1. Purpose
This clinical guideline supports the testing and management of vitamin D deficiency and women at risk of Vitamin D deficiency in pregnancy at the Women’s and the early management of their babies.
This guideline does not cover babies with gestational age < 32 weeks or birth weight < 2kg. For these babies please refer to the NISC Vitamin D guideline available under Neonatal Medicines Information on the Pharmacy intranet page.

2. Definitions
Vitamin D deficiency is a state of insufficient vitamin D to meet the body’s requirements.
For more information on effects of vitamin D deficiency, see Appendix 1.

3. Responsibilities
Obstetricians, obstetric fellows, O & G registrars and residents, general practitioners, midwives, lactation consultants, pharmacists and dieticians should be guided by this policy in their testing and management of vitamin D deficiency in pregnant women at the Women’s and the early management of their babies.

4. Guideline
4.1 Screening and Assessment
Pregnant women at risk of vitamin D deficiency who:
- have not had their vitamin D level tested prior to their first hospital booking appointment
  Should be recommended vitamin D supplementation of 2,000 International Units per day orally, with a Vitamin D level performed once at 26-28 weeks; with supplementation subsequently individualised.
- have had their vitamin D level tested prior to their first hospital booking appointment.
  Should be recommended vitamin D supplementation according to their levels.
Retesting for Vitamin D levels is not currently indicated, nor the policy of the Royal Women’s Hospital.
Calcium levels do not require testing.
Women at risk criteria of vitamin D deficiency for the purpose of this policy are pregnant women with:
- deeply pigmented skin
- chronic and severe lack of sun exposure for cultural, medical, occupational or residential reasons
- malabsorption (eg cystic fibrosis, short bowel syndrome, inflammatory bowel disease or untreated coeliac disease, or has had bariatric surgery).
For more information about risk factors for vitamin D deficiency in pregnant women and newborns, see Appendix 2.
Level <50 nmol/L is considered deficient in vitamin D. Levels≥50 nmol/L are considered adequate.
- Vitamin D sufficiency: 25(OH)D ≥50 nmol/L
- Mild vitamin D deficiency: 25(OH)D between 40 nmol/L to 49 nmol/L
- Moderate vitamin D deficiency: 25(OH)D 26 to 39 nmol/L
- Moderate to severe vitamin D deficiency: 25(OH)D ≤25 nmol/L.
For more information on vitamin D levels, see Appendix 3.

4.2 Management of Vitamin D Deficiency
General Advice for all women
1. Advice to increase safe sun exposure
For moderately fair-skinned people, a walk with arms exposed for 6–7 minutes mid-morning or mid-afternoon in
summer, is likely to be helpful in maintaining adequate vitamin D levels in the body. In winter months as much bare skin exposed as feasible for 25 minutes at noon, on most days, should achieve adequate vitamin D levels in the body [33].

2. Advice to increase food intake of vitamin D
Dietary sources include oily fish, eggs, and fortified foods such as margarines and some milk products. These foods contain only small amounts of vitamin D, but may help to increase vitamin D levels.

3. Advice to ensure adequate calcium supplementation
Sufficient quantities of calcium can be provided through dietary sources alone. Milk, cheeses and yoghurt provide rich natural sources of calcium and are the major food contributors of calcium. Non-dairy sources include vegetables, such as Chinese cabbage, kale, and broccoli. Spinach provides calcium, but its bioavailability is poor. Foods available with added calcium include many fruit juices and drinks, tofu, and cereals.

NHRMC RDI for calcium in pregnancy is 1000mg/day [30]. Calcium supplementation is available if unable to reach recommended daily intake though diet alone. Calcium tablets contain varying quantities of calcium, most between 500mg to 600mg calcium per tablet. Multivitamins (including antenatal vitamins) also include calcium in smaller quantities (see pregnancy vitamin table on page 2 below).

4. Advice to consider needs of other family members
For other family members of vitamin D deficient mothers or who are high risk for vitamin D deficiency similar principles apply with respect to safely increasing sun exposure and food intake of vitamin D where possible.

Supplementation for pregnant women
Universal supplementation of pregnant women with vitamin D is not currently recommended.

The NHMRC recommends the upper level of intake from all sources of vitamin D in pregnancy is 3200 IU (80 µg/day) [3] and IOM recommends an upper limit of 3,000IU [30]

Consequently RWH does not routinely recommend supplementation of >3,000IU per day or parenteral vitamin D. Supplementation is indicated:

- For at risk women who have not had their Vitamin D level tested.
  In this case, women should be recommended an oral supplementation of vitamin D 2,000 International Units per day. The recommendation for supplementation is then individualised according to the results of a 26-28 week vitamin D level.

- If, after blood testing the vitamin D level is <50nmol/l.

If screened: The following vitamin supplementation (at least to the end of exclusive breastfeeding) should be recommended according to a woman's vitamin D test results:

<table>
<thead>
<tr>
<th>Pregnancy Vitamin Table</th>
<th>&lt;25 nmol/l</th>
<th>25 - 39 nmol/l</th>
<th>40 - 49 nmol/l</th>
<th>≥50 nmol/l</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pregnancy Multivitamin containing Vitamin D (min 400IU/day)</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Patient Choice</td>
</tr>
<tr>
<td>Vitamin D (Cholecalciferol) 1,000 IU (Dosage for 3 months)</td>
<td>2-3 tablets daily</td>
<td>2 tablets daily</td>
<td>1 tablet daily</td>
<td>N/A</td>
</tr>
<tr>
<td>Ongoing vitamin D dosage 1,000 IU until end of exclusive breastfeeding</td>
<td>2 tablets daily</td>
<td>1 to 2 tablets daily</td>
<td>1 tablet daily</td>
<td>N/A</td>
</tr>
</tbody>
</table>

The range provided allows for clinician assessment of issues including the actual figure, seasonality (due to normal seasonal variation summer would support higher supplementation), the gestation of pregnancy (later gestation would support higher supplementation), patient preference and ability to increase natural Vitamin D intake.
Vitamin D retesting

Retesting of vitamin D is not required and is not the policy of the Royal Women's Hospital.

For more information on Vitamin D requirements, sources, supplementation and safety, see Appendix 4.

Vitamin D supplementation for babies

*For NISC babies, refer to the NISC Vitamin D guideline*

Even if a mother is vitamin D deficient, babies do not routinely have their vitamin D levels checked.

Vitamin D supplementation of her baby is required (unless baby is fully formula fed on a vitamin fortified formula) if the mother has a vitamin D deficiency or is at risk of a Vitamin D deficiency and has not been adequately supplemented in the last trimester of pregnancy.

Vitamin D supplementation of baby is usually provided by the oral administration of 400IU of cholecalciferol daily.

<table>
<thead>
<tr>
<th>Ostelin® vitamin D Liquid for Kids</th>
<th>OsteVit-D® Liquid for Kids</th>
<th>Penta-vite® 0-3 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Strength: 0.5mL = 200IU</td>
<td>Strength: 1 drop = 200IU</td>
<td>Strength: 0.45mL = 400IU</td>
</tr>
<tr>
<td>Dose: 1mL daily</td>
<td>Dose: 2 drops daily</td>
<td>Dose: 0.45mL daily</td>
</tr>
</tbody>
</table>

*Can be purchased over the counter and without a prescription*

**Length of supplementation:** Supplementation should occur at least throughout the first year of life (or else until the baby is fully fed with a vitamin D fortified formula). It should be noted that the child may share risk factors of a vitamin D deficient mother and this should be addressed holistically by the family’s GP.

### 4.3 Follow-up and Communication with GPs

It should be noted that as the woman is deficient both the baby and the rest of her family may share risk factors.

All women with vitamin D deficiency should be advised to follow up with their GP for the lifelong management of her and her family.

For women who have been found to have levels < 50nmol/l in pregnancy, discharge summaries to a woman’s GP should include vitamin D deficiency as a secondary diagnosis, her vitamin D status and the planned management of her and her baby.

### 5. Evaluation, monitoring and reporting of compliance to this guideline

Compliance with this guideline will be monitored, evaluated and reported through the team leader’s management meeting. Outcomes will be measured by review of incidents, and periodically auditing the compliance with the guideline.
6. References


4. Pearce and Cheetham, BMJ 340, b5664

5. SACN, Update on Vitamin D: Position Statement by the Scientific Advisory Committee on Nutrition, (2007)


14. Cochrane intervention review Feb 2012 Vitamin D supplementation for women during pregnancy Luz Maria De-Regil, Cristina Palacios, Ali Ansary, Regina Kulier, Juan Pablo Peña-Rosas


17. IARC, Vitamin D and Cancer, ed. (IARC, Lyon, 2008).


33. Position statement – Vitamin D and health in adults in Australia and New Zealand; MJA 196(11) – 18 June 2012

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Ines Rio: Senior Medical staff

7. Legislation/Regulations related to this guideline

Not Applicable.

8. Appendices

Appendix 1: Information on Effects of Vitamin D Deficiency

Appendix 2: Risk Factors for Vitamin D Deficiency in Pregnant Women and Newborns

Appendix 3: Vitamin D Levels

Appendix 4: Vitamin D Requirements, Sources, Supplementation and Safety

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Background information

Vitamin D is essential in the maintenance of skeletal growth and bone health – vitamin D regulates calcium and phosphate absorption and metabolism. Vitamin D is a fat-soluble vitamin that can be obtained from food or dietary supplements. However, most vitamin D is produced by the following direct exposure of the skin to the sun. Vitamin D is produced in the body through the conversion of 7-dehydrocholesterol, which is produced in the sebaceous glands of the skin. Exposure to sunlight (UVB) converts this precursor into cholecalciferol over a 2-3 day period [1, 2].

Serum 25-hydroxyvitamin D (25-OHD) reflects the vitamin D derived from all sources and is considered to be an indicator of the individual's vitamin D status. Supplementation during pregnancy does increase serum vitamin D concentrations as measured by 25-hydroxy vitamin D at term [14].

Insufficient quantities of vitamin D are associated with osteomalacia and an increased risk of osteoporosis [1-3]. In children it is associated with rickets and in rare cases fitting secondary to hypocalcaemia [12-13].

Other Gestational Outcomes

Vitamin D deficiency has been proposed as a risk factor for a number of gestational problems including gestational diabetes, preterm birth and preeclampsia. Supplementation during pregnancy is suggested as an intervention to protect against these adverse gestational outcomes [26]. However, there is insufficient evidence to support intervention with vitamin D supplementation [14].
Appendix 2

Risk Factors for Vitamin D Deficiency in Pregnant Women and Newborns

Risk Factors for vitamin D deficiency in pregnant women
The at risk criteria for Vitamin D testing under the Medical Benefits Schedule (from 1/11/14; item 66833) are:

- malabsorption (e.g. cystic fibrosis, short bowel syndrome, inflammatory bowel disease or untreated coeliac disease, or has had bariatric surgery).
  Conditions that impair fat absorption are associated with inadequate vitamin D absorption from the gut e.g. crohn’s disease, celiac disease, cystic fibrosis; and
- deeply pigmented skin
  Vitamin D deficiency is particularly common in dark-skinned pregnant mothers, especially those living at higher latitudes and in the winter months [33]; and,
- chronic and severe lack of sun exposure for cultural, medical, occupational or residential reasons. Veiled, people working in an enclosed environment, such as office workers, factory or warehouse workers, taxi drivers, night-shift workers

The above at risk criteria are those currently utilised at the Royal Women’s Hospital to determine women at risk of Vitamin D deficiency that require testing.

Obesity is also a risk factor for Vitamin D deficiency. An inverse association exists between obesity and 25(OH) D levels [24] that have been attributed to the storage of vitamin D in fat. Vitamin D requirements are thus higher in obese compared with normal weight individuals. However, as the clinical significance of low serum 25(OH) D levels in this group of patients is uncertain, obesity itself is not a criteria at RWH for either testing or routine supplementation.

Risk factors for vitamin D deficiency in the newborn

- Maternal vitamin D deficiency — vitamin D is transferred from the mother to the fetus across the placenta, and reduced vitamin D stores in the mother are associated with lower vitamin D levels in the infant. [18].
- Prematurity — vitamin D levels are particularly low in premature infants, who have less time to accumulate vitamin D from the mother through transplacental transfer [19].

The third trimester is a critical time for vitamin D transfer, because this is when the fetal skeleton becomes calcified, requiring increased activation of 25(OH)D in the maternal kidneys and placenta. Vitamin D deficiency in the mother during this period or prematurity can cause fetal vitamin D deficiency, and in severe cases, fetal rickets [20]

- Exclusive breast feeding — Even in a vitamin D sufficient mother, the vitamin D content of breast milk is low (15 to 50 IU/L), with exclusively breast-fed infants consuming an average of 750 mL of breast milk daily ingest only 10 to 40 IU/day of vitamin D in the absence of sun exposure or supplement use [21]. The vitamin D content of breast milk is lower in mothers who are vitamin D deficient [22]. Vitamin D supplementation increases the vitamin D in breast milk, however breast milk is not a good source of vitamin D and the baby relies on the stores achieved in the third trimester in utero. One study that included infants of different skin colour estimates that most breast-fed infants need to be exposed to sunlight for at least 30 minutes/week while wearing only a nappy in order to maintain 25(OH)D levels at 50 nmol/L[29]. This amount of sun exposure is unlikely given current recommendations to limit sun exposure in infants younger than six months old. Despite most formulas having a higher amount of vitamin D than breast milk, women should be advised to breastfeed for its many benefits and because babies normally rely on the stores they have achieved in the last trimester.

Note on Formula Feeding - Although vitamin D deficiency is uncommon in formula fed infants because of the vitamin D fortification of infant formulas, it should be noted that it can still occur if the infant had low vitamin D stores at birth. In one study, 50% of children with rickets at 0 to 5 years old who presented with hypocalcaemic convulsions had been formula fed [23]. However, additional vitamin D supplementation is not routine.
Vitamin D deficiency is thought to be common among pregnant women; however standards for defining vitamin D deficiency are not well established and certainly not established for pregnancy.

Although there is general consensus that levels below 25nmol/L qualify as ‘deficient’ [4] [5], beyond this there is currently no standard definition of ‘optimal’ 25(OH) D levels as evidence is lacking.

1. The committee of obstetric practice of the American College of Obstetricians and Gynaecologists has proposed the conservative approach stating: “vitamin D supplementation during pregnancy beyond that contained in a prenatal vitamin should await the completion of ongoing randomized clinical trials” [28].

2. The Endocrine Society of Australia and The Institute of Medicine (IOM), Washington suggests > 50 nmol/L is ‘sufficient’.

3. United States Endocrine Society recommends an optimal target 25(OH) D levels of > 75nmol/L, which the IOM and the Endocrine Society concur as an optimal target levels.

4. The Endocrine Society of Australia and defined deficiency below 50nmol/L [2].

Of note, there is thought to be a normal a seasonal variation in 25(OH) D levels with levels 10-20nmol/l higher at the end of summer [30].

In determining our definitions for vitamin D status we considered the reporting limits of the pathology laboratories that reports are commonly received from, including:

- RWH/RCH: lower limit <23nmol/L
- Melbourne Pathology: lower limit <10nmol/L
- Healthscope: lower limit <20nmol/L
- Dorevitch: lower limit <10nmol/L.

In view of the above reporting limits, the general consensus in the literature that below 25nmol/L qualifies as ‘deficient’. Whilst awaiting further evidence The Women’s currently uses the following definitions in order to guide the management of women and their babies:

- Vitamin D sufficiency: 25(OH)D ≥50 nmol/L
- Mild vitamin D deficiency: 25(OH)D between 40 nmol/L to 49 nmol/L
- Moderate vitamin D deficiency: 25(OH)D 26 to 39 nmol/L
- Moderate to severe vitamin D deficiency: 25(OH)D ≤25 nmol/L
Appendix 4

Vitamin D Requirements, Sources, Supplementation and Safety

Vitamin D requirements
Vitamin D recommended daily requirements to maintain healthy levels in pregnancy and breastfeeding vary with the 2006 NHMRC nutrient reference values for Australia and New Zealand recommending 200 IU, and the 2010 USA Institute of Medicine report recommending 600 IU per day.

Sources of Vitamin D

Sun exposure
Exposure to UVB radiation in sunlight is the most efficient way to boost vitamin D supply, but it is still unclear how much sunlight is required to produce a given level of 25 (OH) D. Environmental and personal factors greatly affect vitamin D production in the skin, making it impossible to recommend a generalised approach to level of exposure for the general population.

However, the best estimates suggest that for most people, everyday casual exposure to sunlight produces sufficient vitamin D in the summer months, provided optimal environmental conditions, such as lack of cloud cover [15].

The true amount of time may be greater and will vary depending on other factors including skin type, posture, time of day, outdoor activities, atmospheric conditions, and the presence of shading structures.

People with darker skin and older people require more sun exposure to generate the same level of vitamin D as fairer people.

In addition, vitamin D levels have been demonstrated to vary with sunlight exposure and therefore a seasonal variability in the normal range is expected. During winter months there is less UVB for vitamin D synthesis and population serum vitamin D levels are generally lower. However, a person’s stores can be built up when they have higher levels, such as in the summer months and these can be utilised as serum levels drop in the winter. [7-9].

Dietary sources
The primary source of vitamin D (90%) for most Australians is synthesis triggered by sun exposure. Dietary sources make up only 5-10% and include oily fish, eggs, and fortified foods such as margarines and some milk products [1].

Supplements

Routine Supplements
Recommendations for routine supplementation in pregnancy vary with the NHMRC not recommending routine supplementation but the UK National Institute for Health and Clinical Excellence (NICE) suggesting women may choose to take 400 IU of vitamin D a day during pregnancy and breastfeeding. Vitamin D of at least 400 IU is contained in many Australian pregnancy and breastfeeding multivitamins. NHRMC RDI for calcium in pregnancy is 1000mg/day [30].

Popular Pregnancy Vitamins:

<table>
<thead>
<tr>
<th>Brand Name</th>
<th>Dosage</th>
<th>Vitamin D (Cholecalciferol)</th>
<th>Calcium</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elevit with Iodine</td>
<td>1 daily</td>
<td>500IU (12.5 microgram)</td>
<td>125mg</td>
</tr>
<tr>
<td>Blackmore’s Pregnancy and Breast-Feeding Gold</td>
<td>2 daily</td>
<td>500IU (12.5 microgram)</td>
<td>59mg</td>
</tr>
<tr>
<td>Swisse Pregnancy + Ultivite</td>
<td>1 daily</td>
<td>600IU (15 microgram)</td>
<td>20mg</td>
</tr>
<tr>
<td>Nature’s Own Pregnancy Platinum Multivitamin</td>
<td>1 daily</td>
<td>200IU (5 microgram)</td>
<td>75mg</td>
</tr>
<tr>
<td>Cenovis Pregnancy and Breastfeeding Formula</td>
<td>2 daily</td>
<td>NIL</td>
<td>137.7mg</td>
</tr>
<tr>
<td>Ethical Nutrients Pregnancy Support</td>
<td>1 daily</td>
<td>1000IU (25 microgram)</td>
<td>250mg</td>
</tr>
</tbody>
</table>
Supplementation, blood levels and safety

Supplementation and blood 25 (OH) D levels

Supplementation is indicated after blood testing indicates a level of <50nmol/l (as per the guideline attached). Some studies suggest an average increase of 17nmol/l for each 1,000IU per day in a non pregnant sample. However at any given dose there is considerable variation in the levels achieved [33]. After supplementation with vitamin D, studies suggest that 25-OHD levels reach a plateau after about 8 weeks but with considerable variation of 2-5 months [31, 32]. Retesting should therefore not take place before 2 months (and ideally before 3 months).

Supplements and safety

An extensive review has confirmed that the long term safety data on vitamin D supplementation remains limited. NHMRC recommends an upper level intake of vitamin D from all sources of 3,200IU and IOM recommends an upper limit of 3,000IU.

Consequently high dose and parenteral vitamin D preparations should not be used in pregnancy [28]. In addition, supplements that contain vitamin A, including cod liver oil, are unsuitable for pregnant women (26).