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Article in Public Health · January 2021

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Review Paper

Does vitamin D deficiency increase the risk of obesity in adults and the elderly? A systematic review of prospective cohort studies

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ARTICLE INFO

Article history:

Received 23 July 2019

Received in revised form

9 April 2020

Accepted 25 April 2020

Keywords:

Vitamin D

Vitamin D deficiency

Systematic review

Cohort studies

ABSTRACT

Objectives: Epidemiological studies indicate an association between vitamin D deficiency and obesity. However, there is no consistent evidence of the direction or causal relationship between these conditions. Thus, we analysed the longitudinal relationship between vitamin D deficiency and obesity/adiposity in different age groups.

Study design: This study was a systematic review with PROSPERO registry (CRD42016047523).

Methods: Electronic searches were undertaken in Lilacs, Medline, Science Direct, Scopus and Web of Science databases until April 2020. For each study, we collected the frequency of vitamin D deficiency and obesity.

Results: In total, 5071 articles were identified and 8 were ultimately included in this systematic review. Five cohort studies involved adults, two of which recorded a positive association between vitamin D deficiency and obesity. The other three studies found a borderline or null association between vitamin D deficiency and obesity. Three studies investigated the elderly population; two of these recorded an association between vitamin D and greater adiposity, and one study recorded that 25-hydroxyvitamin D levels ≥ 30 ng/ml were associated with less weight gain in the follow-up.

Conclusions: This review reports that the majority of studies included show that vitamin D deficiency can contribute to the occurrence of obesity in adults and the elderly. It is recommended that prospective studies are conducted, with varying age groups and weather conditions, designed to test the longitudinal relationship between vitamin D deficiency and obesity outcomes.

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Introduction

Vitamin D deficiency is an important public health issue worldwide.^{1,2} A deficiency in vitamin D is defined as a serum 25-hydroxyvitamin D [25(OH)D] level of <20 ng per millilitre (50 nmol per litre).¹ Vitamin D deficiency underpins the aetiology of several chronic endocrine and metabolic disorders.^{3,4} In this regard, observational studies have identified the relationship between vitamin D and obesity, and there is evidence that vitamin D metabolism, storage and action are influenced by adiposity.⁵

Obesity and overweight are important nutritional issues in the field of public health, and there has been an increased prevalence of these in recent decades.⁶ Obesity is a risk factor for mortality, and it also coexists with vitamin D deficiency. Therefore, obesity and vitamin D deficiency are known to be associated, but the direction of this association and whether it is causal or not are uncertain.⁷

Observational evidence supports the association of obesity and vitamin D deficiency. A meta-analysis study reported that vitamin D deficiency was 35% higher in patients who are obese compared with the control group and 24% higher than in the overweight group.⁸ Other studies observed that a 10% higher body mass index (BMI) was associated with 4.2% lower 25(OH)D concentrations.⁷ However, cross-sectional associations are susceptible to confounding and reverse causation. Nonetheless, there is no consistent evidence of the causal relationship between vitamin D deficiency

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and the risk of obesity. This limitation contributed to the discussion about these events^{9,10} and encouraged this new systematic review of cohort studies investigating the causal connection and direction of the relationship between obesity and vitamin D deficiency.

Therefore, the aims of this study were to aggregate evidence of cohort studies that evaluate the relationship between vitamin D deficiency and the risk of obesity in adults and the elderly.

Methods

A systematic review was conducted in accordance with the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) standards¹¹ on studies that evaluated the causal relationship between vitamin D deficiency and obesity. We attempted to answer the following PICO (population, intervention, control and outcomes) question: in cohort studies, does vitamin D deficiency increase the occurrence of overweight and obesity in adults and the elderly when compared with individuals with healthy levels of vitamin D? To answer this question, the PROSPERO protocol was prepared, which was registered for commencing the literature research (CRD42016047523).

Research strategy and eligibility criteria

Three authors (M.P., E.M.P. and P.R.d.F.C.) independently searched Lilacs, Medline, Science Direct, Scopus and Web of Science databases applying the search terms 'vitamin D', 'cholecalciferol', 'ergocalciferol' combined with 'obesity', 'body mass index', 'overweight', 'weight' and 'cohort studies' or 'prospective studies' (see [Table S1](#) in the supplementary material). In addition, the references of the articles were evaluated to identify studies that were not indexed in the databases but may be relevant to this review. The first search was conducted in May 2018 and was subsequently reviewed in April 2020. The publications identified in the databases were entered in Mendeley® software to apply the eligibility criteria.

Articles were independently selected by two authors using eligibility criteria. The titles and abstracts of the publications identified were independently reviewed by two authors after removing duplicates. Eligible publications were original prospective cohort studies that carried out 25(OH)D serum assays, analysed the relationship between vitamin D status and anthropometric profiles and identified the prevalence of vitamin D deficiency and studies involving adults and the elderly that included any measures of body weight status or fat distribution.

The 25(OH)D serum level was used as an indicator for vitamin D status because this metabolite reflects the combined effect of intake, skin synthesis, storage, blood transport protein and catabolism.¹ Moreover, hydroxylation of 25(OH)D to 1,25(OH)2D3 (active vitamin D) occurs in several tissues: the half-life of 25(OH)D ranges from 2 to 3 weeks, while that of 1,25(OH)2D3 is approximately 6 h.¹² Consequently, 25(OH)D is the best indicator.

Studies were excluded if they involved pregnant women or individuals who had undergone bariatric surgery or if they were literature reviews or evaluated the relationship between vitamin D deficiency and nutritional status without explaining the methodology and the parameters applied to evaluate these events. There were no language restrictions. Articles were screened and selected for full-text review if they met the selection criteria. Disagreements were resolved through consensus between two authors who discussed the eligibility and tried to reach an agreement. In the absence of consensus, a third author (P.R.d.F.C.) evaluated whether the given study was eligible.

Quality assessment of studies

Two authors (M.P. and E.M.P.) independently scored the quality of the cohort studies included in the systematic review in accordance with the Newcastle–Ottawa Scale (NOS).¹³ This NOS scores nine questions that cover selection of the cohort (4 points), comparability of the cohort (2 points) and assessment of outcome (3 points) [total score ranging from 0 to 9 points]. The quality of the study was considered high if the sum score was ≥ 8 points or moderate if it ranged from 6 to 7 points. The final score was agreed between the two authors.

The risk of bias was evaluated in accordance with the Research Triangle Institute Item Bank (RTI–Item Bank),¹⁴ which contains 29 items for evaluating observational studies, 6 of which were applied to the studies included in this review. A high risk of bias was assigned to studies presenting one or more negative responses, and a moderate risk of bias was given to studies with one or more 'partially' or 'cannot be determined' outcomes. A low risk of bias was defined when all study questions presented a positive response.

Data extraction and analysis

Eligible articles were read in full, and information about their year of publication, sample size, follow-up duration, vitamin D and obesity measurements, vitamin D and obesity outcome at baseline, frequency of obesity in the follow-up, effect estimate (95% confidence interval [CI]) and adjustment was noted. The data obtained from the selected studies refer to vitamin D deficiency, vitamin D insufficiency and vitamin D sufficiency groups. An electronic correspondence was submitted to the authors of the selected articles requesting unavailable data for the inclusion in a possible meta-analysis. However, we did not receive any additional requested information.

Results

Research results

The initial search identified 5071 publications, 1187 of which were duplicates. After screening, 56 studies were analysed for their eligibility and 8 were selected for inclusion in the systematic review^{15–22} (see [Fig. 1](#)). The reasons for excluding articles included non-prospective design (11), lack of analysis of the vitamin D status and anthropometric profile relationship (12), non-inclusion of adiposity indicators as the outcome (14) and incorrect age group (11) (see [Fig. 1](#) and [Table S2](#) in the supplementary material).

Description of included studies

Included articles were published between 2009 and 2020; the majority ($n = 6$) were European studies published between 2012 and 2017.^{15–17,20–22} The sample at baseline ranged from 1079 to 9922 individuals (mean: 3965 participants). The follow-up time ranged from 2.9 to 15 years (mean: 7.8 years), and a total of 2636 people completed the studies (see [Table 1](#)).

The analysis of the serum concentration of 25(OH)D, regarded as a risk factor of adiposity, was determined by high-performance liquid chromatography (HPLC) and radioimmunoassay (RIA) in most studies. Obesity and adiposity, the outcome of the cohort studies, were measured by different methods, including body fat, waist circumference and BMI ([Table 1](#)).

The quality of the studies included in this review was evaluated using the NOS (see [Table 2](#)). High methodological quality was observed. Two cohorts obtained a maximum score.^{16,21} The main

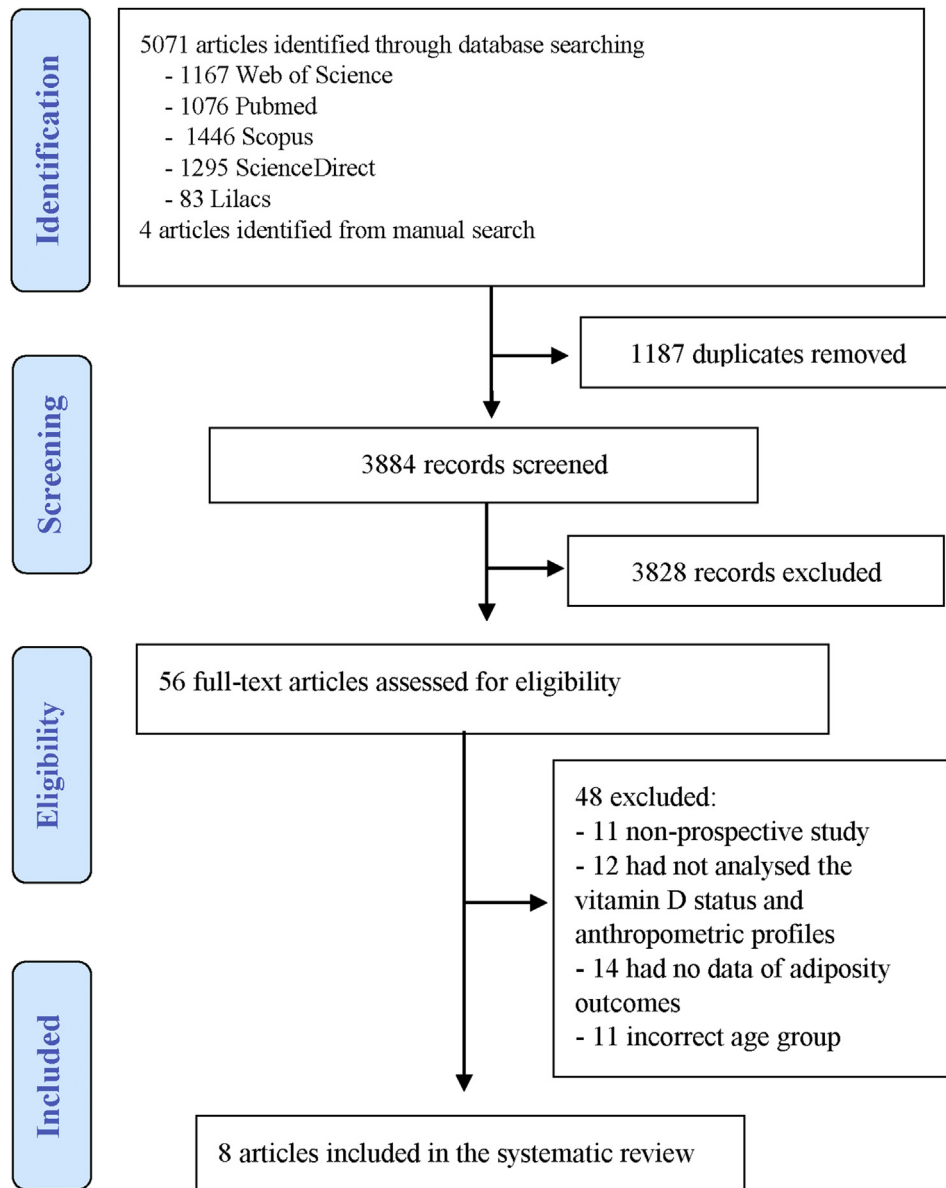


Fig. 1. Study selection flowchart.

problems identified in the studies refer to the absence of planning for the evaluation between the concentration of vitamin D and the development of obesity because the evaluated hypothesis was from cohorts designed to investigate other outcomes. In addition, a large number of participants were lost to follow-up (with values more than 20%), which can influence the validity of study results. In terms of the risk of bias, two of the selected articles showed a high risk of bias, three showed moderate risk and three showed low risk (see Table S3 in the supplementary material).

Main results

Considering the baseline of cohort studies, adiposity and/or obesity have occurred in different stages of life (i.e. different age groups). In five cohorts, the baseline started in the adult phase^{15,16,18,20,22}, and three cohorts evaluated the changes of adiposity indicators in the elderly^{17,19,21} (Table 1). In the five cohort studies involving adults,^{15,16,18,20,22} two showed a positive

association between vitamin D deficiency and obesity.^{15,16,22} The other two studies^{20,22} found a borderline or null association between vitamin D deficiency and obesity. Regarding the elderly population, two of three studies^{19,21} observed an association between vitamin D and greater adiposity.^{19,21} One cohort study¹⁹ showed that 25(OH)D levels ≥ 30 ng/ml were associated with less weight gain between visits. We could not carry out a meta-analysis for the studies included in the systematic review because of the variations in the exposure and outcomes measured.

Discussion

Eight investigations evaluating vitamin D concentrations and the occurrence of obesity and/or adiposity in different age groups were systematically reviewed. This review shows that vitamin D deficiency can be considered as one of the risk factors for obesity.

The relationship between vitamin D concentration and the increase in the amount of body fat in different age groups is

Table 1
Results of studies included in the systematic review.

Study	Country/ region	Sample	Follow-up duration, years	Outcome	Vitamin D measurement	Baseline 25 (OH)D level	Obesity measurement	% Obesity at baseline	% Obesity at follow-up	Effect estimate (95% CI)	Adjustment
González-Molero, 2013 ¹⁵ Pizarra study	Pizarra, Málaga, in southern Spain	Baseline 1996–1998: 1226 subjects, aged 18–68 years; Follow-up: 2002–2004: 988 subjects aged 23–72 years; 2005–2007: 961 subjects aged 27–77 years	12 years	Obesity	ECLIA VDD: ≤ 20 ng/ml	22.8 ng/ml, (SD = 6.2) VDD: 34.7%	Weight, height, waist and hip circumferences.	36.2%	39.5%	Risk of developing obesity between the second and third study by VD ≤ 17 ng/ml: OR: 2.35 (95% CI = 1.03–5.34) Risk of weight increase higher than 3.7 kg in non-obese (2->3) by VD ≤ 17 ng/ml: OR: 2.37 (95% CI = 1.23–4.58)	Sex, age, season, iPTH
Mai et al., 2012 ¹⁶ ; Study HUNT 2 and HUNT 3	Norway, Nord-Trøndelag Health	Baseline Sample = 10% random of HUNT 2 to HUNT 3: <i>n</i> = 2,584 HUNT 2 (1995–1997) adults aged 19–55 years Follow-up: HUNT 3 (2006–008) <i>n</i> = 2165	11 years	Obesity	Chemiluminescence assay VDD: <50 nmol/L	VDD: <50.0 nmol/L = 40% 50.0–74.9 nmol/L: 37%	Body weight, height and WC	Obesity: 12% BMI (kg/m ²): 25.8 (SD = 3.7) WC: 84.1 (SD = 11.2) VD-sufficient obesity: BMI (kg/m ²): 4.8% (<i>n</i> = 27) WC: 8.0% (<i>n</i> = 47) VD-insufficient obesity: BMI (kg/m ²): 10.5% (<i>n</i> = 97) OR: 2.19 (95% CI = 1.40, 3.41) WC: 12.2% (<i>n</i> = 112) OR: 1.43 (0.99, 2.08) VDD obesity: BMI (kg/m ²): 17.6% (<i>n</i> = 1.71) OR: 3.96 (95% CI = 2.58, 6.08) WC: 19.4 (<i>n</i> = 189) OR: 2.63 (95% CI = 1.84, 3.76)	Obesity: 15% VD-sufficient obesity: BMI (kg/m ²): 10.8% (<i>n</i> = 58) WC: 32.7% (<i>n</i> = 170) VD-insufficient obesity: BMI (kg/m ²): 14.8% (<i>n</i> = 122) WC: 36.8% (<i>n</i> = 298) VDD: BMI (kg/m ²): 18.3% (<i>n</i> = 147) WC: 43.4% (<i>n</i> = 340)	VD-insufficient obesity: BMI (kg/m ²): 1.38 (95% CI = 0.99, 1.94) WC: 1.13 (95% CI = 0.89, 1.44) VDD: BMI (kg/m ²): 1.73 (95% CI = 1.24, 2.41) WC: OR: 1.56 (1.22, 1.99)	Sex, age, smoking, education, physical activity, social benefits and economic difficulties at baseline.
Vogt et al., 2016 ¹⁷ ; KORA Cooperative Health Research in the Region of Augsburg	Southern Germany	Baseline in 2009: 1079 participants aged 65–90 years Follow-up 2012: 822 participants	2.9 (SD = 0.1) years	Change in weight and total body fat	ECLIA	21.47 ng/ml (SD = 11.24) VDD: <30 ng/ml = 79%	Total body fat: bioelectrical impedance analysis, weight	Total body fat 34.19 (SD = 6.94)	Body fat change per year (%) −0.37 (SD = 4.24)	1 ng/ml higher 25(OH)D Weight: 0.21 kg (95% CI = −0.31; −0.12) Body fat: 0.07% [95% CI = −0.11; −0.03]	Weight: disability, diabetes medication, heart disease Body fat: smoking status, kidney disease
Young et al., 2009 ¹⁸ ; Insulin Resistance Atherosclerosis	San Antonio, TX, San Luis Valley, CO; Los Angeles, CA	Baseline between 1999 and 2002: 917 Hispanics and 439 African-Americans Follow-up: 1081	5.3 yr	Adiposity	RIA	Hispanic: 17.9 ng/ml (SD = 6.7) Female 15.7 ng/ml (SD = 7.7) African-Americans:	SAT, VAT; Computed tomography scan Height and weight BMI	Hispanic: Male: BMI (kg/m ²): 27.9 (SD = 5.1) SAT: 264(SD = 128) VAT: 121(SD = 60) Female BMI (kg/m ²): 28.6(SD = 6.3)	Change Hispanic: Male: BMI (KG/M ²):0.8, (SD = 2.2) SAT:25,(SD = 55) VAT: 4, (SD = 36) Female BMI ((KG/M2));	25 (OH)D was inversely associated with BMI (KG/M2), VAT, and SAT in both populations at baseline (<i>P</i> = 0.001), but were not associated with 5-yr change in adiposity	Energy expenditure from vigorous activity, current smoking status, and education status

Table 1 (continued)

Study	Country/ region	Sample	Follow-up duration, years	Outcome	Vitamin D measurement	Baseline 25 (OH)D level	Obesity measurement	% Obesity at baseline	% Obesity at follow-up	Effect estimate (95% CI)	Adjustment
Vitezova et al., 2016 ²¹ Rotterdam Study	Rotterdam, the Netherlands	Follow-up in 2013, 2,916 individuals aged 46 years Baseline: 1990 to 1993 (<i>n</i> = 4787) Follow-up: 2002–2004 (<i>n</i> = 2158)	7 years	Body composition	ECLIA VDD: <50 nmol/L	VDD: 52% VDI: 29%	DXA, body weight	VDD: BMI 3rd visit (kg/m ²): 27.30 (SD = 4.1) WC 3rd visit (cm): 93.7 (SD = 12.0) VDS: BMI 3rd visit (kg/ m ²):26.2 (SD = 3.4) WC 3rd visit (cm): 92.6 (SD = 10.29)	VDD: BMI 4th visit (kg/ m ²): 27.8 (SD = 4.4) BMI 5th visit (kg/ m ²): 27.9 (SD = 4.6) WC 4th visit (cm): 93.6 (SD = 12.1) WC 5th visit (cm): 92.5 (SD = 12.9) VDS BMI 4th visit (kg/ m ²): 26.2(SD = 3.4) BMI 5th visit (kg/ m ²): 26.9 (SD = 3.4) WC 4th visit (cm): 92.8 (SD = 11.03) WC 5th visit (cm): 92.2 (SD = 11.8)	VDD: BMI β = 0.95 (95% CI = 0.53; 1.37) WC β = 3.07 (95% CI = 1.97; 4.17) Total fat (%) β = 1.56 (95% CI = 0.81; 2.31) Android fat (%) β = 0.18(95% CI = 0.01; 0.35) Gynoid fat (%) β = −0.08 (95% CI = 0.29; 0.14)	age and gender
Jääskeläinen et al., 2020 ²² H2000 and H2011	Finland	Baseline: 2000 –2001 (<i>n</i> = 9922) participants aged 30–64 years Follow-up: 2011 (<i>n</i> = 8135)	11 years	Weight gain or increase in waist circumference	RIA VDD: <30 nmol/L VDI: 30–49 nmol/L	Men: 45 nmol/l Women: 46 nmol	Height, weight and bioimpedance	Men VDD WC (cm): 97.8 (95% CI = 96.3; 99.3) Women: VDD WC (cm): 87.9 (95% CI = 86.2; 89.5)	Men: VD: \geq 10% increase in WC (OR for sufficient v. VVD OR = 0.41; 95% CI = 0.25 0.67) Weight gain >10%: OR = 0.60 (95% CI = 0.37, 0.97) Women: WC: VD: \geq 10% (sufficient v. VDD = 0.80; 95% CI = 0.55; 1.16) Weight gain >10%: OR = 0.83 (CI 95% = 0.57; 1.20)	Adjusted for age at baseline	

OR, odds ratio; RR, relative risk; BMI (kg/m²), body mass index; BW, body weight; WC, waist circumference, BFM, body fat mass; ECLIA, electrochemiluminescence immunoassay; RIA, radioimmunoassay; HPLC, high-performance liquid chromatography; MAC, mid-arm circumference; DXA, percent body dual-energy X-ray absorptiometry.

Table 2

Quality assessment using the Newcastle–Ottawa quality assessment scale for the studies included in the systematic review.

Authors, year	Selection				Comparability		Outcome			Score	Overall judgement
	Representativeness of the exposed Cohort	Selection of the non-exposed cohort	Exposure Ascertainment	Outcome not present at the start of the study	Study controls for sex and age	Study controls for any additional important factor	Assessment of outcome	Length of follow-up	Adequacy of follow-up		
González-Molero, 2013 ¹⁵	★	★	★		★	★	★	★	★	8	High
Mai et al., 2012 ¹⁶	★	★	★	★	★	★	★	★	★	9	High
Vogt, 2016 ¹⁷	★	★	★		★	★	★			6	Moderate
Young, 2009 ¹⁸	★	★	★		★	★	★	★	★	7	Moderate
LeBlanc et al., 2012 ¹⁹	★	★	★		★	★	★			6	Moderate
Larsen et al., 2016 ²⁰	★	★	★		★	★	★		★	7	Moderate
Vitezova et al., 2016 ²¹	★	★	★	★	★	★	★	★	★	9	High
Jääskeläinen et al., 2020 ²²	★	★	★	★	★	★	★		★	8	High

biologically plausible because of the vitamin D participation in the regulation of adipogenesis. Therefore, vitamin D deficiency can favour a greater adiposity by promoting an increase in parathyroid hormone levels and the inflow of calcium in adipocytes, thus increasing lipogenesis and inhibiting the lipolysis in adipocytes.²³ It is also suggested that the depletion of vitamin D storage can lead to excessive differentiation between preadipocytes and adipocytes. Other proposed mechanisms include high expressions of the vitamin D receptor in adipose tissue and the possibility of vitamin D playing a role in the pathogenesis of the metabolic syndrome.²⁴

Evidence from epidemiological studies suggests that obesity can be the result of an excessive adaptive winter response and that the decline in vitamin D skin synthesis due to reduced sunlight exposure contributes to the tendency towards increasing fat mass during the colder periods of the year.^{7,25} Thus, it is possible that the high concentrations of vitamin D increase the energy expenditure because of the uncoupling of oxidative phosphorylation in adipose tissues.

In addition, possible antiobesity mechanisms of calcium and vitamin D include control of adipocyte death, regulation of adipogenesis and improvement of lipid metabolism.²⁶ It is also suggested

that in the occurrence of high concentrations of vitamin D, the skeletal muscle can store vitamin D and gradually release 25(OH)D in the blood flow, preventing the 25(OH)D deterioration in the liver. Vitamin D retention in the muscle tissue can activate 25(OH)D to 1,25(OH)2D, via connection with vitamin D receptor (VDR), promoting the increase and improvement of muscle function.²⁶ This fact could explain the relationship between sufficient vitamin D (>75 nmol/L) and lower amount and percentage of body fat identified in some of the studies analysed in this review.

The relationship between vitamin D concentrations and adiposity is bidirectional, that is, a disorder in one of the events constitutes a risk factor for the occurrence of the other.^{8,15} In this regard, the classical observational studies suggest that obesity contributes to vitamin D deficiency. One of them says that, in subjects who are obese, there is the fat-soluble vitamin D sequestration in the adipose tissue⁵ and volumetric dilution,²⁷ which imply that vitamin D plasma levels decrease as body size and, hence, fat stores increase. As a result, if fat stores decrease, there ought to be a greater return of vitamin D into plasma, resulting in increased vitamin D status.²⁸ It has been suggested that individuals who are obese have limited mobility and avoid outdoor activities,

Table 3

Risk-of-bias assessment using the Research Triangle Institute Item Bank for the studies included in the systematic review.

Authors, year	Question numbers						Overall judgement on risk of bias
	Q1	Q2	Q3	Q6	Q7	Q8	
González-Molero, 2013	–	+	+	+	+	–	High
Mai et al., 2012	+	+	+	+	+	+	Moderate
Vogt, 2016	+	+	+	+	+	?	Moderate
Young 2009	?	+	+	+	+	+	Moderate
LeBlanc et al., 2012	+	+	+	+	+	+	Low
Larsen et al., 2016	+	–	+	+	+	–	High
Vitezova et al., 2016	+	+	+	+	+	+	Low
Jääskeläinen et al., 2020	+	+	+	+	+	+	Low

Key: + = low risk of bias; – = high risk of bias; ? = unclear risk of bias.; Q1: Do the inclusion/exclusion criteria vary across the comparison groups of the study; Q2: Does the strategy for recruiting participants into the study differ across groups?; Q3: Is the selection of the comparison group inappropriate, after taking into account feasibility and ethical considerations?; Q6: Were valid and reliable measures, implemented consistently across all study participants used to assess inclusion/exclusion criteria, exposure outcomes and confounding?; Q7: Was the length of follow-up different across study groups?; Q8: In cases of tall loss to follow-up (or differential loss to follow-up), was the impact assessed (e.g., through sensitivity analysis or other adjustment method)?

which limits exposure to the sun and, consequently, cutaneous vitamin D synthesis. Other mechanisms involve the relationship between vitamin D and inflammatory adipocytes and different genomic and non-genomic mechanisms exerted by vitamin D.^{19,29}

The Pizarra study,¹⁵ which included 961 subjects in three follow-up steps, observed a lack of association between vitamin D and the risk of obesity during the 4 years of follow-up. In addition, this study showed, at the second evaluation carried out 4 years later, that 25-hydroxyvitamin D values ≤ 17 ng/ml (≤ 42.5 nmol/l) in participants who are not obese (BMI <30 kg/m²) were significantly associated with an increased risk of developing obesity after diverse adjustments.¹⁵ Corroborating with such results, the Trøndelag Health Study (HUNT) study, which evaluated 2165 subjects with a BMI <30 kg/m², found that 25(OH)D values ≤ 50 nmol/l were associated with an increased risk of obesity. A prospective population-based study demonstrated that vitamin D insufficiency may be a risk factor for abdominal obesity in men but not in women.²¹

Low vitamin D concentrations in the elderly are associated with a higher body fat percentage,²¹ and higher 25(OH)D levels are associated with lower weight gains.¹⁹ For each ten-unit increase in serum 25(OH)D, there was a 0.03-unit decrease in android fat.²¹ In addition, it has been shown that 25(OH)D levels were associated with a lower body fat gain in women but not in men.¹⁷

It should be noted that cohort studies that did not include long-term follow-up stages found an association between 25(OH)D and changes in adiposity measures; however, this association appears to be marginal²⁰ or absent when considering a five-year change in adiposity.¹⁸ The absence of a more detailed evaluation of the participants during the follow-up is a critical limitation to these studies, favouring the non-detection of potentially confounding variables or effect modifiers of the relationship between vitamin D and the modification in the amount of body fat in the elderly.

Limitations and recommendations of the study

To the best of our knowledge, this is the first systematic review reporting the longitudinal relationship between vitamin D concentrations and the development of adiposity in adults and the elderly. However, it should be noted that this systematic review has some limitations. Most of the included studies were not designed to observe the relationship between vitamin D concentrations and the occurrence of high adiposity/obesity. The relationship between vitamin D and adiposity was analysed in both completed and current/ongoing study cohorts. In addition, there was a low prevalence of the exposure occurrence and the outcome incidence, making it difficult to compare the groups and the confounding control. This can be a result of the lack of sampling calculation and insufficient capacity to test the hypothesis that vitamin D can influence the occurrence of outcomes related to adipose tissue excess.

Most of the statistical analyses applied to the data did not consider the repeated measures, common to cohort studies. In addition, the results of the studies included in this review were not stratified based on gender. This limitation can impair the validity of some findings because body composition and fat percentage differ between men and women. Furthermore, the studies showed several methodological divergences preventing the exploration of the meta-analysis heterogeneity. In addition, the studies showed a high risk of bias. Some factors contributing to high risk of bias included the selection criteria of the study participants, the exposure evaluation and the outcome and the number of participants lost to follow-up. In terms of study locations, there was a greater frequency of studies conducted in countries with a predominance of cold weather, preventing the comparison between latitudes,

climatic conditions and occurrence of vitamin D deficiency and obesity.

Despite these limitations, this systematic review of cohort studies is consistent from the methodological perspective, considering its rigorous selection method. There was a greater frequency of studies reporting that vitamin D deficiency can contribute to obesity occurrence in adults and the elderly. Therefore, we recommend the development of prospective studies, with varying age groups and weather conditions, designed to test the relationship between vitamin D deficiency and outcomes related to obesity/adiposity. The sample size should be suitable for comparison between the groups, confounding control and reverse causation assessment. If the relationship between vitamin D deficiency and adverse effects on body composition in distinct populations is confirmed in future cohort studies and meta-analyses, the adoption of intervention strategies to prevent and control vitamin D deficiency is recommended, at both individual and population levels, with the aim of promoting obesity prevention.

Author statements

Ethical approval

Not required.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial or not-for-profit sectors.

Competing interests

The authors declare that they have no conflicts of interest.

Authors' contributions

M.P. contributed to conception, design, search, data interpretation and manuscript drafting. P.R.d.F.C. contributed to design, data interpretation and manuscript drafting. E.M.P. and I.R.d.L.L. contributed to data collection and manuscript drafting. A.M.O. supervised the study and contributed to design, data interpretation and manuscript drafting. All authors approved the final manuscript for submission.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.puhe.2020.04.031>.

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