

Vitamin D Supplementation in Pregnancy

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Key Recommendations

- Vitamin D supplementation should be discussed with all pregnant and breastfeeding women
- All pregnant/breastfeeding women should receive at least 400 units/day cholecalciferol from OTC preparations or “Healthy Start” if eligible.
- Women should be assessed for their risk of vitamin D deficiency at their booking appointment.
- ‘At risk’ groups for vitamin D deficiency or insufficiency should be started on 1000 units cholecalciferol daily (Figure 1)
- Women at moderate or high risk of vitamin D deficiency should be tested with their booking blood tests.
- All pregnant women with Vitamin D deficiency should have their Vitamin D replaced according to the level of insufficiency to ensure it is adequately replaced by the third trimester.
- All babies should have 400 units per day unless fully formula fed.

Background

There has been increasing awareness of the benefits of vitamin D supplementation during pregnancy and studies demonstrating current levels of deficiency in the UK population. The National Diet and Nutrition Survey have demonstrated that a quarter of the inhabitants in UK have low vitamin D levels. In 2012, the UK Health Department identified at risk groups for vitamin D deficiency, this included pregnant and breastfeeding women, especially teenagers and young women (Vitamin D – advice on supplements for at risk groups – letter from UK Chief Medical Officers Department of Health http://www.dh.gov.uk/en/Publicationsandstatistics/Lettersandcirculars/Dearcolleagueletters/DH_132509).

In June 2014, the RCOG Scientific Impact Paper No. 43 discusses the benefits of Vitamin D in pregnancy. The NICE public health guidance 56 (Nov 2014) aims to identify and prevent vitamin D deficiency in at risk populations, which include pregnant and breastfeeding women.

Aims

- To inform clinicians and other practitioners caring for pregnant women about the need for Vitamin D in pregnancy and breastfeeding
- To recognise the ‘at risk’ population in need of Vitamin D supplementation
- To guide the optimal management for Vitamin D supplementation in pregnant and breastfeeding women
- To enable all pregnant and breastfeeding women to have optimal supplementation of Vitamin D by the third trimester

Scope

- To incorporate these latest recommendations from NICE and RCOG to improve the care of pregnant and breastfeeding women within the Oxford University Hospitals NHS Foundation Trust, by raising the awareness of Health Care Professionals within the Maternity Services.

Definitions

Term	Definition
CKD	Chronic kidney disease
TB	Tuberculosis
MMRA	Maternal Medicine Risk Assessment
OTC	Over the counter
PET	Pre-eclampsia

Executive Summary

Around 20% of adults in the United Kingdom have low Vitamin D levels because of the lack of ambient sunlight and other extenuating risk factors. Rickets has now re-emerged, within the UK. 'At risk' populations are likely to have low Vitamin D levels, so their infants are also likely to be born with low vitamin D stores that are further depleted by the lack of vitamin D in maternal breastmilk. These children are at high risk of childhood rickets.

Key aims of Vitamin D supplementation

To ensure:

1. Maternal Vitamin D levels are replete to avoid neonatal rickets.
2. Vitamin D deficiency is reversed in a timely manner.
3. Avoid (or reverse) the consequences of Vitamin D deficiency.

How to deliver excellent care	How to document that care
All women should be assessed for Vitamin D sufficiency at booking or when there is any contact with antenatal care.	To fill the MMRA or EPR booking form for risk assessment of Vitamin D status. This should be documented in the EPR record or the antenatal notes.
All pregnant and breastfeeding women should have at least 400 units (10mcg) cholecalciferol a day.	Antenatal vitamins should be included in the medications history of the antenatal notes.
<p>Women who belong to the 'at risk' group should have a higher dose of Vitamin D supplementation.</p> <ul style="list-style-type: none"> • Non-white skin • Obese BMI $\geq 30 \text{ kg/m}^2$ • Housebound women or who remain covered • Women with delivery date in November to March • At risk of pre-eclampsia 	Recommendations for OTC cholecalciferol 1,000 units daily and be documented in the antenatal notes.
<p>Women with high risk conditions should have their Vitamin D levels quantified and adequately replaced.</p> <ul style="list-style-type: none"> • Possible osteomalacia (bone pain, insufficiency or fragility fractures or proximal muscle weakness) • Known previous Vitamin D deficiency • Multiple sclerosis • Malabsorption due to inflammatory bowel disease, gluten enteropathy, gastric surgery, biliary disease, or intestinal overgrowth. • Inflammatory rheumatic diseases. • Drugs that impair Vitamin D e.g. steroids, antacids, antiepileptics, tacrolimus, rifampicin, anti-retrovirals, cholestyramine, diuretics 	<p>Vitamin D levels should be documented and replacement commenced according to the guideline. (see flowchart)</p> <p>Levels should be rechecked if indicated.</p>
Women with CKD 3-5, hyperparathyroidism, granulomatous disease (i.e. sarcoidosis and TB) should be referred to Silver Star or Obstetric Medicine.	Referral letter along with Vitamin D levels and current supplementation should be included in the woman's antenatal notes.

<p>After delivery, all women who are breastfeeding should be risk assessed for Vitamin D sufficiency. All breastfeeding women should be on at least 400 units (10mcg) cholecalciferol at discharge.</p>	<p>This should be included in the discharge summary.</p>
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Full Guideline

All pregnant and breastfeeding women will require screening for Vitamin D sufficiency, preferably at the booking visit, to ensure there is adequate time for replacing her Vitamin D by the third trimester.

The importance of screening for Vitamin D sufficiency

There has been a re-emergence of rickets in the UK and internationally as a result of depleted Vitamin D stores and lack of sunlight exposure. National surveys suggest that around a fifth of adults and 8 to 24% of children may have low vitamin D status.(2) This is compounded by the lack of ambient sunlight of the appropriate ultraviolet wavelength to facilitate synthesis of Vitamin D on exposed skin between mid-October till April, in the UK. Women belonging to the 'at risk' population are particularly vulnerable. They are likely to have low Vitamin D levels and therefore their infants will be born with low vitamin D stores that are further exacerbated by the lack of vitamin D in maternal breastmilk. There is no definitive maternal Vitamin D levels that are directly associated with childhood (or congenital) rickets, but studies have indicated that rickets in children less than 3 years is usually associated with maternal vitamin D deficiency. (3)

Data regarding the association between Vitamin D levels and low neonatal birthweight, wheezing and infection risks are not robust. Similarly, Vitamin D supplementation to reduce the risk of gestational diabetes, preterm delivery and bacterial vaginosis remains controversial. Women should only receive Vitamin D supplementation to ensure sufficiency, and not to prevent the conditions listed. The RCOG 2014 guideline however does suggest a higher dose of cholecalciferol supplementation (1,000 units daily) for women at high risk of pre-eclampsia. (1)

The 'at risk' population (NEW)

All pregnant women need a minimum of 10 mcg (400 units) cholecalciferol daily.

Women belonging to the 'at risk' population are at greater risk of Vitamin D insufficiency (or deficiency) in pregnancy and should be considered for a higher dose of Vitamin D supplementation or are at risk of pre-eclampsia (as per NICE CG107) and RCOG guidelines recommend a higher dose of vitamin D.

The 'at risk' population are:

- Non-white skin
- Obese BMI ≥ 30 kg/m²
- Housebound women or who remain covered

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- Women with delivery date in November to March
- At risk of pre-eclampsia (as per NICE CG107)

When to test Vitamin D levels (NEW)

Not all pregnant and breastfeeding women need to have their Vitamin D levels quantified. Quantification of Vitamin D level costs £9.95.

Testing Vitamin D levels is only necessary when the quantification of level of insufficiency is required to determine intensity of Vitamin D supplementation.

25-OH Vitamin D levels should be quantified if the woman has any of the following:

- Possible osteomalacia (bone pain, insufficiency or fragility fractures or proximal muscle weakness)
- Known previous Vitamin D deficiency
- Multiple sclerosis
- Malabsorption due to inflammatory bowel disease, gluten enteropathy, gastric surgery, biliary disease, or intestinal overgrowth.
- Inflammatory rheumatic diseases.
- Drugs that impair Vitamin D e.g. steroids, antacids, antiepileptics, tacrolimus, rifampicin, anti-retrovirals, cholestyramine, diureticsHyperparathyroidism
- Multiple sclerosis
- CKD 3-5
- Granulomatous disorders (e.g. TB or sarcoidosis)

Consider discussing with an Obstetric Physician before testing for other indications.

Additional laboratory investigations

These can be considered when the woman is found to be Vitamin D deficient, but does not fall into the 'at risk' population.

- Renal function
- Calcium and phosphate
- FBC (severe anaemia may suggested underlying malabsorption)
- Parathyroid hormone levels
- ESR / CRP / CK / Thyroid function – only if there are additional clinical indicators of connective tissue disease (i.e. muscle weakness)

Key aims of Vitamin D supplementation

To ensure:

1. Maternal Vitamin D levels are replenished to avoid neonatal rickets
2. Vitamin D deficiency is reversed in a timely manner
3. Avoid (or reverse) the consequences of Vitamin D deficiency.

Supplementing Vitamin D based on levels of sufficiency

Levels of Vitamin D sufficiency remain contentious and normal ranges are not available on EPR. The reasons for these are:

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1. Different laboratories often have different 'normal ranges'
2. The precision and accuracy of the assays, especially in non-reference laboratories, remain problematic (6)
3. 25-hydroxyvitamin D levels change with the seasons, exposure to sunlight, and dietary intake

Definition of Vitamin D Sufficiency (NEW)

Vitamin D sufficiency (values from the institute of Medicine and the National Osteoporosis Society Clinical Guideline 2013)	
25-hydroxyvitamin D levels	Vitamin D doses
Deficiency * (less than 30nmol/l)	Cholecalciferol 4000 units daily for 6 weeks †
Insufficiency (30-50 nmol/l)	Cholecalciferol 2,000 units daily
Sufficient (greater than 50 nmol/l)	Health promotion advice. To continue whatever treatment they are currently on, or at least cholecalciferol 1000 units a day.
Ensure that the woman is also on a calcium-replete diet of $\geq 1,000$ mg of calcium a day which is roughly equivalent to 1 pint of milk.	
* The Department of Health defines less than 25nmol/l (equal to 10 ng/ml) of 25-hydroxyvitamin D as low.	
† Cholecalciferol 300,000 units IM is associated with an increased risk of fractures and therefore not suitable in pregnant women.	

Safety of Vitamin D

Safety of Vitamin D in pregnancy

Vitamin D is naturally occurring nutrient manufactured by skin when exposed to sunlight (UVB). Oral supplementation of cholecalciferol (maximum dose of 4,000 units daily) started less than 16 weeks gestation has been shown to be safe in pregnancy. (7)

Safety of Vitamin D in the general population (risk of toxicity)

Vitamin D toxicity results in hypercalcaemia, and only occurs with protracted use of excessively high doses of supplementation. The Food and Nutrition Board of the IOM has extensively reviewed the evidence and concluded that vitamin D below 10,000 IU/day is not usually associated with toxicity, whereas doses equal to or above 50,000 IU/day for several weeks or months are frequently associated with toxicity, including documented hypercalcaemia. Less severe symptoms include hypercalciuria and renal stones.

In the non-parous population, toxicity not seen at serum vitamin D levels less than 250nmol/l; and seldom poses a problem until greater than 500nmol/l. However, the caveats are if there is a history of renal calculi, renal impairment (CKD 3 or 4),

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granulomatous disease (i.e. TB or sarcoidosis) or parathyroid disorders - refer for secondary care advice. (8)

Monitoring

Dosing regimens suggested in pregnancy, are unlikely to result in Vitamin D toxicity except those with hyperparathyroidism, CKD 3-4, granulomatous disease (i.e. sarcoidosis or TB).

Routine monitoring of Vitamin D levels is not necessary in pregnancy and breastfeeding unless:

1. Have known past or current Vitamin D deficiency
2. Have completed loading regimen for Vitamin D deficiency (Figure 1)
3. Poor adherence is suspected.

Dosing – intensity and timing

The aim of Vitamin D replacement is to ensure that the pregnant woman's vitamin D levels are replenished by the third trimester to prevent the development of rickets in the offspring. Due to this larger doses and/or loading doses may be required.

At 'at risk' women who have a delayed diagnosis of Vitamin D deficiency (after 12 weeks gestation), require more vigorous replacement therapy with loading doses. (Figure 1) (Appendix 1 – reasons for more intensive vitamin D replacement).

Special circumstances for Vitamin D supplementation

Women with hyperparathyroidism, chronic kidney disease (CKD Stage 3-4), granulomatous disease (i.e. TB and sarcoidosis) require special monitoring and or different formulations of Vitamin D. Please refer to Obstetric Medicine

Vitamin D replacement algorithm in pregnant and breastfeeding women (NEW)

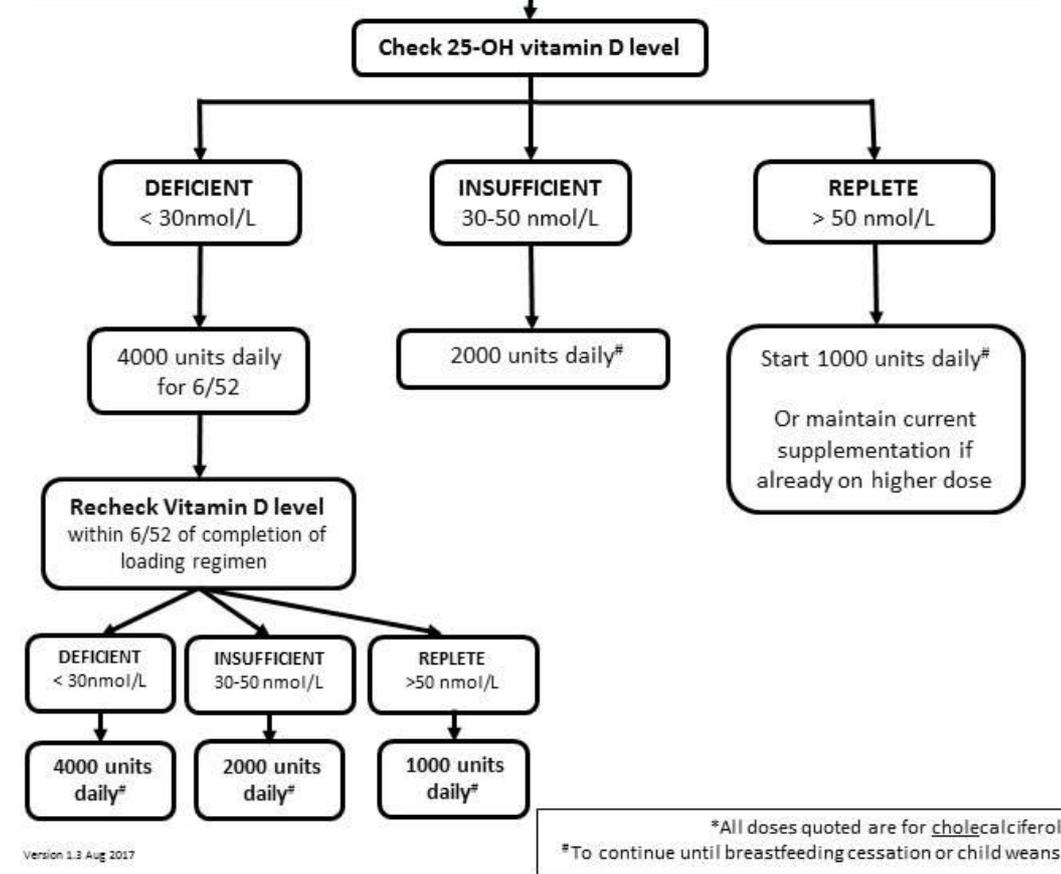
- All pregnant/breastfeeding women should receive at least 400 units/day cholecalciferol* from OTC preparations or "Healthy Start" if eligible.
- All women should be given advice about their calcium intake. Suggested daily intake of ≥ 1 g calcium a day (or equivalent of 1 pint of milk)

- 'AT RISK' POPULATION**
- Non-white skin
 - Obese (BMI ≥ 30 kg/m²)
 - Housebound women or who remain covered
 - Women with delivery date in November to March
 - At risk of pre-eclampsia (as per NICE CG107)

1000 units/day

This algorithm EXCLUDES those with CKD 3-4, hyperparathyroidism, granulomatous disease (sarcoidosis, TB)
Please check Vitamin D level and refer to Obstetric Medicine. Silver.star@nhs.net

- HIGH RISK CONDITIONS**
- Possible osteomalacia (bone pain, insufficiency or fragility fractures or proximal muscle weakness)
 - Previous Vitamin D deficiency (<30nmol/L)
 - Multiple sclerosis
 - Malabsorption (inflammatory bowel disease, gluten enteropathy, gastric surgery, biliary disease, or intestinal overgrowth)
 - Drugs that impair Vitamin D e.g. steroids, antacids, antiepileptics, tacrolimus, rifampicin, anti-retrovirals, cholestyramine, diuretics
 - Inflammatory rheumatic diseases



Post-natal follow up

All women who are breastfeeding should remain on their pregnancy multivitamins or continue their Vitamin D supplementation at the same doses (and dosing interval) as when they were pregnant till she completes breastfeeding or child weans. All women should be advised that their babies should have 400 units of vitamin D per day unless fully formula fed.

Appendix 1 – The need for more intensive Vitamin D supplementation in pregnancy

Studies in high risk groups who have documented Vitamin deficiency between 12-16 weeks gestation have shown that replacement with 4,000 units of cholecalciferol a day led to 91% of the women treated having a Vitamin D level greater than 50nmol/L; but in maintenance doses 2,000 units a day of cholecalciferol, only 75.6% of women were replete at the time of delivery. Furthermore, despite more than 90% of mothers (on cholecalciferol 4,000 units a day) having replete Vitamin D levels, only 79.1% of the offspring had achieved Vitamin D sufficiency at the levels measured at birth. (9)

While childhood (or congenital rickets) has been linked to maternal Vitamin D deficiency, it remains unclear what the maternal threshold is. Most children diagnosed with rickets present several months (median 0.9 years after birth in New Zealand) after birth and maternal levels are seldom quantified. Common clinical presentations in New Zealand children presenting with Vitamin D deficiency rickets include: skeletal abnormalities (29.3%), poor growth (29.3%), motor delay (20.7%), symptomatic hypercalcaemia with seizures and tetany (15.5%), bone pain (12.1%), respiratory disease (8.6%), fractures (8.6%), etc. (3)

Hence, women at high risk who have a delayed diagnosis of Vitamin D deficiency (after 12 weeks gestation), require more vigorous replacement therapy with loading doses.

Appendix 2 – Monitoring and Compliance

Compliance Standard	Monitoring method	Frequency of monitoring	Review Group/Committee
Women who require Vitamin D are treated according to Protocol	Audit	Annual	WCGC
Collect and analyse all cases of neonatal hypocalcaemic	Service improvement project	Annual	WCGC
Calculate the number of vitamin D tests done in maternity patients over a 6 month period	Service improvement project	After 1 st 6 months	WCGC

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