·2
Kenya - Toko 2016 (infants)	40	54	74·07	[60·35; 85·04]	2·3
Nigeria - Owie 2019 (infants)	60	166	36·14	[28·84; 43·95]	2·4
Nigeria - Pfitzner 1998	162	198	81·82	[75·73; 86·93]	2·4
South Africa - Poopedi 2011	89	295	30·17	[24·98; 35·76]	2·4
Tanzania - Boillat-Blanco 2016	111	358	31·01	[26·25; 36·08]	2·4
Tunisia - Ayadi 2016 (infants)	87	87	100·00	[95·85; 100·00]	2·4
Tunisia - Maalmi 2013	108	225	48·00	[41·31; 54·74]	2·4
Uganda - Cusick 2014	16	20	80·00	[56·34; 94·27]	2·2
Uganda - Nabeta 2015	15	41	36·59	[22·12; 53·06]	2·3
Random effects meta-analyis		**2121**	**58·06**	**[43·26; 72·17]**	**33·2**
Heterogeneity: $I^2 = 98\%$, $\tau^2 = 0{\cdot}07$, $p < 0{\cdot}01$					
Random effects meta-analyis		**7133**	**57·59**	**[48·38; 66·55]**	**100·0**
Heterogeneity: $I^2 = 98\%$, $\tau^2 = 0{\cdot}09$, $p = 0$					
Residual heterogeneity: $I^2 = 98\%$, $p = 0$					
Test for subgroup differences: $\chi^2_1 = 0{\cdot}01$, df = 1 ($p = 0{\cdot}94$)					



Supplementary Figure 2. Pooled prevalence of low vitamin D status in the general population in Africa using <75 nmol/L cut-off. Events were defined as number of participants in a study with 25(OH)D levels <75 nmol/L; total, the total number of participants in the study.

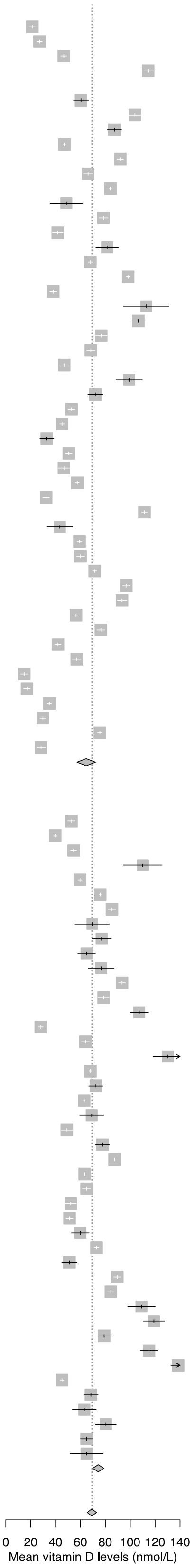


Supplementary Figure 3. Funnel plot asymmetry tests. The asymmetry of the funnel plots for the meta-analyses of prevalence was tested using Egger test of bias[20], where a linear regression method was used. P <0·1 indicated significant publication bias**.**

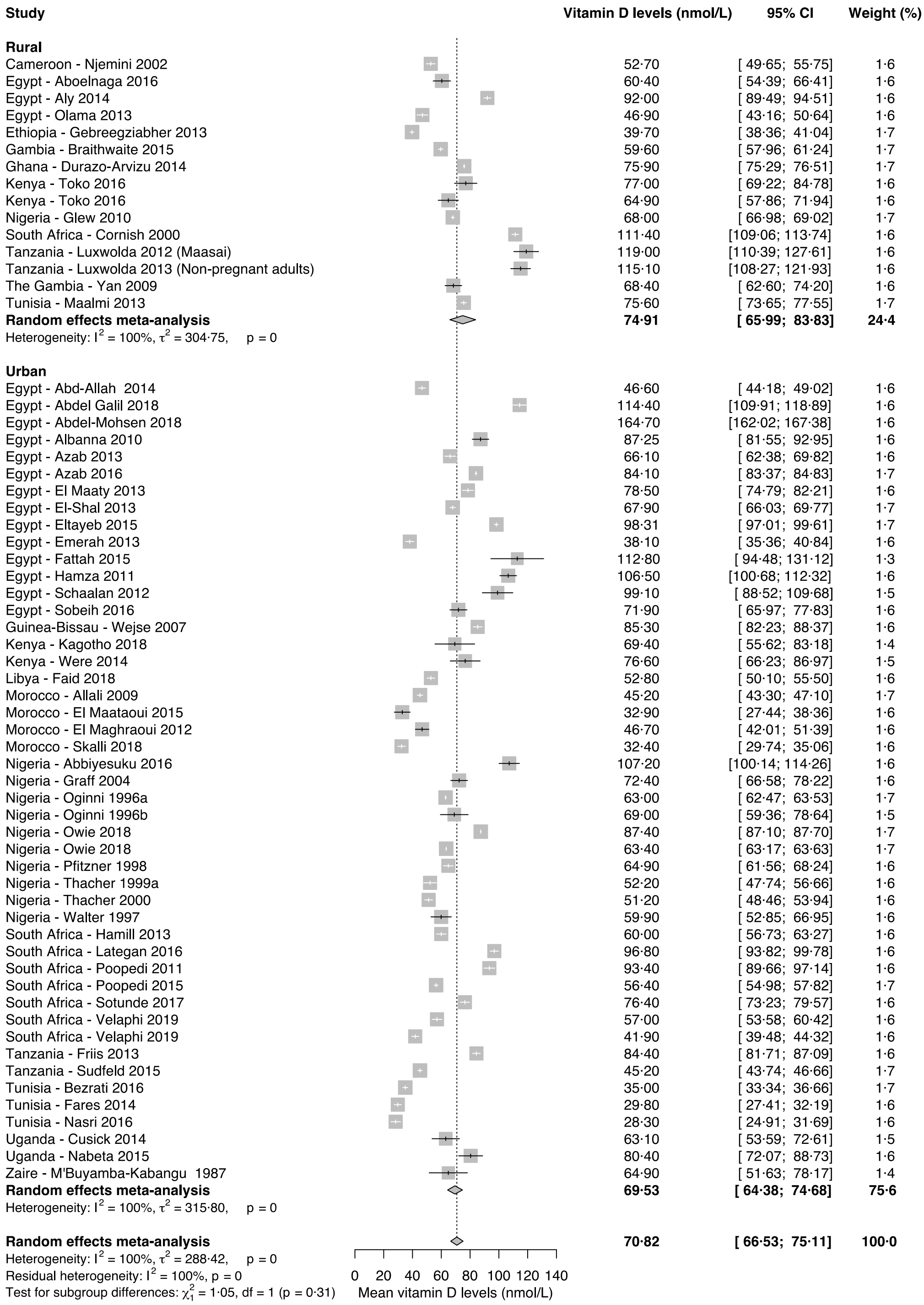


Supplementary Figure 4. Pooled mean 25(OH)D levels in the general population in Africa stratified by age groups. Studies that only reported median 25(OH)D values were excluded from this meta-analysis.

Study	Vitamin D levels (nmol/L)	95% CI	Weight (%)
Northern and Southern Africa			
Algeria - Garabedian 1991 (Infants)	21.30	[18.78; 23.82]	1.1
Algeria - Garabedian 1991 (Women)	27.10	[25.09; 29.11]	1.1
Egypt - Abd-Allah 2014	46.60	[44.18; 49.02]	1.1
Egypt - Abdel Galil 2018	114.40	[109.91; 118.89]	1.1
Egypt - Abdel-Mohsen 2018	164.70	[162.02; 167.38]	1.1
Egypt - Aboelnaga 2016	60.40	[54.39; 66.41]	1.1
Egypt - Abu Shady 2015	103.70	[99.10; 108.30]	1.1
Egypt - Albanna 2010	87.25	[81.55; 92.95]	1.1
Egypt - Alsayed 2007	47.10	[46.37; 47.83]	1.1
Egypt - Aly 2014	92.00	[89.49; 94.51]	1.1
Egypt - Azab 2013	66.10	[62.38; 69.82]	1.1
Egypt - Azab 2016	84.10	[83.37; 84.83]	1.1
Egypt - Bakeer 2018	48.65	[35.67; 61.63]	1.0
Egypt - El Maaty 2013	78.50	[74.79; 82.21]	1.1
Egypt - El Rifai 2014 (infants)	41.70	[37.48; 45.92]	1.1
Egypt - El Rifai 2014 (mothers)	81.40	[72.39; 90.41]	1.0
Egypt - El-Shal 2013	67.90	[66.03; 69.77]	1.1
Egypt - Eltayeb 2015	98.31	[97.01; 99.61]	1.1
Egypt - Emerah 2013	38.10	[35.36; 40.84]	1.1
Egypt - Fattah 2015	112.80	[94.48; 131.12]	0.9
Egypt - Hamza 2011	106.50	[100.68; 112.32]	1.1
Egypt - Ibrahim 2018	76.70	[72.00; 81.40]	1.1
Egypt - Kazem 2014	68.30	[64.97; 71.63]	1.1
Egypt - Olama 2013	46.90	[43.16; 50.64]	1.1
Egypt - Schaalan 2012	99.10	[88.52; 109.68]	1.0
Egypt - Sobeih 2016	71.90	[65.97; 77.83]	1.1
Libya - Faid 2018	52.80	[50.10; 55.50]	1.1
Morocco - Allali 2009	45.20	[43.30; 47.10]	1.1
Morocco - El Maataoui 2015	32.90	[27.44; 38.36]	1.1
Morocco - El Maataoui 2016	50.60	[47.96; 53.24]	1.1
Morocco - El Maghraoui 2012	46.70	[42.01; 51.39]	1.1
Morocco - Ibn Yacoub 2012	57.41	[55.91; 58.91]	1.1
Morocco - Skalli 2018	32.40	[29.74; 35.06]	1.1
South Africa - Cornish 2000	111.40	[109.06; 113.74]	1.1
South Africa - Daniels 2000	43.40	[33.19; 53.61]	1.0
South Africa - Durazo-Arvizu 2014	59.20	[57.39; 61.01]	1.1
South Africa - Hamill 2013	60.00	[56.73; 63.27]	1.1
South Africa - Kruger 2011	71.40	[69.72; 73.08]	1.1
South Africa - Lategan 2016	96.80	[93.82; 99.78]	1.1
South Africa - Poopedi 2011	93.40	[89.66; 97.14]	1.1
South Africa - Poopedi 2015	56.40	[54.98; 57.82]	1.1
South Africa - Sotunde 2017	76.40	[73.23; 79.57]	1.1
South Africa - Velaphi 2019	41.90	[39.48; 44.32]	1.1
South Africa - Velaphi 2019	57.00	[53.58; 60.42]	1.1
Tunisia - Ayadi 2016 (infants)	14.80	[11.69; 17.91]	1.1
Tunisia - Ayadi 2016 (mothers)	17.00	[14.31; 19.69]	1.1
Tunisia - Bezrati 2016	35.00	[33.34; 36.66]	1.1
Tunisia - Fares 2014	29.80	[27.41; 32.19]	1.1
Tunisia - Maalmi 2013	75.60	[73.65; 77.55]	1.1
Tunisia - Nasri 2016	28.30	[24.91; 31.69]	1.1
Random effects meta-analysis	**64.63**	**[57.21; 72.05]**	**53.5**
Heterogeneity: $I^2 = 100\%$, $\tau^2 = 710.22$, $p = 0$			
Western, Eastern and Central Africa			
Cameroon - Njemini 2002	52.70	[49.65; 55.75]	1.1
Ethiopia - Gebreegziabher 2013	39.70	[38.36; 41.04]	1.1
Ethiopia - Wakayo 2015	54.50	[52.14; 56.86]	1.1
Gabon - Nguema-Asseko 2005	110.00	[94.37; 125.63]	0.9
Gambia - Braithwaite 2015	59.60	[57.96; 61.24]	1.1
Ghana - Durazo-Arvizu 2014	75.90	[75.29; 76.51]	1.1
Guinea-Bissau - Wejse 2007	85.30	[82.23; 88.37]	1.1
Kenya - Kagotho 2018	69.40	[55.62; 83.18]	0.9
Kenya - Toko 2016	77.00	[69.22; 84.78]	1.0
Kenya - Toko 2016	64.90	[57.86; 71.94]	1.0
Kenya - Were 2014	76.60	[66.23; 86.97]	1.0
Malawi - Amukele 2012	93.40	[90.62; 96.18]	1.1
Malawi - Amukele 2012	78.60	[74.15; 83.05]	1.1
Nigeria - Abbiyesuku 2016	107.20	[100.14; 114.26]	1.0
Nigeria - Akinlade 2017	28.06	[26.05; 30.07]	1.1
Nigeria - Durazo-Arvizu 2013	64.00	[60.59; 67.41]	1.1
Nigeria - Gbadegesin 2017	130.30	[118.46; 142.14]	1.0
Nigeria - Glew 2010	68.00	[66.98; 69.02]	1.1
Nigeria - Graff 2004	72.40	[66.58; 78.22]	1.1
Nigeria - Oginni 1996a	63.00	[62.47; 63.53]	1.1
Nigeria - Oginni 1996b	69.00	[59.36; 78.64]	1.0
Nigeria - Okonofua 1986 (children)	49.00	[44.42; 53.58]	1.1
Nigeria - Okonofua 1986 (mothers)	77.70	[72.05; 83.35]	1.1
Nigeria - Owie 2018	87.40	[87.10; 87.70]	1.1
Nigeria - Owie 2018	63.40	[63.17; 63.63]	1.1
Nigeria - Pfitzner 1998	64.90	[61.56; 68.24]	1.1
Nigeria - Thacher 1999a	52.20	[47.74; 56.66]	1.1
Nigeria - Thacher 2000	51.20	[48.46; 53.94]	1.1
Nigeria - Walter 1997	59.90	[52.85; 66.95]	1.0
Seychelles - Durazo-Arvizu 2014	72.90	[71.18; 74.62]	1.1
Sudan - Derar 2017	51.10	[45.03; 57.17]	1.1
Tanzania - Boillat-Blanco 2016	89.60	[86.81; 92.39]	1.1
Tanzania - Friis 2013	84.40	[81.71; 87.09]	1.1
Tanzania - Luxwolda 2012 (Hadzabe)	109.00	[98.02; 119.98]	1.0
Tanzania - Luxwolda 2012 (Maasai)	119.00	[110.39; 127.61]	1.0
Tanzania - Luxwolda 2013 (Infants)	79.00	[73.29; 84.71]	1.1
Tanzania - Luxwolda 2013 (Non-pregnant adults)	115.10	[108.27; 121.93]	1.1
Tanzania - Luxwolda 2013 (Pregnant women)	138.50	[132.66; 144.34]	1.1
Tanzania - Sudfeld 2015	45.20	[43.74; 46.66]	1.1
The Gambia - Yan 2009	68.40	[62.60; 74.20]	1.1
Uganda - Cusick 2014	63.10	[53.59; 72.61]	1.0
Uganda - Nabeta 2015	80.40	[72.07; 88.73]	1.0
Uganda - Nansera 2011	64.90	[60.05; 69.75]	1.1
Zaire - M'Buyamba-Kabangu 1987	64.90	[51.63; 78.17]	1.0
Random effects meta-analysis	**74.27**	**[69.78; 78.76]**	**46.5**
Heterogeneity: $I^2 = 100\%$, $\tau^2 = 220.50$, $p = 0$			
Random effects meta-analysis	**69.12**	**[65.41; 72.83]**	**100.0**
Heterogeneity: $I^2 = 100\%$, $\tau^2 = 329.00$, $p = 0$			
Residual heterogeneity: $I^2 = 100\%$, $p = 0$			
Test for subgroup differences: $\chi^2_1 = 4.75$, df = 1 ($p = 0.03$)			



Supplementary Figure 5. 25(OH)D levels stratified by WHO African Regions. Northern African countries and South Africa were compared with West, East and Central African regions.

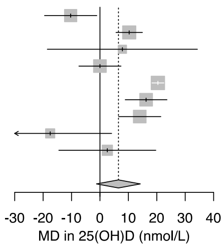


Supplementary Figure 6. 25(OH)D levels stratified by area (rural vs urban)

A· Mean differences in 25(OH)D levels between men and women

Study	Men Total	Men Mean	Men SD	Women Total	Women Mean	Women SD	MD in 25(OH)D (nmol/L)	95% CI	Weight (%)
Egypt - Abu Shady 2015	98	98·50	30·90	102	108·80	35·40	-10·30	[-19·50; -1·10]	12·1
Ethiopia - Wakayo 2015	75	60·30	16·90	99	50·00	13·50	10·30	[5·64; 14·96]	13·9
Kenya - Kagotho 2018	191	70·50	111·00	62	62·60	85·20	7·90	[-18·51; 34·31]	5·4
Libya - Faid 2018	75	52·80	30·00	380	52·80	29·30	0·00	[-7·40; 7·40]	12·9
Nigeria - Glew 2010	22	79·60	4·00	29	59·20	3·50	20·40	[18·30; 22·50]	14·5
South Africa - Lategan 2016	76	108·60	29·45	263	92·35	26·46	16·25	[8·90; 23·60]	12·9
South Africa - Poopedi 2011	155	100·00	34·40	144	86·00	31·10	14·00	[6·58; 21·42]	12·9
Tanzania - Luxwolda 2013 (Hadzabe)	21	106·30	29·20	4	123·80	18·00	-17·50	[-39·11; 4·11]	6·8
Tanzania - Luxwolda 2013 (Maasai)	15	120·90	24·00	20	118·30	27·40	2·60	[-14·48; 19·68]	8·5
Random effects meta-analysis	**728**			**1103**			**6·51**	**[-1·19; 14·20]**	**100·0**

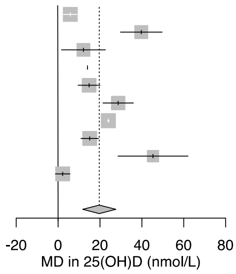
Heterogeneity: $I^2 = 90\%$, $\tau^2 = 105{\cdot}11$, $p < 0{\cdot}01$



B· Mean differences in 25(OH)D levels between mothers and their infants

Study	Mothers Total	Mothers Mean	Mothers SD	Infants Total	Infants Mean	Infants SD	MD in 25(OH)D (nmol/L)	95% CI	Weight (%)
Algeria - Garabedian 1991	84	27·10	9·40	84	21·30	11·80	5·80	[2·57; 9·03]	12·1
Egypt - El Rifai 2014	135	81·40	53·40	135	41·70	25·00	39·70	[29·75; 49·65]	10·4
Kenya - Toko 2016	63	77·00	31·50	54	64·90	26·40	12·10	[1·61; 22·59]	10·2
Libya - Markestad 1984	19	34·00	0·00	14	20·00	0·00	14·00		0·0
Malawi - Amukele 2012	21	93·40	6·50	21	78·60	10·40	14·80	[9·55; 20·05]	11·7
Nigeria - Okonofua 1986	30	77·70	15·80	30	49·00	12·80	28·70	[21·42; 35·98]	11·2
Nigeria - Owie 2018	166	87·40	2·00	166	63·40	1·50	24·00	[23·62; 24·38]	12·4
South Africa - Velaphi 2019	290	57·00	29·70	290	41·90	21·00	15·10	[10·91; 19·29]	12·0
Tanzania - Luxwolda 2013	25	135·90	32·00	25	90·60	28·20	45·30	[28·58; 62·02]	8·0
Tunisia - Ayadi 2016	87	17·00	12·80	87	14·80	10·40	2·20	[-1·27; 5·67]	12·1
Random effects meta-analysis	**920**			**906**			**19·65**	**[11·75; 27·55]**	**100·0**

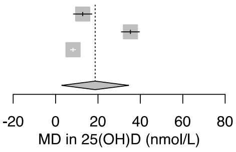
Heterogeneity: $I^2 = 97\%$, $\tau^2 = 131{\cdot}17$, $p < 0{\cdot}01$



C· Mean differences in 25(OH)D levels between rural and urban inhabitants

Study	Rural Total	Rural Mean	Rural SD	Urban Total	Urban Mean	Urban SD	MD in 25(OH)D (nmol/L)	95% CI	Weight (%)
Ethiopia - Wakayo 2015	85	61·00	15·10	89	48·20	14·00	12·80	[8·47; 17·13]	33·1
Nigeria - Durazo-Arvizu 2013	100	64·40	17·40	95	29·10	12·70	35·30	[31·04; 39·56]	33·1
South Africa - Kruger 2011	324	76·40	10·03	324	68·17	5·27	8·23	[7·00; 9·46]	33·8
Random effects meta-analysis	**509**			**508**			**18·70**	**[2·92; 34·48]**	**100·0**

Heterogeneity: $I^2 = 99\%$, $\tau^2 = 191{\cdot}13$, $p < 0{\cdot}01$



Supplementary Figure 7. Mean difference (MD) in 25(OH)D levels between men and women (A), between mothers and their infants (B) and between rural and urban inhabitants (C). These were differences in mean 25(OH)D levels between the groups in the same study.

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