National Institute for Health and Care Excellence

Final

Maternal and child Nutrition

[D] Evidence reviews for optimum vitamin D dose during pregnancy for those medically classified as being in the overweight or obesity weight categories

NICE guideline NG247

Evidence reviews underpinning research recommendation on optimum vitamin D dose during pregnancy for people with a BMI medically classified as being in the overweight or obesity weight categories in the NICE guideline

January 2025

Final

These evidence reviews were developed by NICE

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The recommendations in this guideline represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, professionals are expected to take this guideline fully into account, alongside the individual needs, preferences and values of their patients or service users. The recommendations in this guideline are not mandatory and the guideline does not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or their carer or guardian.

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Review question

What dose of vitamin D is appropriate during pregnancy for women with a BMI medically classified as being in the overweight or obesity weight categories?

Introduction

Vitamin D demands increase during pregnancy and during lactation. There is a lack of scientific consensus on the amount of vitamin D intake that is deemed optimal in populations of pregnant women, regardless of additional risk factors that contribute to low vitamin D status, but current advice in the United Kingdom (UK) is that the reference nutrient intake for vitamin D is 10µg/day throughout pregnancy and during lactation, the same as for the general population (SACN 2016). For majority of the population (including those pregnant and breastfeeding, this means a 10µg/day supplement is recommended during winter months when sunlight exposure is more limited. For population at an increased risk, such as people with darker skin or less skin exposure to sunlight, the supplementation is recommended throughout the year.

Observational studies have reported a relationship between low vitamin D status, pre-term birth, and low birth weight. There is suggestion that low vitamin D status is associated with gestational diabetes mellitus (GDM) and preeclampsia, although these relationships are not established. In the infant there is some suggestion of an association with low bone mass and poor respiratory function in childhood.

While limited in number, observational studies have shown that pregnant women with body mass indexes (BMIs) above 29kg/m^2 have significantly lower vitamin D status than those with a BMI ≤ 29k g/m^2. Vitamin D status of the neonate has been shown to be highly correlated with maternal 25 hydroxyvitamin D (25(OH)D) concentrations. It has been suggested that circulating 25(OH)D in newborns should be maintained above a minimum of 25–30 nmol/L. There are no known thresholds for 25(OH)D concentrations in umbilical cord indicative of improved infant health outcomes. The aim of this review is to assess what dose of vitamin D supplementation is appropriate during pregnancy for women medically classified as being in the overweight or obesity weight categories.

Summary of the protocol

See Table 1 for a summary of the Population, Intervention, Comparison and Outcome (PICO) characteristics of this review.

Table 1: Summary of the protocol (PICO table)

Population	Women during a single or multiple pregnancy, who have a BMI medically classified as being in the overweight or obesity weight categories at booking or first scan
Intervention	• Low dose vitamin D supplementation (<10µg/400IU daily) • Medium dose vitamin D supplementation (≥10µg/400IU to 20µg/800IU daily)

	• High dose vitamin D supplementation (≥20µg/800IU daily) In combination or not with other vitamins and minerals
Comparison	• A different vitamin D supplementation dose daily (same dose category) • A different vitamin D supplementation dose daily (different dose category) • Standard care (as defined by the study) • Placebo • No intervention
Outcome	**Critical** • Maternal serum 25(OH)D concentration • Preterm birth (before 37 weeks gestational age) • Low birth weight (<2500g) **Important** • Pre-eclampsia • Gestational diabetes • Bone mass in infant • Childhood respiratory function

25(OH)D: 25 hydroxyvitamin D; BMI: body mass index; IU: international unit

For further details see the review protocol in appendix A.

Methods and process

This evidence review was developed using the methods and process described in Developing NICE guidelines: the manual. Methods specific to this review question are described in the review protocol in appendix A and the methods document (supplementary document 1).

Declarations of interest were recorded according to NICE's conflicts of interest policy.

Effectiveness evidence

Included studies

Two randomised trials were included for this review (Alhomaid 2021, Corcoy 2020).

The included studies are summarised in Table 2.

The study population included women with singleton pregnancies and mixed BMI population. However, only evidence on women with a BMI ≥ 25kg/m^2 was extracted from the studies and reported in this review. There was no evidence for women with multiple pregnancies.

There was evidence for 2 of the intervention groups stated in the protocol – medium dose vitamin D supplementation (≥10µg/ 400IU to 20µg/800IU daily) and high dose vitamin D supplementation (≥20µg/800IU daily). One study compared medium dose vitamin D supplementation of 10µg (400IU)/day with another medium dose vitamin D supplementation of 20µg (800IU)/day (Alhomaid 2021) and one study compared no vitamin D supplementation to a high dose vitamin D supplementation of 40µg (1600IU)/day (Corcoy 2020). There was no evidence for low dose vitamin D supplementation (<10µg/ 400IU daily) as defined in the protocol, standard care or no intervention.

Two studies reported on maternal serum 25(OH)D concentration and 1 study reported on preterm birth (before 37 weeks gestational age), low birth weight (<2500 g), pre-eclampsia and gestational diabetes. There was no evidence for bone mass in infant or childhood respiratory function.

Evidence was stratified according to pre-specified BMI ranges where possible.

Pre-specified sub-group analysis (deprived socioeconomic groups, under/over 40 years of age, women and parents with disabilities, including learning disabilities and other physical and mental health conditions, women going through assisted conception, LGBTQ+ women and parents, children with developmental problems, geographical variation and religion and cultural considerations) could not be conducted as there was no information within the studies to conduct the analysis.

See the literature search strategy in appendix B and study selection flow chart in appendix C.

Excluded studies

Studies not included in this review are listed, and reasons for their exclusion are provided in appendix K.

Summary of included studies

Summaries of the studies that were included in this review are presented in Table 2.

Table 2: Summary of included studies.

Study	Population	Intervention	Comparison	Outcomes
Alhomaid 2021 RCT Northern Ireland	N = 240 pregnant women Age in years [Mean (SD)]: Intervention (20µg/d) = 29.5 (5.5) Control (10µg/d) = 29.7 (5.1) Gestational age in weeks [Mean (SD)]: Intervention (20µg/d) = 12.8 (1.4) Control (10µg/d) = 13.0 (1.4) BMI in kg/m^2 [Mean (SD)]: Intervention (20µg/d) = 27.8 (5.4)	20µg (800IU) vitamin D supplement from 12 weeks gestational age until birth 1 multivitamin tablet containing 10µg (400IU) vitamin D and 1 tablet containing 10µg (400IU) vitamin D	10µg (400IU) vitamin D supplement from 12 weeks gestational age until birth 1 multivitamin tablet containing 10µg (400IU) vitamin D and 1 tablet containing 0µg vitamin D (placebo)	• Maternal serum 25(OH)D concentration at 28- and 36-weeks gestation – data was presented separately for overweight and obese women

Study	Population	Intervention	Comparison	Outcomes
	Control (10µg/d) = 28.1 (5.7) Singleton pregnancies only			
Corcoy 2020 Cluster RCT 7 European countries • United Kingdom • Ireland • Australia • Poland • Italy • Spain • Belgium	N = 154 pregnant women Age in years [Mean (SD)]: Intervention (40µg/d) = 32.3 (5.2) Control (Placebo) = 32.8 (5.4) Gestational age in years [Mean (SD)]: Intervention (40µg/d) = 15.0 (2.9) Control (Placebo) = 15.4 (2.5) BMI in kg/m^2 [Mean (SD)]: Intervention (40µg/d) = 34.2 (4.3) Control (Placebo) = 34.2 (4.2) Singleton pregnancies only	40µg (1600IU)/day vitamin D3 supplement from ~ 15 weeks gestational age until birth 4 tablets each containing 10µg (400IU) of vitamin D3	Placebo from ~ 15 weeks gestational age until birth 4 tablets identical to the intervention tablets	• Maternal serum 25(OH)D concentration at 24-28 weeks, 35-37 weeks and at delivery • Preterm birth at delivery • Low birth weight at delivery (<2500g) • Preeclampsia at delivery • Gestational diabetes mellitus at 24-28 weeks and 35-37 weeks

25(OH)D: 25 hydroxyvitamin D; BMI: body mass index; IU: international unit; RCT: randomised controlled trial

See the full evidence tables in appendix D. No meta-analysis was conducted (and so there are no forest plots in appendix E).

Summary of the evidence

See appendix F for full GRADE tables.

The below paragraphs summarise the evidence for 2 comparisons: medium dose vitamin D supplementation (≥10µg/ 400IU to 20µg/800IU daily) versus a different vitamin D supplementation dose daily (same dose category) and high dose vitamin D supplementation (≥20µg/800IU daily) versus placebo.

Comparison 1: Comparison between 20µg/day and 10µg/day vitamin D supplementation in pregnant women medically classified as being in the overweight or obesity weight categories (BMI ≥25.0 kg/m^2) - singleton pregnancies only

One study was included in this comparison.

Overall 20µg (800IU)/day of vitamin D supplementation showed inconsistent findings for maternal serum 25(OH)D concentration when compared to 10µg (400IU)/day in women in overweight or obesity weight categories by gestational age. In women medically classified as overweight, the evidence showed a possible important benefit at 36 weeks gestational age, and no important difference at 28 weeks gestational age. No important difference or no evidence of an important difference was found in women medically classified as being in the obesity weight category at the same time points. No other relevant outcomes were reported for this comparison group. The quality of the evidence in this comparison was moderate.

Comparison 2: Comparison between 40µg/day vitamin D supplementation and no supplementation in pregnant women medically classified as being in the overweight or obesity weight categories (BMI ≥ 29.0kg/m^2) - singleton pregnancies only

One study was included in this comparison.

Overall 40µg (1600 IU)/day of vitamin D supplementation in pregnant women medically classified as being in the overweight or obesity weight categories showed an important benefit over placebo in terms of maternal serum 25(OH)D concentration at 24 to 28 and 35 to 37 weeks gestational age, and at delivery. There was no evidence of important difference or no important difference for other outcomes such as preterm birth, low birth weight (<2.5kg), preeclampsia and gestational diabetes. The quality of the evidence in this comparison was very low to moderate.

Economic evidence

Included studies

No economic studies were identified which were applicable to this review question. See the literature search strategy in appendix B and economic study selection flow chart in appendix G.

Excluded studies

No economic studies were reviewed at full text and excluded from this review.

Economic model

No economic modelling was undertaken for this review because the committee agreed that other topics were higher priorities for economic evaluation.

The committee's discussion and interpretation of the evidence

The outcomes that matter most

Maternal serum 25(OH)D concentration, preterm birth (before 37 weeks gestational age) and low birth weight (<2500g) were prioritised as critical outcomes by the committee. The main aim of this review was to determine the optimal dose of vitamin D during pregnancy for women medically classified as being in the overweight or obesity weight categories. Maternal serum 25(OH)D was prioritised as a critical outcome because it is a key measure of vitamin D concentration in the blood, which will help to determine what dosage will achieve optimal blood vitamin D levels. Preterm birth and low birth weight were prioritised as critical

outcomes because these outcomes are crucial to the health of the neonate and are impacted by maternal vitamin D levels.

Pre-eclampsia, gestational diabetes, bone mass in infants and childhood respiratory function were prioritised as important outcomes as they are associated with vitamin D levels and may have long-term effects on the mother and the infant. In addition, the committee recognised that preeclampsia and gestational diabetes have been prioritised as outcomes in published literature. Bone mass in infants was agreed as an important outcome because bone formation is directly associated with vitamin D and the fetus obtains vitamin D from the mother. The committee acknowledged that there is evidence that shows the relationship between vitamin D supplementation and reduced risk of severe asthma attacks, but agreed that studies' follow up may not be long enough to capture this. Therefore, they agreed to include any childhood respiratory function as an important outcome.

Evidence was available for all outcomes except for bone mass in infants and childhood respiratory function.

The quality of the evidence

The quality of the evidence was assessed using GRADE and ranged from moderate to very low, with most of the evidence being of moderate quality. The main issues with the quality were due to methodological risk of bias due to issues with randomisation and missing outcome data, and bias arising from seriously imprecise findings. Studies were assessed for quality using the Cochrane Risk of Bias (Rob) 2.0 tool for randomised studies and the Cochrane RoB 2.0 Cluster randomised trials tool for cluster randomised studies.

Benefits and harms

The committee discussed the evidence from the review and agreed that whilst there was some evidence suggesting a benefit for vitamin D for some outcomes, given the low quality and uncertainty in evidence, the committee decided not to make any recommendations.

Evidence for 20µg (800IU) versus 10µg (400IU) of vitamin D supplementation showed that there was minimal increase in maternal serum 25(OH)D concentration for women medically classified as overweight, and no difference in women medically classified as being in the obesity weight categories. Therefore, due to insufficient evidence and inconsistency in the evidence, the committee agreed not to make any recommendations for this specific dosage.

The evidence for 40µg (1600IU) vitamin D supplementation showed that there was increased maternal serum concentration levels at various timepoints during pregnancy and at birth but there was no difference for any other outcomes when compared to placebo. Therefore, due to lack of sufficient evidence, the committee did not make any recommendation for this vitamin D dose.

All available evidence was in those with single pregnancies. There was no evidence for women with multiple pregnancies. The committee cross referred to the section on diet, lifestyle and nutritional supplements in the NICE guideline on Twin and triplet pregnancy, as this provides advice on nutritional supplements including Vitamin D for multiple pregnancies.

The committee from their knowledge and experience discussed that there was increased insufficiency of vitamin D (vitamin D sufficiency in the UK is set at 25mmol) in pregnant women who are medically classified as being in the overweight or obesity weight categories. However, they agreed that the evidence reviewed was not sufficient to make recommendations on optimum dose of vitamin D for pregnant women who are medically classified as being in the overweight or obesity weight categories. The committee agreed that further research should be undertaken in this area to determine the optimum dose of vitamin D during pregnancy for women with a BMI medically classified as being in the overweight or obesity weight categories. They therefore developed a research recommendation to inform

future guidance (see appendix K for full details of the research recommendation). The research recommendation includes both singleton and multiple pregnancy populations.

Cost effectiveness and resource use

No economic evidence was identified for this review. As the committee made no recommendations relevant to this review question, there are no resource implications.

Other factors the committee took into account

For this review question, the population in the evidence was women and no evidence was identified or reviewed for trans men or non-binary people. The protocol and literature searches were not designed to specifically look for evidence on trans men or non-binary people but they were also not excluded. However, there is a small chance evidence on them may not have been captured, if such evidence exists. In discussing the evidence, the committee considered whether the recommendations could apply to a broader population, and used gender inclusive language to promote equity, respect and effective communication with everyone. Healthcare professionals should use their clinical judgement when implementing the recommendations, taking into account each person's circumstances, needs and preferences, and ensuring all people are treated with dignity and respect throughout their care.

Recommendations supported by this evidence review

This evidence review supports the research recommendation on optimum vitamin D dose during pregnancy for people with a BMI medically classified as being in the overweight or obesity weight categories.

References – included studies

Alhomaid 2021

Alhomaid, Raghad M, Mulhern, Maria S, Strain, Jj et al. (2021) Maternal obesity and baseline vitamin D insufficiency alter the response to vitamin D supplementation: a double-blind, randomized trial in pregnant women. The American journal of clinical nutrition 114(3): 1208-1218

Corcoy 2020

Corcoy, Rosa, Mendoza, Lilian C, Simmons, David et al. (2020) The DALI vitamin D randomized controlled trial for gestational diabetes mellitus prevention: No major benefit shown besides vitamin D sufficiency. Clinical nutrition (Edinburgh, Scotland) 39(3): 976-984

Appendices

Appendix A Review protocols

Review protocol for review question: What dose of vitamin D is appropriate during pregnancy for women with a BMI medically classified as being in the overweight or obesity weight categories?

Table 3: Review protocol

Field	Content
PROSPERO registration number	CRD42022346781
Review title	Optimum vitamin D dose during pregnancy for women medically classified as being in the overweight or obesity weight categories
Review question	What dose of vitamin D is appropriate during pregnancy for women with a BMI medically classified as being in the overweight or obesity weight categories?
Objective	To determine the optimal vitamin D dose during pregnancy for women medically classified as being in the overweight or obesity weight categories.
Searches	The following databases will be searched: • Cochrane Central Register of Controlled Trials (CENTRAL) • Cochrane Database of Systematic Reviews (CDSR) • Embase • MEDLINE • Epistemonikos • CINAHL • International HTA Database • Health Technology Assessment (HTA) database (last updated October 2016) Searches will be restricted by: • No date restriction

Field	Content
	• English language only • Human studies only Other searches: • Inclusion lists of systematic reviews The full search strategies for MEDLINE database will be published in the final review. For each search, the principal database search strategy is quality assured by a second information scientist using an adaptation of the PRESS 2015 Guideline Evidence-Based Checklist.
Condition or domain being studied	Vitamin D supplementation
Population	• Women during a single or multiple pregnancy, who have a BMI medically classified as being in the overweight or obesity weight categories (in line with NICE guideline on Obesity: identification and classification of overweight and obesity [update]) at booking or first scan Note: other anthropometric measures, such as weight to height ratio, that have been reported in the NICE guidance on Obesity: identification and classification of overweight and obesity (update) will be considered Note: if BMI is measured after the 1st trimester, the study will be included if eligible, but downgraded for indirectness.
Intervention	• Low dose vitamin D supplementation (<10µg/ 400IU daily) • Medium dose vitamin D supplementation (≥10µg/ 400IU to <20µg/800IU daily) • High dose vitamin D supplementation (≥20µg/800IU daily) In combination or not with other vitamins and minerals
Comparator	• A different vitamin D supplementation dose daily (same dose category) • A different vitamin D supplementation dose daily (different dose category) • Standard care (as defined by the study) • Placebo

Field	Content
	• No intervention

Types of study to be included	Include published full-text papers:
	• Systematic reviews of RCTs
	• Parallel RCTs
	• If insufficient parallel RCTs*:
	  ○ Quasi-randomised controlled trials
	  ○ Non-randomised controlled trials/prospective cohort studies
	  ○ Retrospective cohort studies
	  ○ Historically controlled studies
	
	*Non-randomised studies will be considered for inclusion if insufficient RCT evidence is available for guideline decision making. Sufficiency will be judged taking into account factors including number/quality/sample size of RCTs, outcomes reported and availability of data from subgroups of interest.
	
	Non-randomised studies will only be included if they adjust for confounding factors in the analysis.
	
	Conference abstracts will not be included because these do not typically have sufficient information to allow full critical appraisal.

Other exclusion criteria	Setting: • Countries other than high income countries (as defined by the OECD) If any study or systematic review includes <1/3 of women who received care in the above setting, it will be considered for inclusion but, if included, the evidence will be downgraded for indirectness.
Context	The population of this guideline may overlap with the population of women included in other NICE guidelines (such as postnatal care, antenatal care, intrapartum care, pregnancy and complex social factors or obesity prevention).
Primary outcomes (critical outcomes)	• Maternal serum 25(OH)D concentration • Preterm birth (before 37 weeks gestational age)

Field	Content
	• Low birth weight (<2500 g)
Secondary outcomes (important outcomes)	• Pre-eclampsia • Gestational diabetes • Bone mass in infant • Childhood respiratory function
Data extraction (selection and coding)	All references identified by the searches and from other sources will be uploaded into EPPI and de-duplicated. Titles and abstracts of the retrieved citations will be screened to identify studies that potentially meet the inclusion criteria outlined in the review protocol. Duplicate screening will not be undertaken for this question. Full versions of the selected studies will be obtained for assessment. Studies that fail to meet the inclusion criteria once the full version has been checked will be excluded at this stage. Each study excluded after checking the full version will be listed, along with the reason for its exclusion. A standardised form will be used to extract data from studies. The following data will be extracted: study details (reference, country where study was carried out, type and dates), participant characteristics, inclusion and exclusion criteria, details of the interventions if relevant, setting and follow-up, relevant outcome data and source of funding. One reviewer will extract relevant data into a standardised form, and this will be quality assessed by a senior reviewer.
Risk of bias (quality) assessment	Quality assessment of individual studies will be performed using the following checklists: • ROBIS tool for systematic reviews • Cochrane RoB tool v.2 for RCTs and quasi-RCTs • Cochrane ROBINS-I tool for non-randomised (clinical) controlled trials The quality assessment will be performed by one reviewer and this will be quality assessed by a senior reviewer.
Strategy for data synthesis	Quantitative findings will be formally summarised in the review. Where multiple studies report on the same outcome for the same comparison, meta-analyses will be conducted using Cochrane Review Manager software.

Field	Content
	A fixed effect meta-analysis will be conducted and data will be presented as risk ratios if possible or odds ratios when required (for example, if only available in this form in included studies) for dichotomous outcomes, and mean differences or standardised mean differences for continuous outcomes. Heterogeneity in the effect estimates of the individual studies will be assessed using the I2 statistic. Alongside visual inspection of the point estimates and confidence intervals, I2 values of greater than 50% and 80% will be considered as significant and very significant heterogeneity, respectively. Heterogeneity will be explored as appropriate using sensitivity analyses and pre-specified subgroup analyses. If heterogeneity cannot be explained through subgroup analysis then a random effects model will be used for meta-analysis, or the data will not be pooled. The confidence in the findings across all available evidence will be evaluated for each outcome using an adaptation of the 'Grading of Recommendations Assessment, Development and Evaluation (GRADE) toolbox' developed by the international GRADE working group: http://www.gradeworkinggroup.org/ **Minimally important differences:** • Preterm birth (before 37 weeks gestational age), low birth weight (<2500g), pre-eclampsia, gestational diabetes, childhood respiratory function: statistical significance • Validated scales/continuous outcomes: published MIDs where available • All other outcomes & where published MIDs are not available: 0.8 and 1.25 for all relative dichotomous outcomes ; +/- 0.5x control group SD for continuous outcomes
Analysis of subgroups	Evidence will be stratified by: • BMI thresholds on booking: ○ Overweight range: 25 to 29.99 kg/m^2 ○ Obesity range 1: 30 to 34.99 kg/m^2 ○ Obesity range 2: 35 to 39.99 kg/m^2 ○ Obesity range 3: >40 kg/m^2 ○ Follow the NICE guidance on Obesity: identification and classification of overweight and obesity (update) for people with a South Asian, Chinese, other Asian, Middle Eastern, Black 24 African or African-Caribbean family background • Single versus multiple pregnancy • Comorbidities (yes versus no) • Season (summer versus winter) • Ethnicity

Field	Content
	○ White/White British ○ Asian/Asian British ○ Black/African/Caribbean/Black British ○ Mixed/Multiple ethnic groups ○ Other ethnic group Evidence will be sub-grouped by the following only in the event that there is significant heterogeneity in outcomes: • Deprived socioeconomic group • Age ○ Under 40 years of age ○ Over 40 years of age • Women and parents with disabilities, including learning disabilities and other physical and mental health conditions • Women going through assisted conception • LGBTQ+ women and parents • Children with developmental problems • Geographical variation e.g. places without adequate provision of primary care (outside cities). • Religion and cultural considerations Where evidence is stratified or sub-grouped the committee will consider on a case by case basis if separate recommendations should be made for distinct groups. Separate recommendations may be made where there is evidence of a differential effect of interventions in distinct groups. If there is a lack of evidence in one group, the committee will consider, based on their experience, whether it is reasonable to extrapolate and assume the interventions will have similar effects in that group compared with others.
Type and method of review	☒ Intervention ☐ Diagnostic ☐ Prognostic ☐ Qualitative ☐ Epidemiologic

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5b. Named contact e-mail
mandcnutrition@nice.org.uk
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Field	Content
	National Institute for Health and Care Excellence (NICE)
Review team members	From the National Guideline Alliance: • Senior Systematic Reviewer • Systematic Reviewer
Funding sources/sponsor	This systematic review is being completed by the National Institute for Health and Care Excellence
Conflicts of interest	All guideline committee members and anyone who has direct input into NICE guidelines (including the evidence review team and expert witnesses) must declare any potential conflicts of interest in line with NICE's code of practice for declaring and dealing with conflicts of interest. Any relevant interests, or changes to interests, will also be declared publicly at the start of each guideline committee meeting. Before each meeting, any potential conflicts of interest will be considered by the guideline committee Chair and a senior member of the development team. Any decisions to exclude a person from all or part of a meeting will be documented. Any changes to a member's declaration of interests will be recorded in the minutes of the meeting. Declarations of interests will be published with the final guideline.
Collaborators	Development of this systematic review will be overseen by an advisory committee who will use the review to inform the development of evidence-based recommendations in line with section 3 of Developing NICE guidelines: the manual. Members of the guideline committee are available on the NICE website: https://www.nice.org.uk/guidance/indevelopment/gid-ng10191
Other registration details	None
URL for published protocol	https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=346781
Dissemination plans	NICE may use a range of different methods to raise awareness of the guideline. These include standard approaches such as: notifying registered stakeholders of publication publicising the guideline through NICE's newsletter and alerts issuing a press release or briefing as appropriate, posting news articles on the NICE website, using social media channels, and publicising the guideline within NICE.
Keywords	Vitamin D, pregnancy, overweight, obesity
Details of existing review of same topic by same authors	Not applicable

Field	Content
Current review status	☒ Ongoing ☐ Completed but not published ☐ Completed and published ☐ Completed, published and being updated ☐ Discontinued
Additional information	None
Details of final publication	www.nice.org.uk

BMI: body mass index; CDSR: Cochrane Database of Systematic Reviews; CENTRAL: Cochrane Central Register of Controlled Trials; EPPI: Evidence for policy and practice information; GRADE: Grading of Recommendations Assessment, Development and Evaluation; HTA: Health Technology Assessment; MID: minimally important difference; NGA: National Guideline Alliance; NICE: National Institute for Health and Care Excellence; OECD: organisation for economic cooperation and development; (OH)D: hydroxyvitamin D; RCT: randomised controlled trial; RoB: risk of bias; ROBINS-I: risk of bias in non-randomised studies; ROBIS: risk of bias in systematic reviews; SD: standard deviation

Appendix B Literature search strategies

Literature search strategies for review question: What dose of vitamin D is appropriate during pregnancy for women with a BMI medically classified as being in the overweight or obesity weight categories?

Effectiveness Searches

Databases: MEDLINE

Date of last search: 05/12/2023

#	Searches
1	exp Pregnancy/ or Pregnant Women/ or Prenatal Care/
2	(antenatal* or ante-natal* or gestational or maternal* or pregnan* or prenatal* or pre-natal*).ti,ab,kf.
3	1 or 2
4	adiposity/ or body mass index/ or body size/ or body weight/ or overweight/ or obesity/ or obesity, abdominal/ or obesity, maternal/ or obesity, metabolically benign/ or obesity, morbid/ or waist circumference/ or waist-hip ratio/ or Waist-Height Ratio/ or Weight Gain/ or Skinfold Thickness/ or Body Fat Distribution/
5	exp Adipose Tissue/
6	(obes* or overweight or over weight or corpulen* or heavy or heavier or fat or adipos* or (weight adj2 (manag* or gain* or increas* or excess or chang*))).ti,ab,kf.
7	(body mass index or BMI or quetelet index).ti,ab,kf.
8	(waist circumference* or waist hip ratio* or waist height ratio* or weight height ratio*).ti,ab,kf.
9	(skin fold* or skinfold* or body composition or (body fat adj3 percent*)).ti,ab,kf.
10	((arm or midarm or upperarm or brachial) adj4 (circumferen* or measure* or area* or fat* or diameter* or anthropometr*)).ti,ab,kf.
11	or/4-10
12	3 and 11
13	exp Vitamin D/
14	(calciferol* or calcifediol* or calciol* or cholecalciferol* or hydroxycholecalciferol* or dihydroxycholecalciferol* or calcitriol* or 24,25-dihydroxyvitamin D* or ergocalciferol* or ergosterol* or viosterol or vitamin d* or vitamind* or 25 hydroxy* or 25-?OH*).ti,ab,kf.
15	or/13-14
16	12 and 15
17	letter/
18	editorial/
19	news/
20	exp historical article/
21	Anecdotes as Topic/
22	comment/
23	case report/
24	(letter or comment*).ti.
25	or/17-24
26	randomized controlled trial/ or random*.ti,ab.
27	25 not 26
28	animals/ not humans/
29	exp Animals, Laboratory/
30	exp Animal Experimentation/
31	exp Models, Animal/
32	exp Rodentia/
33	(rat or rats or mouse or mice).ti.
34	or/27-33
35	16 not 34

#	Searches
36	limit 35 to English language
37	randomized controlled trial.pt.
38	controlled clinical trial.pt.
39	pragmatic clinical trial.pt.
40	randomi#ed.ab.
41	placebo.ab.
42	drug therapy.fs.
43	randomly.ab.
44	trial.ab.
45	groups.ab.
46	or/37-45
47	Meta-Analysis/
48	Meta-Analysis as Topic/
49	(meta analy* or metanaly* or metaanaly*).ti,ab.
50	((systematic* or evidence*) adj2 (review* or overview*)).ti,ab.
51	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
52	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
53	(search* adj4 literature).ab.
54	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
55	cochrane.jw.
56	or/47-55
57	36 and (46 or 56)
58	Observational Studies as Topic/
59	Observational Study/
60	Epidemiologic Studies/
61	exp Case-Control Studies/
62	exp Cohort Studies/
63	Cross-Sectional Studies/
64	Controlled Before-After Studies/
65	Historically Controlled Study/
66	Interrupted Time Series Analysis/
67	Comparative Study.pt.
68	case control$.tw.
69	case series.tw.
70	(cohort adj (study or studies)).tw.
71	cohort analy$.tw.
72	(follow up adj (study or studies)).tw.
73	(observational adj (study or studies)).tw.
74	longitudinal.tw.
75	prospective.tw.
76	retrospective.tw.
77	cross sectional.tw.
78	or/58-77
79	36 and 78
80	afghanistan/ or africa/ or africa, northern/ or africa, central/ or africa, eastern/ or "africa south of the sahara"/ or africa, southern/ or africa, western/ or albania/ or algeria/ or andorra/ or angola/ or "antigua and barbuda"/ or argentina/ or armenia/ or azerbaijan/ or bahamas/ or bahrain/ or bangladesh/ or barbados/ or belize/ or benin/ or bhutan/ or bolivia/ or borneo/ or "bosnia and herzegovina"/ or botswana/ or brazil/ or brunei/ or bulgaria/ or burkina faso/ or burundi/ or cabo verde/ or cambodia/ or cameroon/ or central african republic/ or chad/ or exp china/ or comoros/ or congo/ or cote d'ivoire/ or croatia/ or cuba/ or "democratic republic of the congo"/ or cyprus/ or djibouti/ or dominica/ or dominican republic/ or ecuador/ or egypt/ or el salvador/ or equatorial guinea/ or eritrea/ or eswatini/ or ethiopia/ or fiji/ or gabon/ or gambia/ or "georgia (republic)"/ or ghana/ or grenada/ or guatemala/ or guinea/ or guinea-bissau/ or guyana/ or haiti/ or honduras/ or independent state of samoa/ or exp india/ or indian ocean islands/ or indochina/ or indonesia/ or iran/ or

#	Searches
	iraq/ or jamaica/ or jordan/ or kazakhstan/ or kenya/ or kosovo/ or kuwait/ or kyrgyzstan/ or laos/ or lebanon/ or liechtenstein/ or lesotho/ or liberia/ or libya/ or madagascar/ or malaysia/ or malawi/ or mali/ or malta/ or mauritania/ or mauritius/ or mekong valley/ or melanesia/ or micronesia/ or monaco/ or mongolia/ or montenegro/ or morocco/ or mozambique/ or myanmar/ or namibia/ or nepal/ or nicaragua/ or niger/ or nigeria/ or oman/ or pakistan/ or palau/ or exp panama/ or papua new guinea/ or paraguay/ or peru/ or philippines/ or qatar/ or "republic of belarus"/ or "republic of north macedonia"/ or romania/ or exp russia/ or rwanda/ or "saint kitts and nevis"/ or saint lucia/ or "saint vincent and the grenadines"/ or "sao tome and principe"/ or saudi arabia/ or serbia/ or sierra leone/ or senegal/ or seychelles/ or singapore/ or somalia/ or south africa/ or south sudan/ or sri lanka/ or sudan/ or suriname/ or syria/ or taiwan/ or tajikistan/ or tanzania/ or thailand/ or timor-leste/ or togo/ or tonga/ or "trinidad and tobago"/ or tunisia/ or turkmenistan/ or uganda/ or ukraine/ or united arab emirates/ or uruguay/ or uzbekistan/ or vanuatu/ or venezuela/ or vietnam/ or west indies/ or yemen/ or zambia/ or zimbabwe/
81	"organisation for economic co-operation and development"/
82	australasia/ or exp australia/ or austria/ or baltic states/ or belgium/ or exp canada/ or chile/ or colombia/ or costa rica/ or czech republic/ or exp denmark/ or estonia/ or europe/ or finland/ or exp france/ or exp germany/ or greece/ or hungary/ or iceland/ or ireland/ or israel/ or exp italy/ or exp japan/ or korea/ or latvia/ or lithuania/ or luxembourg/ or mexico/ or netherlands/ or new zealand/ or north america/ or exp norway/ or poland/ or portugal/ or exp "republic of korea"/ or "scandinavian and nordic countries"/ or slovakia/ or slovenia/ or spain/ or sweden/ or switzerland/ or turkey/ or exp united kingdom/ or exp united states/
83	european union/
84	developed countries/
85	or/81-84
86	80 not 85
87	57 not 86
88	79 not 86

Databases: Embase

Date of last search: 05/12/2023

#	Searches
1	exp pregnancy/ or pregnant woman/ or prenatal care/ or prenatal period/
2	(antenatal* or ante natal* or gestation* or maternal* or mother* or pregnan* or prenatal* or pre natal*).ti,ab,kf.
3	1 or 2
4	body mass/ or body size/ or body weight/ or body weight gain/ or obesity/ or abdominal obesity/ or fat mass/ or maternal obesity/ or metabolically benign obesity/ or morbid obesity/ or normal weight obesity/ or waist circumference/ or waist hip ratio/ or waist to height ratio/ or weight height ratio/ or skinfold thickness/ or body fat distribution/
5	exp adipose tissue/ or exp obese patient/
6	(obes* or overweight or over weight or corpulen* or heavy or heavier or fat or adipos* or (weight adj2 (manag* or gain* or increas* or excess or chang*))).ti,ab,kf.
7	(body mass index or BMI or quetelet index).ti,ab,kf.
8	(waist circumference* or waist hip ratio* or waist height ratio* or weight height ratio*).ti,ab,kf.
9	(skin fold* or skinfold* or body composition or (body fat adj3 percent*)).ti,ab,kf.
10	((arm or midarm or upperarm or brachial) adj4 (circumferen* or measure* or area* or fat* or diameter* or anthropometr*)).ti,ab,kf.
11	or/4-10
12	3 and 11
13	exp vitamin D/
14	(calciferol* or calcifediol* or calciol* or cholecalciferol* or hydroxycholecalciferol* or dihydroxycholecalciferol* or calcitriol* or 24,25-dihydroxyvitamin D* or ergocalciferol* or ergosterol* or viosterol or vitamin d* or vitamind* or 25 hydroxy* or 25-?OH*).ti,ab,kf.
15	or/13-14
16	12 and 15
17	letter.pt. or letter/
18	note.pt.
19	editorial.pt.
20	case report/ or case study/
21	(letter or comment*).ti.
22	or/17-21

#	Searches
23	randomized controlled trial/ or random*.ti,ab.
24	22 not 23
25	animal/ not human/
26	nonhuman/
27	exp Animal Experiment/
28	exp Experimental Animal/
29	animal model/
30	exp Rodent/
31	(rat or rats or mouse or mice or rodent*).ti.
32	or/24-31
33	16 not 32
34	(conference abstract* or conference review or conference paper or conference proceeding).db,pt,su.
35	33 not 34
36	limit 35 to English language
37	random*.ti,ab.
38	factorial*.ti,ab.
39	(crossover* or cross over*).ti,ab.
40	((doubl* or singl*) adj blind*).ti,ab.
41	(assign* or allocat* or volunteer* or placebo*).ti,ab.
42	crossover procedure/
43	single blind procedure/
44	randomized controlled trial/
45	double blind procedure/
46	or/37-45
47	systematic review/
48	meta-analysis/
49	(meta analy* or metanaly* or metaanaly*).ti,ab.
50	((systematic or evidence) adj2 (review* or overview*)).ti,ab.
51	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
52	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
53	(search* adj4 literature).ab.
54	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
55	((pool* or combined) adj2 (data or trials or studies or results)).ab.
56	cochrane.jw.
57	or/47-56
58	36 and (46 or 57)
59	Clinical study/
60	Case control study/
61	Family study/
62	Longitudinal study/
63	Retrospective study/
64	comparative study/
65	Prospective study/
66	Randomized controlled trials/
67	65 not 66
68	Cohort analysis/
69	cohort analy$.tw.
70	(Cohort adj (study or studies)).tw.
71	(Case control$ adj (study or studies)).tw.
72	(follow up adj (study or studies)).tw.
73	(observational adj (study or studies)).tw.

#	Searches
74	(epidemiologic$ adj (study or studies)).tw.
75	(cross sectional adj (study or studies)).tw.
76	case series.tw.
77	prospective.tw.
78	retrospective.tw.
79	or/59-64,67-78
80	36 and 79
81	afghanistan/ or africa/ or "africa south of the sahara"/ or albania/ or algeria/ or andorra/ or angola/ or argentina/ or "antigua and barbuda"/ or armenia/ or exp azerbaijan/ or bahamas/ or bahrain/ or bangladesh/ or barbados/ or belarus/ or belize/ or benin/ or bhutan/ or bolivia/ or borneo/ or exp "bosnia and herzegovina"/ or botswana/ or exp brazil/ or brunei darussalam/ or bulgaria/ or burkina faso/ or burundi/ or cambodia/ or cameroon/ or cape verde/ or central africa/ or central african republic/ or chad/ or exp china/ or comoros/ or congo/ or cook islands/ or cote d'ivoire/ or croatia/ or cuba/ or cyprus/ or democratic republic congo/ or djibouti/ or dominica/ or dominican republic/ or ecuador/ or el salvador/ or egypt/ or equatorial guinea/ or eritrea/ or eswatini/ or ethiopia/ or exp "federated states of micronesia"/ or fiji/ or gabon/ or gambia/ or exp "georgia (republic)"/ or ghana/ or grenada/ or guatemala/ or guinea/ or guinea-bissau/ or guyana/ or haiti/ or honduras/ or exp india/ or exp indonesia/ or iran/ or exp iraq/ or jamaica/ or jordan/ or kazakhstan/ or kenya/ or kiribati/ or kosovo/ or kuwait/ or kyrgyzstan/ or laos/ or lebanon/ or liechtenstein/ or lesotho/ or liberia/ or libyan arab jamahiriya/ or madagascar/ or malawi/ or exp malaysia/ or maldives/ or mali/ or malta/ or mauritania/ or mauritius/ or melanesia/ or moldova/ or monaco/ or mongolia/ or "montenegro (republic)"/ or morocco/ or mozambique/ or myanmar/ or namibia/ or nauru/ or nepal/ or nicaragua/ or niger/ or nigeria/ or niue/ or north africa/ or oman/ or exp pakistan/ or palau/ or palestine/ or panama/ or papua new guinea/ or paraguay/ or peru/ or philippines/ or polynesia/ or qatar/ or "republic of north macedonia"/ or romania/ or exp russian federation/ or rwanda/ or sahel/ or "saint kitts and nevis"/ or "saint lucia"/ or "saint vincent and the grenadines"/ or saudi arabia/ or senegal/ or exp serbia/ or seychelles/ or sierra leone/ or singapore/ or "sao tome and principe"/ or solomon islands/ or exp somalia/ or south africa/ or south asia/ or south sudan/ or exp southeast asia/ or sri lanka/ or sudan/ or suriname/ or syrian arab republic/ or taiwan/ or tajikistan/ or tanzania/ or thailand/ or timor-leste/ or togo/ or tonga/ or "trinidad and tobago"/ or tunisia/ or turkmenistan/ or tuvalu/ or uganda/ or exp ukraine/ or exp united arab emirates/ or uruguay/ or exp uzbekistan/ or vanuatu/ or venezuela/ or viet nam/ or western sahara/ or yemen/ or zambia/ or zimbabwe/
82	exp "organisation for economic co-operation and development"/
83	exp australia/ or "australia and new zealand"/ or austria/ or baltic states/ or exp belgium/ or exp canada/ or chile/ or colombia/ or costa rica/ or czech republic/ or denmark/ or estonia/ or europe/ or exp finland/ or exp france/ or exp germany/ or greece/ or hungary/ or iceland/ or ireland/ or israel/ or exp italy/ or japan/ or korea/ or latvia/ or lithuania/ or luxembourg/ or exp mexico/ or netherlands/ or new zealand/ or north america/ or exp norway/ or poland/ or exp portugal/ or scandinavia/ or sweden/ or slovakia/ or slovenia/ or south korea/ or exp spain/ or switzerland/ or "Turkey (republic)"/ or exp united kingdom/ or exp united states/ or western europe/
84	european union/
85	developed country/
86	or/82-85
87	81 not 86
88	58 not 87
89	81 not 87

Database: The Cochrane Library: Cochrane Database of Systematic Reviews, Issue 12 of 12, December 2023 and Cochrane Central Register of Controlled Trials, Issue 12 of 12, December 2023

Date of last search: 07/12/2023

#	Searches
#1	MeSH descriptor: [Pregnancy] explode all trees
#2	MeSH descriptor: [Pregnant Women] this term only
#3	MeSH descriptor: [Prenatal Care] this term only
#4	(antenatal* or ante NEXT natal* or gestation* or maternal* or mother* or pregnan* or prenatal* or pre NEXT natal*):ti,ab,kw
#5	{OR #1-#4}
#6	MeSH descriptor: [Adiposity] this term only
#7	MeSH descriptor: [Body Mass Index] this term only
#8	MeSH descriptor: [Body Size] this term only
#9	MeSH descriptor: [Body Weight] this term only

#	Searches
#10	MeSH descriptor: [Overweight] this term only
#11	MeSH descriptor: [Obesity] this term only
#12	MeSH descriptor: [Obesity, Abdominal] this term only
#13	MeSH descriptor: [Obesity, Maternal] this term only
#14	MeSH descriptor: [Obesity, Metabolically Benign] this term only
#15	MeSH descriptor: [Obesity, Morbid] this term only
#16	MeSH descriptor: [Waist Circumference] this term only
#17	MeSH descriptor: [Waist-Hip Ratio] this term only
#18	MeSH descriptor: [Waist-Height Ratio] this term only
#19	MeSH descriptor: [Weight Gain] this term only
#20	MeSH descriptor: [Skinfold Thickness] this term only
#21	MeSH descriptor: [Body Fat Distribution] this term only
#22	MeSH descriptor: [Adipose Tissue] explode all trees
#23	(obes* or overweight or "over weight" or corpulen* or heavy or heavier or fat or adipos* or (weight NEAR/2 (manag* or gain* or increas* or excess or chang*))):ti,ab,kw
#24	("body mass index" or BMI or "quetelet index"):ti,ab,kw
#25	(waist NEXT circumference* or waist NEXT hip NEXT ratio* or waist NEXT height NEXT ratio* or weight NEXT height NEXT ratio*):ti,ab,kw
#26	(skin NEXT fold* or skinfold* or "body composition" or ("body fat" NEAR/3 percent*)):ti,ab,kw
#27	((arm or midarm or upperarm or brachial) NEAR/4 (circumferen* or measure* or area* or fat* or diameter* or anthropometr*)):ti,ab,kw
#28	{OR #6-#27}
#29	#5 AND #28
#30	MeSH descriptor: [Vitamin D] explode all trees
#31	(calciferol* or calcifediol* or calciol* or cholecalciferol* or hydroxycholecalciferol* or dihydroxycholecalciferol* or calcitriol* or 24 NEXT 25 NEXT dihydroxyvitamin NEXT D or ergocalciferol* or ergosterol* or viosterol or "vitamin d" or vitamind or 25 NEXT hydroxy* or 25OH*):ti,ab,kw
#32	#30 OR #31
#33	#29 AND #32
#34	conference:pt or (clinicaltrials or trialsearch):so
#35	#33 NOT #34

Database: CINAHL

Date of last search: 05/12/2023

#	Searches
1	(MH "Pregnancy+")

#	Searches
2	(MH "Expectant Mothers")
3	(MH "Prenatal Care")
4	TI ((antenatal* or ante-natal* or gestational or maternal* or pregnan* or prenatal* or pre-natal*)) OR AB ((antenatal* or ante-natal* or gestational or maternal* or pregnan* or prenatal* or pre-natal*))
5	S1 OR S2 OR S3 OR S4
6	(MH "Body Mass Index")
7	(MH "Body Size")
8	(MH "Body Weight")
9	(MH "Obesity")
10	(MH "Obesity, Maternal") OR (MH "Obesity, Morbid")
11	(MH "Waist Circumference")
12	(MH "Waist-Hip Ratio")
13	(MH "Body Height")
14	(MH "Weight Gain")
15	(MH "Skinfold Thickness")
16	(MH "Adipose Tissue Distribution")
17	(MH "Adipose Tissue+")
18	TI ((obes* or overweight or "over weight" or corpulen* or heavy or heavier or fat or adipos*)) OR AB ((obes* or overweight or "over weight" or corpulen* or heavy or heavier or fat or adipos*))
19	TI ((weight N2 (manag* or gain* or increas* or excess or chang*))) OR AB ((weight N2 (manag* or gain* or increas* or excess or chang*)))
20	TI (("body mass index" or BMI or quetelet index)) OR AB (("body mass index" or BMI or quetelet index))
21	TI (("waist circumference*" or "waist hip ratio*" or "waist height ratio*" or "weight height ratio*")) OR AB (("waist circumference*" or "waist hip ratio*" or "waist height ratio*" or "weight height ratio*"))
22	TI (("skin fold*" or skinfold* or "body composition")) OR AB (("skin fold*" or skinfold* or "body composition"))
23	TI (((arm or midarm or upperarm or brachial) N4 (circumferen* or measure* or area* or fat* or diameter* or anthropometr*))) OR AB (((arm or midarm or upperarm or brachial) N4 (circumferen* or measure* or area* or fat* or diameter* or anthropometr*)))
24	S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16 OR S17 OR S18 OR S19 OR S20 OR S21 OR S22 OR S23
25	S5 AND S24
26	(MH "Vitamin D+")
27	TI ((calciferol* or calcifediol* or calciol* or cholecalciferol* or hydroxycholecalciferol* or dihydroxycholecalciferol* or calcitriol* or "24,25-dihydroxyvitamin D*" or ergocalciferol* or ergosterol* or viosterol or "vitamin d*" or vitamind* or 25 hydroxy* or 25-?OH*)) OR AB ((calciferol* or calcifediol* or calciol* or cholecalciferol* or hydroxycholecalciferol* or dihydroxycholecalciferol* or calcitriol* or "24,25-dihydroxyvitamin D*" or ergocalciferol* or ergosterol* or viosterol or "vitamin d*" or vitamind* or 25 hydroxy* or 25-?OH*))
28	S26 OR S27
29	S25 AND S28

Database: Epistemonikos

Date of last search: 05/12/2023

#	Searches
1	(advanced_title_en:((antenatal* OR ante-natal* OR gestational OR maternal* OR pregnan* OR prenatal* OR pre-natal*)) OR advanced_abstract_en:((antenatal* OR ante-natal* OR gestational OR maternal* OR pregnan* OR prenatal* OR pre-natal*)))
2	((obese OR overweight OR adipos* OR BMI OR skinfold* OR "arm circumference")) OR advanced_abstract_en:((obese OR overweight OR adipos* OR BMI OR skinfold* OR "arm circumference")))
3	(advanced_title_en:("vitamin d") OR advanced_abstract_en:("vitamin d"))
4	1 AND 2 AND 3 [Filters: classification=systematic-review, cochrane=missing, protocol=no]

Economic searches

Databases: MEDLINE

Date of last search: 05/12/2023

#	Searches
1	exp Pregnancy/ or Pregnant Women/ or Prenatal Care/
2	(antenatal* or ante-natal* or gestational or maternal* or pregnan* or prenatal* or pre-natal*).ti,ab,kf.
3	1 or 2
4	adiposity/ or body mass index/ or body size/ or body weight/ or overweight/ or obesity/ or obesity, abdominal/ or obesity, maternal/ or obesity, metabolically benign/ or obesity, morbid/ or waist circumference/ or waist-hip ratio/ or Waist-Height Ratio/ or Weight Gain/ or Skinfold Thickness/ or Body Fat Distribution/
5	exp Adipose Tissue/
6	(obes* or overweight or over weight or corpulen* or heavy or heavier or fat or adipos* or (weight adj2 (manag* or gain* or increas* or excess or chang*))).ti,ab,kf.
7	(body mass index or BMI or quetelet index).ti,ab,kf.
8	(waist circumference* or waist hip ratio* or waist height ratio* or weight height ratio*).ti,ab,kf.
9	(skin fold* or skinfold* or body composition or (body fat adj3 percent*)).ti,ab,kf.
10	((arm or midarm or upperarm or brachial) adj4 (circumferen* or measure* or area* or fat* or diameter* or anthropometr*)).ti,ab,kf.
11	or/4-10
12	3 and 11
13	exp Vitamin D/
14	(calciferol* or calcifediol* or calciol* or cholecalciferol* or hydroxycholecalciferol* or dihydroxycholecalciferol* or calcitriol* or 24,25-dihydroxyvitamin D* or ergocalciferol* or ergosterol* or viosterol or vitamin d* or vitamind* or 25 hydroxy* or 25-?OH*).ti,ab,kf.
15	or/13-14
16	12 and 15
17	letter/
18	editorial/
19	news/
20	exp historical article/
21	Anecdotes as Topic/
22	comment/
23	case reports/
24	(letter or comment*).ti.
25	or/17-24
26	randomized controlled trial/ or random*.ti,ab.
27	25 not 26
28	animals/ not humans/
29	exp Animals, Laboratory/
30	exp Animal Experimentation/
31	exp Models, Animal/
32	exp Rodentia/
33	(rat or rats or mouse or mice).ti.
34	or/27-33
35	16 not 34
36	limit 35 to English language
37	Economics/
38	Value of life/
39	exp "Costs and Cost Analysis"/
40	exp Economics, Hospital/
41	exp Economics, Medical/
42	exp Resource Allocation/

#	Searches
43	Economics, Nursing/
44	Economics, Pharmaceutical/
45	exp "Fees and Charges"/
46	exp Budgets/
47	budget*.ti,ab.
48	cost*.ti,ab.
49	(economic* or pharmaco?economic*).ti,ab.
50	(price* or pricing*).ti,ab.
51	(financ* or fee or fees or expenditure* or saving*).ti,ab.
52	(value adj2 (money or monetary)).ti,ab.
53	resourc* allocat*.ti,ab.
54	(fund or funds or funding* or funded).ti,ab.
55	(ration or rations or rationing* or rationed).ti,ab.
56	ec.fs.
57	or/37-56
58	exp models, economic/
59	*Models, Theoretical/
60	*Models, Organizational/
61	markov chains/
62	monte carlo method/
63	exp Decision Theory/
64	(markov* or monte carlo).ti,ab.
65	econom* model*.ti,ab.
66	(decision* adj2 (tree* or analy* or model*)).ti,ab.
67	or/58-66
68	quality-adjusted life years/
69	sickness impact profile/
70	(quality adj2 (wellbeing or well being)).ti,ab.
71	sickness impact profile.ti,ab.
72	disability adjusted life.ti,ab.
73	(qal* or qtime* or qwb* or daly*).ti,ab.
74	(euroqol* or eq5d* or eq 5*).ti,ab.
75	(qol* or hql* or hqol* or h qol* or hrqol* or hr qol*).ti,ab.
76	(health utility* or utility score* or disutilit* or utility value*).ti,ab.
77	(hui or hui1 or hui2 or hui3).ti,ab.
78	(health* year* equivalent* or hye or hyes).ti,ab.
79	discrete choice*.ti,ab.
80	rosser.ti,ab.
81	(willingness to pay or time tradeoff or time trade off or tto or standard gamble*).ti,ab.
82	(sf36* or sf 36* or short form 36* or shortform 36* or shortform36*).ti,ab.
83	(sf20 or sf 20 or short form 20 or shortform 20 or shortform20).ti,ab.
84	(sf12* or sf 12* or short form 12* or shortform 12* or shortform12*).ti,ab.
85	(sf8* or sf 8* or short form 8* or shortform 8* or shortform8*).ti,ab.
86	(sf6* or sf 6* or short form 6* or shortform 6* or shortform6*).ti,ab.
87	or/68-86
88	36 and (57 or 67 or 87)

Databases: Embase

Date of last search: 05/12/2023

#	Searches
1	exp pregnancy/ or pregnant woman/ or prenatal care/ or prenatal period/
2	(antenatal* or ante natal* or gestation* or maternal* or mother* or pregnan* or prenatal* or pre natal*).ti,ab,kf.
3	1 or 2
4	body mass/ or body size/ or body weight/ or body weight gain/ or obesity/ or abdominal obesity/ or fat mass/ or maternal obesity/ or metabolically benign obesity/ or morbid obesity/ or normal weight obesity/ or waist circumference/ or waist hip ratio/ or waist to height ratio/ or weight height ratio/ or skinfold thickness/ or body fat distribution/
5	exp adipose tissue/ or exp obese patient/
6	(obes* or overweight or over weight or corpulen* or heavy or heavier or fat or adipos* or (weight adj2 (manag* or gain* or increas* or excess or chang*))).ti,ab,kf.
7	(body mass index or BMI or quetelet index).ti,ab,kf.
8	(waist circumference* or waist hip ratio* or waist height ratio* or weight height ratio*).ti,ab,kf.
9	(skin fold* or skinfold* or body composition or (body fat adj3 percent*)).ti,ab,kf.
10	((arm or midarm or upperarm or brachial) adj4 (circumferen* or measure* or area* or fat* or diameter* or anthropometr*)).ti,ab,kf.
11	or/4-10
12	3 and 11
13	exp vitamin D/
14	(calciferol* or calcifediol* or calciol* or cholecalciferol* or hydroxycholecalciferol* or dihydroxycholecalciferol* or calcitriol* or 24,25-dihydroxyvitamin D* or ergocalciferol* or ergosterol* or viosterol or vitamin d* or vitamind* or 25 hydroxy* or 25-?OH*).ti,ab,kf.
15	or/13-14
16	12 and 15
17	letter.pt. or letter/
18	note.pt.
19	editorial.pt.
20	case report/ or case study/
21	(letter or comment*).ti.
22	or/17-21
23	randomized controlled trial/ or random*.ti,ab.
24	22 not 23
25	animal/ not human/
26	nonhuman/
27	exp Animal Experiment/
28	exp Experimental Animal/
29	animal model/
30	exp Rodent/
31	(rat or rats or mouse or mice or rodent*).ti.
32	or/24-31
33	16 not 32
34	(conference abstract* or conference review or conference paper or conference proceeding).db,pt,su.
35	33 not 34
36	limit 35 to English language
37	health economics/
38	exp economic evaluation/
39	exp health care cost/
40	exp fee/
41	budget/
42	funding/
43	resource allocation/
44	budget*.ti,ab.

#	Searches
45	cost*.ti,ab.
46	(economic* or pharmaco?economic*).ti,ab.
47	(price* or pricing*).ti,ab.
48	(financ* or fee or fees or expenditure* or saving*).ti,ab.
49	(value adj2 (money or monetary)).ti,ab.
50	resourc* allocat*.ti,ab.
51	(fund or funds or funding* or funded).ti,ab.
52	(ration or rations or rationing* or rationed).ti,ab.
53	or/37-52
54	statistical model/
55	exp economic aspect/
56	54 and 55
57	*theoretical model/
58	*nonbiological model/
59	stochastic model/
60	decision theory/
61	decision tree/
62	monte carlo method/
63	(markov* or monte carlo).ti,ab.
64	econom* model*.ti,ab.
65	(decision* adj2 (tree* or analy* or model*)).ti,ab.
66	or/56-65
67	quality adjusted life year/
68	"quality of life index"/
69	short form 12/ or short form 20/ or short form 36/ or short form 8/
70	sickness impact profile/
71	(quality adj2 (wellbeing or well being)).ti,ab.
72	sickness impact profile.ti,ab.
73	disability adjusted life.ti,ab.
74	(qal* or qtime* or qwb* or daly*).ti,ab.
75	(qal* or qtime* or qwb* or daly*).ti,ab.
76	(qol* or hql* or hqol* or h qol* or hrqol* or hr qol*).ti,ab.
77	(health utility* or utility score* or disutilit* or utility value*).ti,ab.
78	(hui or hui1 or hui2 or hui3).ti,ab.
79	(health* year* equivalent* or hye or hyes).ti,ab.
80	discrete choice*.ti,ab.
81	rosser.ti,ab.
82	(willingness to pay or time tradeoff or time trade off or tto or standard gamble*).ti,ab.
83	(sf36* or sf 36* or short form 36* or shortform 36* or shortform36*).ti,ab.
84	(sf20 or sf 20 or short form 20 or shortform 20 or shortform20).ti,ab.
85	(sf12* or sf 12* or short form 12* or shortform 12* or shortform12*).ti,ab.
86	(sf8* or sf 8* or short form 8* or shortform 8* or shortform8*).ti,ab.
87	(sf6* or sf 6* or short form 6* or shortform 6* or shortform6*).ti,ab.
88	or/67-87
89	36 and (53 or 66 or 88)

Database: INAHTA HTA

Date of last search: 05/12/2023

#	Searches
1	"Pregnancy"[mhe]

#	Searches
2	"Pregnant Women"[mh]
3	"Prenatal Care"[mh]
4	((antenatal* or ante-natal* or gestational or maternal* or pregnan* or prenatal* or pre-natal*))[Title] OR ((antenatal* or ante-natal* or gestational or maternal* or pregnan* or prenatal* or pre-natal*))[abs]
5	#1 OR #2 OR #3 OR #4
6	"Adiposity"[mh]
7	"Body Mass Index"[mh]
8	"Body Size"[mh]
9	"Body Weight"[mh]
10	"Overweight"[mh]
11	"Obesity"[mh]
12	"Obesity, Abdominal"[mh]
13	"Obesity, Maternal"[mh]
14	"Obesity, Metabolically Benign"[mh]
15	"Obesity, Morbid"[mh]
16	"Waist Circumference"[mh]
17	"Waist-Hip Ratio"[mh]
18	"Waist-Height Ratio"[mh]
19	"Weight Gain"[mh]
20	"Skinfold Thickness"[mh]
21	"Body Fat Distribution"[mh]
22	"Adipose Tissue"[mhe]
23	((obes* or overweight or "over weight" or corpulen* or heavy or heavier or fat or adipos*))[Title] OR ((obes* or overweight or "over weight" or corpulen* or heavy or heavier or fat or adipos*))[abs]
24	((weight AND (manag* or gain* or increas* or excess or chang*)))[Title] OR ((weight AND (manag* or gain* or increas* or excess or chang*)))[abs]
25	(("body mass index" or BMI or "quetelet index"))[Title] OR (("body mass index" or BMI or "quetelet index"))[abs]
26	(("waist circumference*" or "waist hip ratio*" or "waist height ratio*" or "weight height ratio*"))[Title] OR (("waist circumference*" or "waist hip ratio*" or "waist height ratio*" or "weight height ratio*"))[abs]
27	(("skin fold*" or skinfold* or "body composition"))[Title] OR (("skin fold*" or skinfold* or "body composition"))[abs]
28	(("body fat" AND percent*))[Title] OR (("body fat" AND percent*))[abs]
29	(((arm or midarm or upperarm or brachial) AND (circumferen* or measure* or area* or fat* or diameter* or anthropometr*)))[Title] OR (((arm or midarm or upperarm or brachial) AND (circumferen* or measure* or area* or fat* or diameter* or anthropometr*)))[abs]
30	#6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29
31	"Vitamin D"[mhe]
32	((calciferol* or calcifediol* or calciol* or cholecalciferol* or hydroxycholecalciferol* or dihydroxycholecalciferol* or calcitriol* or 24,25-dihydroxyvitamin D* or ergocalciferol* or ergosterol* or viosterol or vitamin d* or vitamind* or 25 hydroxy*))[Title] OR ((calciferol* or calcifediol* or calciol* or cholecalciferol* or hydroxycholecalciferol* or dihydroxycholecalciferol* or calcitriol* or 24,25-dihydroxyvitamin D* or ergocalciferol* or ergosterol* or viosterol or vitamin d* or vitamind* or 25 hydroxy*))[abs]
33	#31 OR #32
34	#5 AND #30
35	#33 AND #34

Database: CRD HTA (last updated October 2016)

Date of last search: 14/07/2022

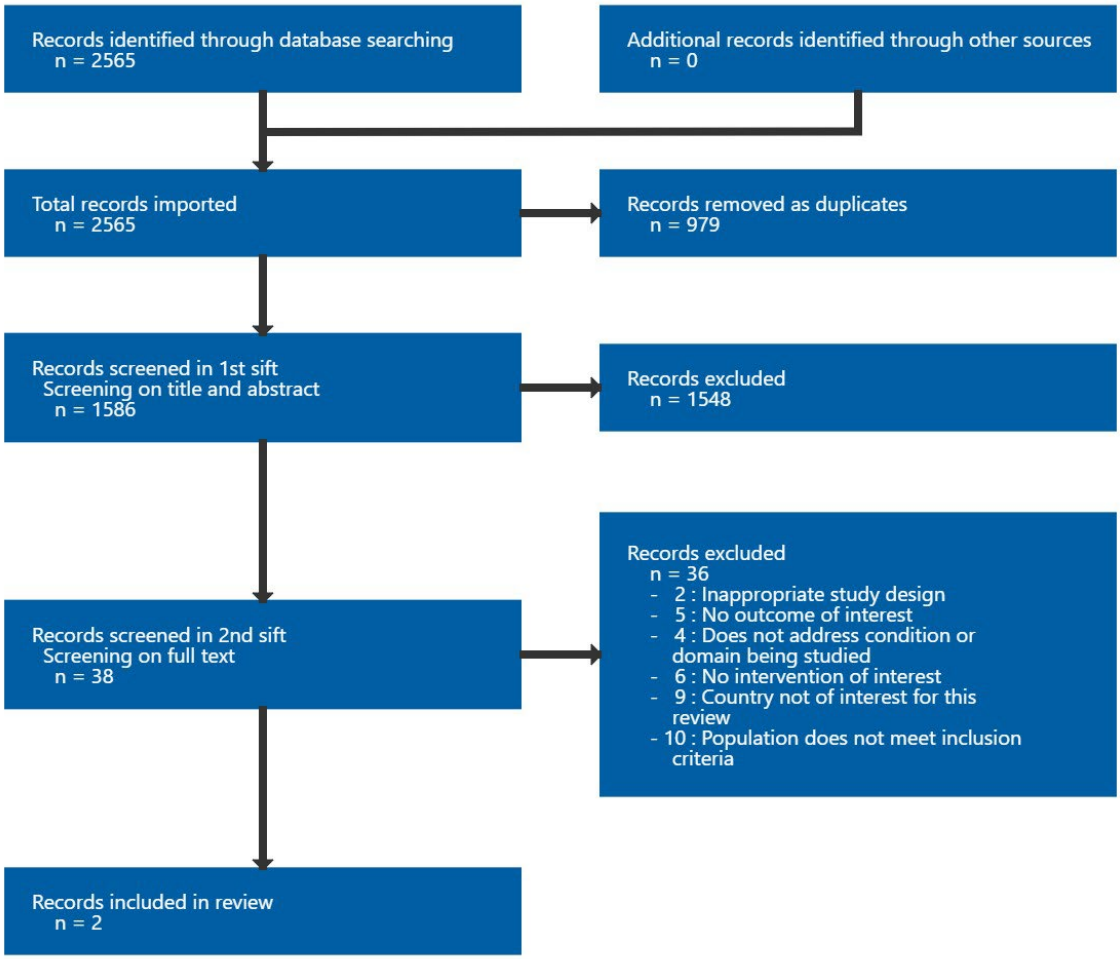
#	Searches
1	MeSH DESCRIPTOR pregnancy EXPLODE ALL TREES IN HTA
2	MeSH DESCRIPTOR pregnant women IN HTA
3	MeSH DESCRIPTOR prenatal care IN HTA

#	Searches
4	(((antenatal* or ante-natal* or gestational or maternal* or pregnan* or prenatal* or pre-natal*))) and (Project record:ZDT OR Full publication record:ZDT) IN HTA
5	#1 OR #2 OR #3 OR #4
6	MeSH DESCRIPTOR adiposity IN HTA
7	MeSH DESCRIPTOR body mass index IN HTA
8	MeSH DESCRIPTOR body size IN HTA
9	MeSH DESCRIPTOR body weight IN HTA
10	MeSH DESCRIPTOR overweight IN HTA
11	MeSH DESCRIPTOR obesity IN HTA
12	MeSH DESCRIPTOR obesity, abdominal IN HTA
13	MeSH DESCRIPTOR obesity, maternal IN HTA
14	MeSH DESCRIPTOR obesity, metabolically benign IN HTA
15	MeSH DESCRIPTOR obesity, morbid IN HTA
16	MeSH DESCRIPTOR waist circumference IN HTA
17	MeSH DESCRIPTOR waist-hip ratio IN HTA
18	MeSH DESCRIPTOR waist-height ratio IN HTA
19	MeSH DESCRIPTOR weight gain IN HTA
20	MeSH DESCRIPTOR skinfold thickness IN HTA
21	MeSH DESCRIPTOR body fat distribution IN HTA
22	MeSH DESCRIPTOR adipose tissue EXPLODE ALL TREES IN HTA
23	(((obes* or overweight or over weight or corpulen* or heavy or heavier or fat or adipos*))) and (Project record:ZDT OR Full publication record:ZDT) IN HTA
24	(((weight adj2 (manag* or gain* or increas* or excess or chang*))))) and (Project record:ZDT OR Full publication record:ZDT) IN HTA
25	(((body mass index or BMI or quetelet index))) and (Project record:ZDT OR Full publication record:ZDT) IN HTA
26	(((waist circumference* or waist hip ratio* or waist height ratio* or weight height ratio*))) and (Project record:ZDT OR Full publication record:ZDT) IN HTA
27	(((skin fold* or skinfold* or body composition))) and (Project record:ZDT OR Full publication record:ZDT) IN HTA
28	(((body fat adj3 percent*))) and (Project record:ZDT OR Full publication record:ZDT) IN HTA
29	((((arm or midarm or upperarm or brachial) adj4 (circumferen* or measure* or area* or fat* or diameter* or anthropometr*)))) and (Project record:ZDT OR Full publication record:ZDT) IN HTA
30	#6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29
31	#5 AND #30
32	MeSH DESCRIPTOR VITAMIN D EXPLODE ALL TREES IN HTA
33	(((calciferol* or calcifediol* or calciol* or cholecalciferol* or hydroxycholecalciferol* or dihydroxycholecalciferol* or calcitriol* or 24,25-dihydroxyvitamin D* or ergocalciferol* or ergosterol* or viosterol or vitamin d* or vitamind*))) and (Project record:ZDT OR Full publication record:ZDT) IN HTA
34	#32 OR #33
35	#31 AND #34

Appendix C Effectiveness evidence study selection

Study selection for: What dose of vitamin D is appropriate during pregnancy for women with a BMI medically classified as being in the overweight or obesity weight categories?

Figure 1: Effective evidence study selection flow chart



Appendix D Evidence tables

Evidence tables for review question: What dose of vitamin D is appropriate during pregnancy for women with a BMI medically classified as being in the overweight or obesity weight categories?

Table 4: Evidence tables

Alhomaid, 2021

Bibliographic Reference	Alhomaid, Raghad M; Mulhern, Maria S; Strain, Jj; Laird, Eamon; Healy, Martin; Parker, Michael J; McCann, Mary T; Maternal obesity and baseline vitamin D insufficiency alter the response to vitamin D supplementation: a double-blind, randomized trial in pregnant women.; The American journal of clinical nutrition; 2021; vol. 114 (no. 3); 1208-1218

Study details

Country/ies where study was carried out	Northern Ireland
Study type	Randomised controlled trial (RCT)
Study dates	Not reported
Inclusion criteria	• pregnant women ≥12 weeks gestational age • aged ≥18 years • BMI ≥18.5kg/m^2 • without current pregnancy-related complications • having a singleton pregnancy
Exclusion criteria	• multiple pregnancy

	• involvement in another research study • history of gastrointestinal, hepatic, renal, vascular, or hematological disorders • in vitro fertilization treatment • a history of neural tube defect pregnancies • active thyroid disease
Patient characteristics	**Age, (mean ±SD), years** Intervention = 29.5 ±5.5 Control = 29.7 ±5.1 **BMI, (mean ±SD), kg/m^2** Intervention = 27.8 ±5.4 Control = 28.1 ±5.7 **BMI categories** **Normal weight, %** Intervention = 33.9 Control = 33.1 **Overweight, %** Intervention = 33.1 Control = 33.1

	Obese, % Intervention = 33.1 Control = 33.9 **Gestation week (mean ±SD)** Intervention = 12.8 ±1.4 Control = 13.0 ±1.4
Intervention(s)/control	**Intervention:** 1 multivitamin tablet containing 10-µg vitamin D and a 10-µg vitamin D tablet **Control:** 1 multivitamin tablet containing 10-µg vitamin D and a 0-µg vitamin D (placebo) tablet
Duration of follow-up	No follow-up (immediately post-intervention)
Sources of funding	Not industry funded
Sample size	N = 240 Intervention group, n =122 (n=1 participant withdrew from 10mcg group after 12-week baseline) Control group, n =118 Note:
Other information	Recruitment took place at the first antenatal visit. Women were enrolled in the study after 12 weeks gestational age, and anthropometric measurements (height and weight) were taken at this point.

	Women taking any vitamin D containing supplement before 12 weeks gestational age were asked to only take the study supplements after enrolment.

BMI: Body mass index; RCT: randomised controlled trial; SD: standard deviation

Study arms
Intervention arm: 20µg/d Vitamin D (N = 121)
Comparison arm: 10µg/d Vitamin D (N = 181)

Outcomes

Study timepoints

- 28 weeks (gestational age)
- 36 weeks (gestational age)

Maternal serum 25(OH)D, nmol/L concentration at various timepoints

Outcome	28 week, Intervention arm: 20ug/d Vitamin D, N = 121	28 week, Comparison arm: 10ug/d Vitamin D, N = 118	36 week, Intervention arm: 20ug/d Vitamin D, N = 121	36 week, Comparison arm: 10ug/d Vitamin D, N = 118
Serum 25(OH)D nmol/L in overweight (25.0 to 29.9 kg/m^2) women Mean (SD)	81.6 (29.6)	72.9 (25.8)	93.9 (31.3)	81.9 (24.9)
Serum 25(OH)D nmol/L in obese (BMI ≥ 30 kg/m^2) women Mean (SD)	74.6 (32.2)	64.3 (27)	82.1 (33.4)	74.8 (30.6)

25 (OH)D: 25 hydroxyvitamin D; BMI: Body mass index; nmol/L: nanomoles per litre; SD: standard deviation

Critical appraisal

Section	Question	Answer
Domain 1: Bias arising from the randomisation process	Risk of bias judgement for the randomisation process	Low *(No serious concerns about the randomisation process)*
Domain 2a: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention)	Risk of bias for deviations from the intended interventions (effect of assignment to intervention)	Low *(Intention-to-treat analysis was used to account for missing data)*
Domain 2b: Risk of bias due to deviations from the intended interventions (effect of adhering to intervention)	Risk of bias judgement for deviations from the intended interventions (effect of adhering to intervention)	Low *(No serious concerns on the effect of adhering to interventions)*
Domain 3. Bias due to missing outcome data	Risk-of-bias judgement for missing outcome data	Low *(No serious concerns about missing outcome data, Intention-to-treat analysis was carried out)*
Domain 4. Bias in measurement of the outcome	Risk-of-bias judgement for measurement of the outcome	Low *(No serious concerns about outcome measurement)*
Domain 5. Bias in selection of the reported result	Risk-of-bias judgement for selection of the reported result	Low *(No serious concerns on the reported results)*
Overall bias and Directness	Risk of bias judgement	Low *(No serious concerns in any domain)*

Section	Question	Answer
Overall bias and Directness	Overall Directness	Directly applicable
Overall bias and Directness	Risk of bias variation across outcomes	N/A

Corcoy, 2020

Bibliographic Reference	Corcoy, Rosa; Mendoza, Lilian C; Simmons, David; Desoye, Gernot; Adelantado, J M; Chico, Ana; Devlieger, Roland; van Assche, Andre; Galjaard, Sander; Timmerman, Dirk; Lapolla, Annunziata; Dalfra, Maria G; Bertolotto, Alessandra; Harreiter, Jurgen; Wender-Ozegowska, Ewa; Zawiejska, Agnieszka; Kautzky-Willer, Alexandra; Dunne, Fidelma P; Damm, Peter; Mathiesen, Elisabeth R; Jensen, Dorte M; Andersen, Lise Lotte T; Tanvig, Mette; Hill, David J; Jelsma, Judith G; Snoek, Frank J; Kofeler, Harald; Trotzmuller, Martin; Lips, Paul; van Poppel, Mireille N M; The DALI vitamin D randomized controlled trial for gestational diabetes mellitus prevention: No major benefit shown besides vitamin D sufficiency.; Clinical nutrition (Edinburgh, Scotland); 2020; vol. 39 (no. 3); 976-984

Study details

Country/ies where study was carried out	7 European countries: • United Kingdom • Ireland • Austria • Poland • Italy (Padua, Pisa) • Spain

	• Belgium
Study type	Cluster randomised controlled trial
Study dates	2012 to 2015
Inclusion criteria	• pregnant women with a pre-pregnancy BMI ≥29 kg/m^2 • ≤19 weeks + 6 days of gestation • singleton pregnancy • aged ≥18 years
Exclusion criteria	• GDM diagnosed by oral glucose tolerance test (OGTT) using IADPSG/WHO 2013 criteria • pre-existing diabetes, chronic medical conditions or a psychiatric disorder • being unable to walk ≥ 100 m safely • requiring complex diets • not fluent in the major language of the country • having current or past abnormal calcium metabolism (hypo/hyperparathyroidism, nephrolithiasis, hypercalciuria), or having hypercalciuria (>0.6 mmol/mmol creatinine in morning spot samples) • hypercalcemia detected at baseline measurement according to trimester cut-offs
Patient characteristics	**Age (mean±SD), years** Intervention = 32.2±5.2 Control = 32.8 ± 5.4

	Parity, % **Multiparous** Intervention = 53 Control = 57 **History of GDM, %** Intervention = 15 Control = 15 **Gestational age at entry (mean±SD), weeks** Intervention = 15.0±2.9 Control = 15.4±2.5 **Pre-pregnancy BMI, (mean±SD), kg/m^2** Intervention = 33.7±4.3 Control = 33.3±4.3 **BMI at entry, (mean±SD), kg/m^2** Intervention = 34.2±4.3 Control = 34.2±4.2

	Taking (multi)vitamins at entry, % Intervention = 86 Control = 84
Intervention(s)/control	**Intervention:** Vitamin D3 supplementation (1600 IU/day) (with and without lifestyle counselling) **Control:** placebo (with and without lifestyle counselling) Study reported that since most women use multivitamins during pregnancy, containing on average 400 IU of vitamin D, the chosen intervention dose was 1600 IU/day. The intervention was delivered in a tablet form. Each tablet contained 400 IU of vitamin D3. Placebo tablets, identical to the intervention tablets in appearance, were produced especially for the DALI trial. Participating women were asked to take 4 tablets daily until delivery.
Duration of follow-up	Immediately post-intervention
Sources of funding	Not industry funded
Sample size	N = 154 Intervention group, n = 79 Placebo group, n=75 Design effect = 1+ (7-1) x 0.231 = 2.386 Adjusted sample size = 154/2.386 = 64.5 ~ **65**

Other information	Study randomised participants into 4 groups: • Lifestyle counselling (healthy eating and physical activity) and placebo, • Lifestyle counselling and vitamin D supplementation, • vitamin D supplementation alone and • placebo alone The study reported that there was no interaction between the lifestyle intervention and the vitamin D intervention for any of the outcomes, and therefore the authors combined the 2 groups randomised to vitamin D supplementation and compared them with the 2 groups randomised to have placebo. Pre-pregnancy BMI (used as an inclusion criterion) was self-reported at recruitment

BMI: Body mass index; IADPSG: the international association of the diabetes and pregnancy study groups; IU: international units; OGTT: oral glucose tolerance test; (OH)D: hydroxyvitamin D: SD: standard deviation; WHO: world health organisation

Study arms
Intervention arm: 1600IU/day (N = 79)
Control arm: Placebo (N = 75)

Outcomes
Study timepoints

- 24 week gestational age (Study reports 24-28weeks)
- 35 week gestational age (Study reports 35-37 weeks)
- 38 week gestational age (Study reports at delivery)

Total serum 25(OH)D concentrations

Outcome	Intervention arm: 1600IU/day, 24 week, N = 32	Intervention arm: 1600IU/day, 35 week, N = 29	Intervention arm: 1600IU/day, 38 week, N = 31	Control arm: Placebo, 24 week, N = 28	Control arm: Placebo, 35 week, N = 25	Control arm: Placebo, 38 week, N = 27
25(OH)D nmol/L level in women with BMI ≥ 29kg/m² Mean (SD)	119.4 (35.5)	122.9 (38.8)	101.2 (32.2)	81.9 (39.4)	84.5 (39.8)	76.9 (34.8)

BMI: body mass index; nmol/L: nanomoles per litre; (OH)D: hydroxyvitamin D; IU: international units
Sample sizes and estimates are adjusted for clustering effect

Preterm birth

Outcome	Intervention arm: 1600IU/day, 38 week, N = 31	Control arm: Placebo, 38 week, N = 27
Preterm birth No of events	n = 1 ; % = 3	n = 0 ; % = 2

IU: international units
Sample sizes and estimates are adjusted for clustering effect

Birth weight <2.5kg

Outcome	Intervention arm: 1600IU/day, 38 week, N = 31	Control arm: Placebo, 38 week, N = 26
Birth weight <2.5kg No of events	n = 0 ; % = 0	n = 0 ; % = 2

IU: international units
Sample sizes and estimates are adjusted for clustering effect

Preeclampsia

Outcome	Intervention arm: 1600IU/day, 38 week, N = 28	Control arm: Placebo, 38 week, N = 24
Preeclampsia No of events	n = 0 ; % = 2	n = 1 ; % = 5

IU: international units
Sample sizes and estimates are adjusted for clustering effect

Gestational diabetes mellitus

Outcome	Intervention arm: 1600IU/day, 24 week, N = 31	Intervention arm: 1600IU/day, 35 week, N = 29	Control arm: Placebo, 24 week, N = 28	Control arm: Placebo, 35 week, N = 22
Gestational Diabetes mellitus No of events	n = 6 ; % = 20	n = 11 ; % = 37	n = 7 ; % = 26	n = 10 ; % = 39

IU: international units
Sample sizes and estimates are adjusted for clustering effect

Critical appraisal - Cochrane Risk of Bias tool (RoB 2.0) Cluster randomised trials NGA

Section	Question	Answer
1a. Bias arising from the randomisation process	Risk of bias judgement for the randomisation process	Some concerns *(No information on the likelihood that allocation sequence was subverted)*
1b. Bias arising from the timing of identification and recruitment of individual participants in relation to timing of randomisation	Risk of bias judgement for the timing of identification and recruitment of individual participants in relation to timing of randomisation	Low

Section	Question	Answer
2. Bias due to deviations from intended interventions (If your aim is to assess the effect of assignment to intervention, answer the following questions).	Risk of bias judgement for deviations from intended interventions	Low
3. Bias due to missing outcome data	Risk of bias judgement for missing outcome data	Some concerns *(16% loss to follow up but ITT analysis conducted)*
4. Bias in measurement of the outcome	Risk of bias judgement for measurement of the outcome	Low
5. Bias in selection of the reported result	Risk of bias for selection of the reported result	Low
Overall bias and Directness	Risk of bias judgement	Some concerns *(Some concerns about the randomisation process and missing outcome data)*
Overall bias and Directness	Overall Directness	Directly applicable

Appendix E Forest plots

Forest plots for review question: What dose of vitamin D is appropriate during pregnancy for women with a BMI medically classified as being in the overweight or obesity weight categories?

No meta-analysis was conducted for this review question and so there are no forest plots.

Appendix F GRADE tables

GRADE tables for review question: What dose of vitamin D is appropriate during pregnancy for women with a BMI medically classified as being in the overweight or obesity weight categories?

Table 5: Evidence profile for comparison between 20µg/day and 10µg/day vitamin D supplementation in pregnant women medically classified as being in the overweight (25.0 to 29.9 kg/m^2) or obesity weight categories (BMI ≥30.0 kg/m^2)

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	20µg/day vitamin D	10µg/day vitamin D	Relative (95% CI)	Absolute		
Maternal serum 25(OH)D concentration (nmol/L) in pregnant women medically classified as being in the overweight weight category (BMI 25.0 to 29.9k/m^2) at 28 weeks gestational age (measured with: LC-tandem MS (LC-MS/MS) using a commercially available kit; Better indicated by higher values)												
1 (Alhomaid 2021)	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[1]	none	40	39	-	MD 8.7 higher (3.54 lower to 20.94 higher)	MODERATE **NO IMP. DIFF.**	CRITICAL
Maternal serum 25(OH)D concentration (nmol/L) in pregnant women medically classified as being in the obesity weight category (BMI ≥30.0kg/m^2) at 28 weeks gestational age (measured with: LC-tandem MS (LC-MS/MS) using a commercially available kit; Better indicated by higher values)												
1 (Alhomaid 2021)	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[1]	none	40	40	-	MD 10.3 higher (2.72 lower to 23.32 higher)	MODERATE **NO. EV. OF. IMP. DIFF.**	CRITICAL
Maternal serum 25(OH)D concentration (nmol/L) in women medically classified as being in the overweight weight category (BMI 25.0 to 29.9kg/m^2) at 36 weeks gestational age (measured with: LC-tandem MS (LC-MS/MS) using a commercially available kit; Better indicated by higher values)												
1 (Alhomaid 2021)	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[1]	none	40	39	-	MD 12 higher (0.46 lower to 24.46 higher)	MODERATE **POSS. IMP. BENEFIT.**	CRITICAL
Maternal serum 25(OH)D concentration (nmol/L) in pregnant women medically classified as being in the obesity weight category (BMI≥30.0kg/m^2) at 36 weeks gestational age (measured with: LC-tandem MS (LC-MS/MS) using a commercially available kit; Better indicated by higher values)												
1 (Alhomaid 2021)	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[1]	none	40	40	-	MD 7.3 higher (6.74 lower to 21.34 higher)	MODERATE **NO. IMP. DIFF.**	CRITICAL

BMI: Body mass index; CI: confidence interval; MD: mean difference; nmol/L: nanomoles per litre; 25(OH)D: 25 hydroxyvitamin D

[1] 95% CI crosses 1 MID (0.5 x control group SD for '25 (OH)D concentration in overweight pregnant women' = ±11.1); (0.5 x control group SD for '25 (OH)D concentration in pregnant women in obesity weight category = ±9.85)

Table 6: Evidence profile for comparison between 40µg /day vitamin D supplementation and no supplementation in pregnant women medically classified as being in the overweight or obesity weight categories (BMI ≥ 29.0kg/m²)

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	1600IU/day vitamin D versus Placebo	Control	Relative (95% CI)	Absolute		
Maternal serum 25(OH)D serum concentration (nmol/L) at 24 to 28 weeks (measured with: ClinMass liquid chromatography-mass spectrometry/mass spectrometry (LC-MS/MS) complete kit; Better indicated by higher values)												
1 (Corcoy 2020)	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	32	28	-	MD 37.5 higher (18.41 to 56.59 higher)	MODERATE **IMP. BENEFIT**	CRITICAL
Maternal serum 25(OH)D serum concentration (nmol/L) at 35 to 37 weeks (measured with: ClinMass liquid chromatography-mass spectrometry/mass spectrometry (LC-MS/MS) complete kit; Better indicated by higher values)												
1 (Corcoy 2020)	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	29	25	-	MD 38.4 higher (17.36 to 59.44 higher)	MODERATE **IMP. BENEFIT**	CRITICAL
Maternal serum 25(OH)D serum concentration (nmol/L) at delivery (number of weeks not specified) (measured with: ClinMass liquid chromatography-mass spectrometry/mass spectrometry (LC-MS/MS) complete kit; Better indicated by higher values)												
1 (Corcoy 2020)	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	31	27	-	MD 24.3 higher (6.96 to 41.64 higher)	LOW **IMP. BENEFIT**	CRITICAL
Preterm birth (not defined in study) at birth												
1 (Corcoy 2020)	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[3]	none	1/31 (3.2%)	0/27 (0%)	POR 6.49 (0.13 to 330.38)	-	MODERATE **NO EV. OF IMP. DIFF.**	CRITICAL
Low birth weight (<2.5kg)												
1 (Corcoy 2020)	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[4]	none	0/31 (0%)	0/26 (0%)	RD 0.00 (-0.07 to +0.07)	-	VERY LOW **NO IMP. DIFF.**	CRITICAL
Preeclampsia at birth												

1 (Corcoy 2020)	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[3]	none	0/28 (0%)	1/24 (4.2%)	POR 0.11 (0 to 5.84)	37 fewer per 1000 (from 42 fewer to 161 more)	VERY LOW **NO IMP. DIFF.**	IMPORTANT
Gestational diabetes mellitus at 24 to 28 weeks												
1 (Corcoy 2020)	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[3]	none	6/31 (19.4%)	7/28 (25%)	RR 0.77 (0.3 to 2.03)	58 fewer per 1000 (from 175 fewer to 257 more)	VERY LOW **NO EV. OF IMP. DIFF.**	IMPORTANT
Gestational diabetes mellitus at 35 to 37 weeks												
1 (Corcoy 2020)	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[3]	none	11/29 (37.9%)	10/22 (45.5%)	RR 0.83 (0.43 to 1.6)	77 fewer per 1000 (from 259 fewer to 273 more)	VERY LOW **NO IMP. DIFF.**	IMPORTANT

BMI: Body mass index; CI: confidence interval; LC-MS/MS: liquid chromatography-mass spectrometry/mass spectrometry; MD: mean difference; nmol/L: nanomoles per litre; (OH)D: hydroxyvitamin D: POR: Peto odds ratio; RD: risk difference: RR: relative risk

[1] Serious risk of bias in the evidence contributing to the outcomes as per RoB 2

[2] 95% CI crosses 1 MID (0.5xcontrol group SD at baseline for maternal serum 25(0H)D serum concentration at birth = ±13.4)

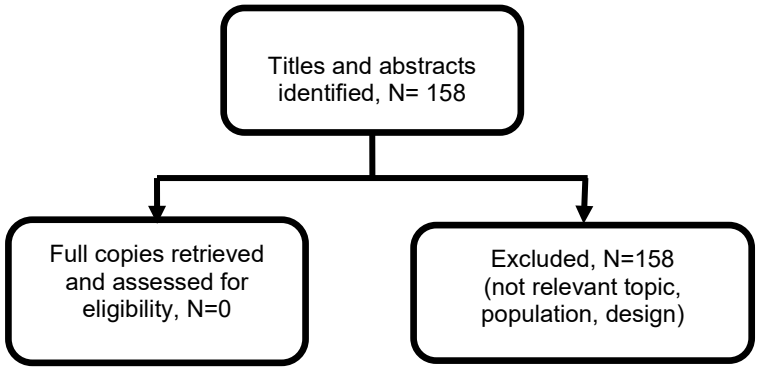
[3] 95% CI crosses 2 MIDs (0.8 and 1.25)

[4] Event rate <150

Appendix G Economic evidence study selection

Study selection for: What dose of vitamin D is appropriate during pregnancy for women with a BMI medically classified as being in the overweight or obesity weight categories?

Figure 2. Flow diagram of selection process for economic evaluations



Appendix H Economic evidence tables

Economic evidence tables for review question: What dose of vitamin D is appropriate during pregnancy for women with a BMI medically classified as being in the overweight or obesity weight categories?

No economic evidence was identified which was applicable to these review question.

Appendix I Economic model

Economic model for review question: What dose of vitamin D is appropriate during pregnancy for women with a BMI medically classified as being in the overweight or obesity weight categories?

No economic analysis was conducted for this review question.

Appendix J Excluded studies

Excluded studies for review question: What dose of vitamin D is appropriate during pregnancy for women with a BMI medically classified as being in the overweight or obesity weight categories?

Excluded effectiveness studies

Table 7: Excluded studies and reasons for their exclusion

Study	Code [Reason]
Amberntsson, Anna, Barebring, Linnea, Winkvist, Anna et al. (2023) Vitamin D intake and determinants of vitamin D status during pregnancy in The Norwegian Mother, Father and Child Cohort Study. Frontiers in nutrition 10: 1111004	- Inappropriate study design *Not an intervention study. Study assessed the total vitamin D intake from food and supplements in pregnant women*
Amberntsson, Anna, Papadopoulou, Eleni, Winkvist, Anna et al. (2021) Maternal vitamin D intake and BMI during pregnancy in relation to child's growth and weight status from birth to 8 years: a large national cohort study. BMJ open 11(10): e048980	- No appropraite intervention *Study assessed total vitamin D intake from both diets and supplements. Vitamin D from supplements alone was not reported.*
Anonymous. (2023) Erratum: Maternal vitamin D intake and BMI during pregnancy in relation to child's growth and weight status from birth to 8 years: a large national cohort study (BMJ Open (2021) 11 (e048980) DOI: 10.1136/bmjopen-2021-048980). BMJ Open 13(3): e048980corr1	- No outcome of interest *Study assessed total vitamin D intake from both diets and supplements. Vitamin D from supplements alone was not reported.*
Begum, R, Coutinho, M L, Dormandy, T L et al. (1968) Maternal malabsorption presenting as congenital rickets. Lancet (London, England) 1(7551): 1048-52	- Inappropriate study design *Case report*
Bhowmik, B., Siddiquee, T., Mdala, I. et al. (2021) Vitamin D3 and B12 supplementation in pregnancy. Diabetes Research and Clinical Practice 174: 108728	- Country not of interest for this review *Study conducted in Bangladesh which is not a high income country as stated in the protocol*
Brustad, Nicklas, Garland, Juri, Thorsen, Jonathan et al. (2020) Effect of High-Dose vs Standard-Dose Vitamin D Supplementation in Pregnancy on Bone Mineralization in Offspring Until Age 6 Years: A Prespecified Secondary Analysis of a Double-Blinded, Randomized Clinical Trial. JAMA pediatrics 174(5): 419-427	- Population does not meet inclusion criteria *All pregnant women were included. Results were not stratified by weight status or BMI categories*
Catov, J.M., Bodnar, L.M., Olsen, J. et al. (2011) Periconceptional multivitamin use and risk of	- No outcome of interest

Study	Code [Reason]
preterm or small-for-gestational-age Births in the Danish National birth cohort. American Journal of Clinical Nutrition 94(3): 906-912	*Observational study which reports an outcome that is already reported in the included RCTs*
Chatzakis, Christos, Goulis, Dimitrios G, Mareti, Evangelia et al. (2019) Prevention of gestational diabetes mellitus in overweight or obese pregnant women: A network meta-analysis. Diabetes research and clinical practice 158: 107924	- Does not address condition or domain being studied *Studies included in this systematic review do not assess vitamin D supplementation except 1(Corcoy 2020), which has been included in this review*
Chawes BL, Bønnelykke K, Stokholm J et al. (2016) Effect of Vitamin D3 Supplementation During Pregnancy on Risk of Persistent Wheeze in the Offspring: A Randomized Clinical Trial. JAMA 315(4): 353-361	- Population does not meet inclusion criteria *All pregnant women were included. Results were not separated by weight status or BMI category.*
Christesen, Henrik T, Falkenberg, Tine, Lamont, Ronald F et al. (2012) The impact of vitamin D on pregnancy: a systematic review. Acta obstetricia et gynecologica Scandinavica 91(12): 1357-67	- Population does not meet inclusion criteria *Systematic review has a mixed study population including all pregnant women irrespective of weight category and outcome data is not stratified by BMI categories. There are no studies relevant for inclusion.*
Dieberger, A.M., Obermayer-Pietsch, B., Harreiter, J. et al. (2023) Physical activity and sedentary time across pregnancy and associations with neonatal weight, adiposity and cord blood parameters: a secondary analysis of the DALI study. International Journal of Obesity 47(9): 873-881	- No outcome of interest *Secondary analysis of DALI trial reported in Corcoy 2020 with no additional relevant outcomes as per protocol.*
Egan, Aoife M, Vellinga, Akke, Harreiter, Jurgen et al. (2017) Epidemiology of gestational diabetes mellitus according to IADPSG/WHO 2013 criteria among obese pregnant women in Europe. Diabetologia 60(10): 1913-1921	- No intervention of interest *Study assessed risk factors for gestational diabetes and there was no intervention.*
Gerveieeha, Z., Siassi, F., Qorbani, M. et al. (2023) The effect of vitamin D supplementation on body composition in nursing mothers with overweight or obesity: a randomized double-blind placebo-controlled clinical trial. BMC Nutrition 9(1): 1	- Population does not meet inclusion criteria *Study included postpartum nursing mothers who delivered at term, and was conducted in Iran which is not a high income country as stated in the protocol.*
Gould, J.F., Gibson, R.A., Green, T.J. et al. (2022) A Systematic Review of Vitamin D during Pregnancy and Postnatally and Symptoms of Depression in the Antenatal and Postpartum Period from Randomized Controlled Trials and Observational Studies. Nutrients 14(11): 2300	- Country not of interest for this review *Systematic review including 2 RCTs conducted in Iran which is not a high income country as stated in the protocol. Other included studies were case control and cohort studies.*

Study	Code [Reason]
Griffith, Rebecca J, Alsweiler, Jane, Moore, Abigail E et al. (2020) Interventions to prevent women from developing gestational diabetes mellitus: an overview of Cochrane Reviews. The Cochrane database of systematic reviews 6: cd012394	- Does not address condition or domain being studied *Included systematic reviews are not relevant to this review as they either assessed dietary or exercise interventions, metformin or pharmacological interventions, which did not include vitamin D. One systematic review had vitamin D as an intervention but individual studies included that stratified population by weight category were carried out in LMICs*
Groth, Susan W, Stewart, Patricia A, Ossip, Deborah J et al. (2017) Micronutrient Intake Is Inadequate for a Sample of Pregnant African-American Women. Journal of the Academy of Nutrition and Dietetics 117(4): 589-598	- No intervention of interest *Study examined dietary micronutrient intake in pregnancy.*
Harreiter, Jurgen, Mendoza, Lilian C, Simmons, David et al. (2022) Vitamin D3 Supplementation in Overweight/Obese Pregnant Women: No Effects on the Maternal or Fetal Lipid Profile and Body Fat Distribution-A Secondary Analysis of the Multicentric, Randomized, Controlled Vitamin D and Lifestyle for Gestational Diabetes Prevention Trial (DALI). Nutrients 14(18)	- No outcome of interest *Secondary analysis of DALI trial reported in Corcoy 2020 with no additional relevant outcomes as per protocol.*
Harvey, Nicholas C, Holroyd, Christopher, Ntani, Georgia et al. (2014) Vitamin D supplementation in pregnancy: a systematic review. Health technology assessment (Winchester, England) 18(45): 1-190	- Does not address condition or domain being studied *Systematic review has a mixed study population including all pregnant women irrespective of weight category and outcome data is not stratified by BMI categories. There are no studies relevant for inclusion.*
Luo, T., Lin, Y., Lu, J. et al. (2022) Effects of vitamin D supplementation during pregnancy on bone health and offspring growth: A systematic review and meta-analysis of randomized controlled trials. PLoS ONE 17(10october): e0276016	- Population does not meet inclusion criteria *Systematic review has a mixed study population including all pregnant women irrespective of weight category and outcome data is not stratified by BMI categories. Individual studies were conducted in HICs and LMICs. There are no studies relevant for inclusion.*
Lutke-dorhoff, M, Schulz, J, Westendarp, H et al. (2022) Comparative Study of the Effects of Two Dietary Sources of Vitamin D on the Bone Metabolism, Welfare and Birth Progress of Sows Fed Protein- and Phosphorus-Reduced Diets. Animals 12(13)	- Does not address condition or domain being studied *Non-human study. Study was on pigs.*

Study	Code [Reason]
Ma, Shuangshuang, Yin, Wanjun, Wang, Peng et al. (2023) Effect of vitamin D supplementation on glucose control in mid-late gestation: A randomized controlled trial. Clinical nutrition (Edinburgh, Scotland) 42(6): 929-936	- Country not of interest for this review *Study conducted in China, which is not a high income country as stated in the protocol*
Mead, Molly J, McWhorter, Caroline A, Rodgers, Megan D et al. (2023) Does maternal vitamin D status influence placental weight or vascular and inflammatory pathology? Secondary analysis from the Kellogg Pregnancy Study. The Journal of steroid biochemistry and molecular biology 233: 106358	- Population does not meet inclusion criteria *All pregnant women were included. Results were not stratified by weight status or BMI categories. Primary study of this secondary analysis equally assessed and was not eligible for inclusion*
Moon, Rebecca J, Harvey, Nicholas C, Cooper, Cyrus et al. (2016) Determinants of the Maternal 25-Hydroxyvitamin D Response to Vitamin D Supplementation During Pregnancy. The Journal of clinical endocrinology and metabolism 101(12): 5012-5020	- Population does not meet inclusion criteria *All pregnant women were included. Results were not stratified by weight status or BMI category*
Morse, Nancy L (2012) Benefits of docosahexaenoic acid, folic acid, vitamin D and iodine on foetal and infant brain development and function following maternal supplementation during pregnancy and lactation. Nutrients 4(7): 799-840	- Inappropriate study design *Not an intervention study. Study compared 25(OH)D concentrations in women who developed GDM to women who did not develop GDM*
Nadeem, Amna, Saeed, Muniza, Sadiqa, Ayesha et al. (2023) The Effect of Vitamin D3 Intervention on the Association Among Vitamin D3, Adiponectin, and Body Mass Index in Pregnant Women With Gestational Diabetes. Cureus 15(8): e43506	- Country not of interest for this review *Study conducted in Pakistan which is not a high income country as stated in the protocol*
Pena, Homero Rabelo, de Lima, Marilia Carvalho, Brandt, Katia Galeao et al. (2015) Influence of preeclampsia and gestational obesity in maternal and newborn levels of vitamin D. BMC pregnancy and childbirth 15: 112	- Country not of interest for this review *Study conducted in Brazil which is not a high income country as stated in the protocol*
Rached, Veronica, Diogenes, Maria Eduarda Leao, Donangelo, Carmen Marino et al. (2023) Calcium plus vitamin D supplementation during pregnancy reduces postpartum fat mass in adolescents: A randomized trial. American journal of human biology : the official journal of the Human Biology Council 35(9): e23911	- Country not of interest for this review *Study conducted in Brazil which is not a high income country as stated in the protocol*

Study	Code [Reason]
Redfern, Kathy M., Hollands, Heidi J., Welch, C. Ross et al. (2022) Dietary Intakes of Folate, Vitamin D and Iodine during the First Trimester of Pregnancy and the Association between Supplement Use and Demographic Characteristics amongst White Caucasian Women Living with Obesity in the UK. Nutrients 14(23): 5135	- No intervention of interest *Study examined dietary micronutrient intake in pregnancy*
Samimi, M, Kashi, M, Foroozanfard, F et al. (2016) The effects of vitamin D plus calcium supplementation on metabolic profiles, biomarkers of inflammation, oxidative stress and pregnancy outcomes in pregnant women at risk for pre-eclampsia. Journal of human nutrition and dietetics 29(4): 505-515	- Country not of interest for this review *Study conducted in Iran which is not a high income country as stated in the protocol*
Sauder, K.A., Harte, R.N., Ringham, B.M. et al. (2021) Disparities in Risks of Inadequate and Excessive Intake of Micronutrients during Pregnancy. Journal of Nutrition 151(11): 3555-3569	- No outcome of interest *Study outcome was the risk of inadequate and excessive nutrients from diet and supplements*
Shahgheibi, S.; Farhadifar, F.; Pouya, B. (2016) The effect of vitamin D supplementation on gestational diabetes in high-risk women: Results from a randomized placebo-controlled trial. Journal of Research in Medical Sciences 21(1)	- Country not of interest for this review *Study conducted in Iran which is not a high income country as stated in the protocol*
Sunarno, Rita Dewi, Kartasurya, Martha Irene, Suwondo, Ari et al. (2023) Vitamin D Supplementation and Sun Exposure Maintain Blood Pressures of Pregnant Women and Increase Birth Weight in a Randomized Controlled Trial. Iranian journal of public health 52(10): 2148-2156	- Country not of interest for this review *Study conducted in Indonesia which is not a high income country as stated in the protocol*
Valkama, Anita J, Meinila, Jelena M, Koivusalo, Saila B et al. (2018) Body size modifies the relationship between maternal serum 25-hydroxyvitamin D concentrations and gestational diabetes in high-risk women. European journal of clinical nutrition 72(3): 460-463	- No intervention of interest *Study assessed the change in 25(OH)D during pregnancy in relation to maternal BMI*
Vanderlelie, Jessica, Scott, Rani, Shibl, Rania et al. (2016) First trimester multivitamin/mineral use is associated with reduced risk of pre-eclampsia among overweight and obese women. Maternal & Child Nutrition 12(2): 339-348	- No intervention of interest *Vitamin D reported as part of multivitamin and the specific dose of vitamin D was not reported*

Study	Code [Reason]
Vestergaard, Anna Louise, Justesen, Signe, Volqvartz, Tabia et al. (2021) Vitamin D insufficiency among Danish pregnant women-Prevalence and association with adverse obstetric outcomes and placental vitamin D metabolism. Acta obstetricia et gynecologica Scandinavica 100(3): 480-488	- No intervention of interest *Study assessed the correlation between vitamin D levels in early pregnancy and pregnancy outcomes*
Zerofsky, Melissa S, Jacoby, Bryon N, Pedersen, Theresa L et al. (2016) Daily Cholecalciferol Supplementation during Pregnancy Alters Markers of Regulatory Immunity, Inflammation, and Clinical Outcomes in a Randomized Controlled Trial. The Journal of nutrition 146(11): 2388-2397	- Population does not meet inclusion criteria *All pregnant women were included. Results were not stratified by weight status or BMI category*

Excluded economic studies

No economic study was reviewed at full text and excluded from this review.

Appendix K Research recommendations – full details

Research recommendations for review question: What dose of vitamin D is appropriate during pregnancy for people with a BMI medically classified as being in the overweight or obesity weight categories?

K.1.1 Research recommendation

What dose of vitamin D is appropriate during pregnancy for people with a BMI that is within the overweight or obesity weight categories?

K.1.2 Why this is important

In the UK it is recommended that all adults take a daily 10µg supplement of Vitamin D. Optimum vitamin D status is associated with better bone health and may be linked to reduced risk of gestational diabetes. Those with higher adiposity may need additional vitamin D, especially during pregnancy, but the identified evidence was not clear.

K.1.3 Rationale for research recommendation

Table 8: Research recommendation rationale

Importance to 'patients' or the population	Those starting pregnancy with a BMI >25 kg/m^2 may be at a greater risk of some adverse pregnancy outcomes compared to those starting pregnancy with a healthy BMI. The risk of some of these outcomes (e.g. gestational diabetes) could potentially be reduced by having a better vitamin D status. Supplementing with vitamin D over and above what is recommended for the general UK population may be a simple preventable action that could improve some pregnancy outcomes for people with a BMI medically classified as being in the overweight or obesity weight categories.
Relevance to NICE guidance	Vitamin supplementation and weight status during pregnancy are important aspects of these guidelines. Only two RCTs were identified for this research question which did not provide enough evidence on the optimum Vitamin D dose in this population group.
Relevance to the NHS	Optimal vitamin D status during pregnancy may be associated with reduced risk of gestational diabetes. In turn, gestational diabetes increases the risk of subsequent type 2 diabetes. Both of these aspects result in poorer health outcomes and greater use of NHS resources.
National priorities	High
Current evidence base	Two RCTs were included in the review. One study compared medium dose vitamin D supplementation of 10µg (400IU)/day with another medium dose vitamin D supplementation of 20µg (800IU)/day (Alhomaid 2021). However, no important difference was found in the same group of women at 28 weeks gestational age. No important difference or no evidence of an important difference was found in women medically classified as being in the obesity weight category at the same time points. No other relevant outcomes were reported for this comparison group. Another study compared no vitamin D supplementation to a high dose vitamin D supplementation of 40µg (1600IU)/day (Corcoy 2020). There was important benefit for Vitamin D supplementation compared to placebo in terms of maternal serum 25(OH)D concentration at 24 to 28 and 35 to 37 weeks gestational age, and at delivery. No important differences were identified in this comparison for other outcomes identified, such as preterm birth, low birth weight (<2.5kg), preeclampsia or gestational diabetes.

	Given the lack of robust evidence, the committee did not make a recommendation and decided to make a research recommendation to help inform future guidelines.
Equality considerations	Ethnicity and socio economic factors

K.1.4 Modified PICO table

Table 9: Research recommendation modified PICO table

Population	Inclusion: • Women during a single or multiple pregnancy, for women with a BMI that is within the overweight or obesity weight categories
Intervention	• Vitamin D supplementation (20µg/800IU daily) • Vitamin D supplementation (40µg/1600IU daily) • Vitamin D supplementation (60-100µg/2400-4000IU daily) Exclude: vitamin D in combination with other vitamins and minerals
Comparator	comparisons • different doses in the intervention vs Vitamin D supplementation (10µg/ 400IU to 20µg/800IU daily) • different doses in the intervention compared to each other
Outcome	Primary outcomes • Maternal serum 25(OH)D concentration and neonatal (umbilical cord) 25(OH) D concentration • Gestational diabetes • Low birth weight (<2500 g) Secondary outcomes • Pre-eclampsia • Bone mass and bone density in infant • Childhood eczema and respiratory function • Infant hypocalcaemia • Cost-effectiveness (including resource use measurements and QALY estimations using a validated preference-based measure such as the EQ-5D or SF-6D).
Study design	• RCTs
Timeframe	For the secondary outcomes listed (bone mass, childhood eczema, infant hypocalcaemia), follow up would need to be until the offspring is age 2 years old at a minimum
Additional information	Sub-group analysis: 1. BMI thresholds on booking: ○ Overweight range: 25 to 29.99 kg/m^2 ○ Obesity range 1: 30 to 34.99 kg/m^2 ○ Obesity range 2: 35 to 39.99 kg/m^2 ○ Obesity range 3: >40 kg/m^2

	2. Single versus multiple pregnancy 3. Comorbidities (yes versus no) 4. Ethnicity ○ White/White British ○ Asian/Asian British ○ Black/African/Caribbean/Black British ○ Mixed/Multiple ethnic groups ○ Other ethnic group 5. Socioeconomic groups (high vs low) (deprivation measured using IMD) 6. Sunlight exposure and use of SPF (sufficient vs not sufficient). To also consider effect of seasons on Vitamin D sufficiency. 7. Baseline vitamin D level (low vs high)

BMI: body mass index; (OH)D: hydroxyvitamin D; QALY: quality-adjusted life year; RCTs: randomised controlled trials; SPF: sun protection factor