Policy on the Diagnosis and Management of Vitamin D Deficiency / Insufficiency

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POLICY AWARENESS	
People who need to know this policy in detail	All clinical staff
People who need to have a broad understanding of this policy	All clinical staff
People who need to know this policy exists	All clinical staff

CHANGE CONTROL DETAILS			
Date (dd/mm/yy)	**Version**	**Description**	**Reason for changes**
July 2012	1.0	New Policy	New Policy
August 2012	1.1	Review: B Jacobs	Paediatric content
August 2012	1.2	Review: H Cohen	Adult content
September 2012	1.3	Review: R Keen	Rheumatology content
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November 2012	1.5	Review: P Julies	Paediatric content
November 2012	2.0	Content update	DTC review
May 2013	2.1	Content update	National Osteoporosis Society guideline published

Location: RNOH web

DISCLAIMER

This Policy is for use by RNOH prescribers and for reference by primary care prescribers – the information contained in it is not suitable to be shared with patients / public or non NHS Organisations.

This Policy has been produced to inform and review local decision making using the best available evidence at the time of publication. The information in this document may be superseded in due course.

The guideline has been adapted from the NHS North Central London Policy with local content written by:

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Acknowledgement:

- NHS North Central London (Camden) – Diagnosis and management of vitamin D deficiency / insufficiency in Camden.
- National Osteoporosis Society – Vitamin D and Bone Health: A Practical Clinical Guideline for Patient Management. April 2013.

Table of Contents

1. Introduction

Public and clinician awareness of an association between vitamin D and health has increased substantially in recent years with the publication of numerous articles on the subject in the medical and lay press.

This has led to a number of publications within the orthopaedic setting which has demonstrated a high prevalence of low serum levels of vitamin D in adult patients who have undergone orthopaedic surgery. Further, NICE guidance on the secondary prevention of osteoporotic fragility fractures in postmenopausal women specifies the importance of ensuring adequate levels of calcium and vitamin D (normal serum concentrations) for optimum effects of treatment for osteoporosis.

Despite the above, there continues to be no formal consensus regarding the ideal levels of vitamin D, the potential consequences of deficiency and insufficiency, and the appropriate approach to managing these clinical scenarios. These factors, alongside important supply problems with licensed pharmacological strength vitamin D preparations, have contributed to confusion about how patients with possible suboptimal vitamin D status should be investigated and managed.

2. Aims and Objectives

This Policy ***aim*** to help clinicians overcome this uncertainty by summarising the best available evidence concerning vitamin D deficiency. This should enable clinicians to:

- Determine which patients at RNOH should be screened for vitamin D deficiency or insufficiency
- Feel confident managing a case where vitamin D deficiency or insufficiency is queried;
- Investigate suspected vitamin D deficiency in a clinically- and cost-effective manner;
- Advise patients about use of lifestyle measures and supplements for raising vitamin D levels;
- Prescribe vitamin D supplementation in an evidence-based, clinically- and cost-effective manner.

The ***objective*** of this Policy is to provide a clear framework for patient access to medication. This document provides the necessary guidance for staff to follow to meet the above aims. The recommendations within this guideline will evolve as new evidence emerges on the association of vitamin D with health outcomes and the effectiveness of supplementation.

Appendix 1 & 2 – Summary of investigations and treatments for adults

Appendix 3 & 4 – Summary of investigations and treatments for children

Appendix 5 – Summary of vitamin D products on the RNOH Formulary

3. Summary Points

General

1. Routine testing of vitamin D level is unnecessary in the absence of clinical symptoms
2. Vitamin D levels <25 nmol/L indicates vitamin D *deficiency*.
3. Vitamin D levels 25-50 nmol/L indicates vitamin D *insufficiency*.
4. Vitamin D levels > 50 nmol/L indicates adequate vitamin D levels.
5. Sunlight is the natural method of maintaining adequate vitamin D levels. In view of the risk of skin cancer, sun beds are not recommended.
6. In addition to lifestyle and sunshine advice, it may be necessary to prescribe high-dose supplementation for a defined period of time where there is evidence of vitamin D deficiency or insufficiency.
7. Oral vitamin D_3 is the treatment of choice in vitamin D deficiency / insufficiency. Over the counter (OTC) supplements can be effective in raising vitamin D levels.
8. There is little or no evidence for harmful effects at vitamin D levels between 50 nmol/L and approximately 220 nmol/L.
9. Only deficient vitamin D levels have been robustly associated with poor bone health outcomes (rickets, osteomalacia, and predisposition to fractures and poor bone mineralization in the elderly and post-menopausal women).
10. The evidence for an association with non-bone health outcomes is inconsistent, conflicting or absent.
11. Excess doses of vitamin D supplementation (greater than 10,000 units/day) may cause toxicity and therefore should be avoided unless clinically justified.

Testing

1. Patients at risk of vitamin D deficiency or insufficiency (and those who present with signs and symptoms) should be identified during the pre-admission clinic. Blood samples should be taken to determine vitamin D levels.
2. Women with osteoporosis who are being considered for treatment should provide a blood sample to determine if they are calcium and/or vitamin D replete. Adequate levels are required to ensure optimum effects of such treatment.
3. For patients being reviewed for elective surgery, results of the blood test should be forwarded to the patients GP for review. Treatment should be prescribed and initiated in primary care (where indicated) ahead of patient elective-admission.
4. For patients being reviewed for non-elective admission (e.g. osteoporosis), results of the blood test will be reviewed in house and treatment provided (via RNOH Pharmacy) where indicated.
5. People in low-risk groups (e.g. middle age adults without disease predisposing to poor vitamin D absorption or metabolism) should be given lifestyle advice (e.g. sunlight exposure and change in diet). Where these measures are not sufficient in raising vitamin D levels, to maintain their health they can be advised to purchase OTC supplements. Prescriptions may be written for specific patient groups (e.g. children and elderly).
6. People in high-risk groups should be targeted for lifestyle advice [as above] as well as prescription of vitamin D supplementation.
7. Prescription for vitamin D supplementation should be initiated in primary care following pre-assessment and ahead of elective admission. Supply of vitamin D from RNOH Pharmacy should therefore be reserved for continuation purposes. For people who have not been admitted to RNOH via the pre-admission clinic, or where the time between pre-admission

and admission is less than 2 weeks, prescription and supply within RNOH is suitable where indicated.

8. Long-term maintenance supplementation (unless clinically not appropriate) should be prescribed to maintain the patients' health.
9. The following patients should be referred to the medical liaison consultant for further advice:
    - Unexplained weight loss
    - Secondary causes i.e. renal disease; liver disease; lymphoma; metastatic cancer; parathyroid disorders; hypercalcaemia; hyperthyroidism; sarcoidosis; and tuberculosis
    - Pregnancy
    - Failure to respond despite 3 months treatment with vitamin D

4. Definition and Prevalence of Vitamin D Deficiency / Insufficiency

4.1 What is vitamin D?

Vitamin D is an essential nutrient, consisting of a group of fat-soluble chemicals, necessary for the healthy metabolism of calcium and phosphate in the body. It is particularly important for maintaining healthy bones and developing muscles but also plays a role in other systems of the body.

Vitamin D exists in two main forms

- Vitamin D_2 (ergocalciferol)
- Vitamin D_3 (colecalciferol)

Active vitamin D is produced after vitamin D_2 or D_3 have been hydroxylated twice to produce first 25-hydroxyvitamin D (25-OHD) in the liver, and then 1,25-hydroxyvitamin D (1,25-OHD) mainly in the kidneys. On the basis of biochemical parameters, ergocalciferol appears to have a quicker clearance and lower tissue bioavailability than colecalciferol, therefore resulting in a preference for prescriptions for the latter.

4.2 What are the sources of vitamin D?

Sunshine is the main natural source of vitamin D. Vitamin D can only be made in the skin (7-dehydrocholesterol is converted to vitamin D_3) by the action of UVB sunlight during the summer-time and only in the middle of the day when the sun is at its highest and strongest point.[1] This is therefore the most efficient natural way of boosting vitamin D levels.

It is not possible to say with great accuracy how much sunlight is required to produce a given level of 25-OHD in an individual, since environmental and personal factors greatly affect vitamin D production in the skin. However, the available evidence suggests that exposure of around one third of the body surface to summer sun for 15-20 minutes (producing mild redness but not burning of the skin) 2-3 times a week may be sufficient to provide adequate levels. People with darker skin pigmentation probably require slightly longer exposures to sunlight. Vitamin D stores obtained during summer are often sufficient to maintain satisfactory levels during the winter months.[2]

Less than 10% of vitamin D is from diet as few foods contain large amounts of vitamin D (Table 1). In the UK, a limited number are foods are fortified with vitamin D, principally powdered milks, breakfast cereals and some margarine products.[2]

The dual sources of vitamin D are one reason why it is difficult to make clear recommendations on what is an ideal average daily intake.[3]

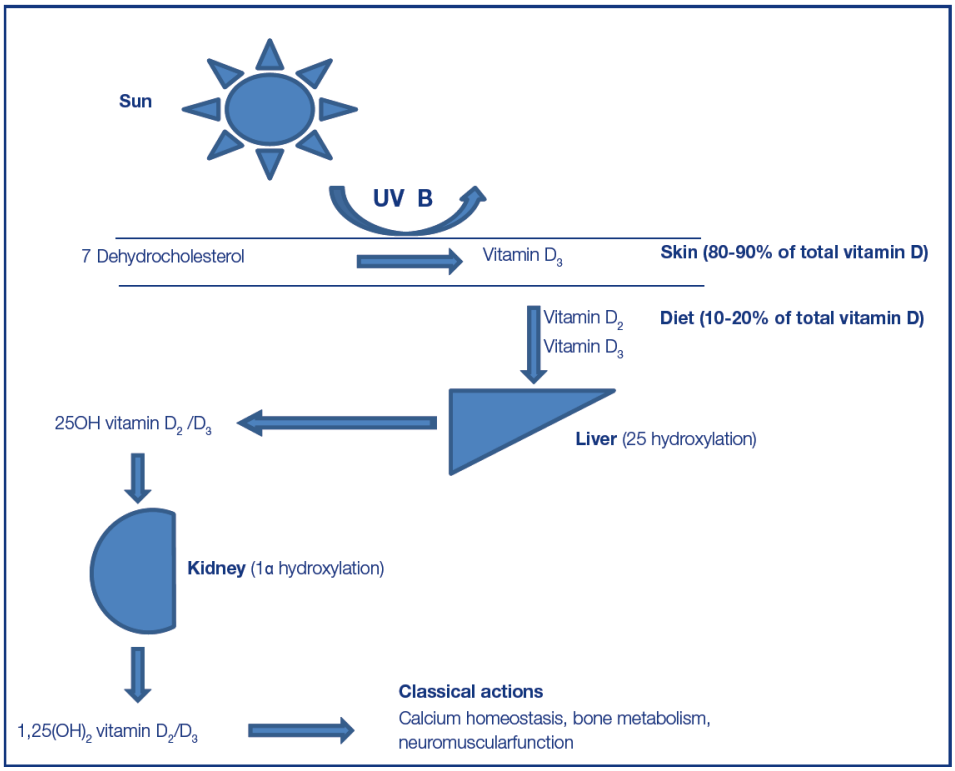
Table 1: Vitamin D content of selected foods

Type of Food	Average amount vitamin D per 100 grams
Oily fish	200 to 400 units
Fortified margarine	280 units
Fortified breakfast cereals	120 to 320 units
Red meat	40 units
Egg yolk	20 units

4.3 *Why is vitamin D important?*

There is good evidence for an association between low levels of vitamin D and adverse bone health outcomes, principally rickets in children, osteomalacia in adults, and fractures and low bone density in older people.[1,4,5,6] With regards to non-bone health outcomes, despite strong claims to the contrary the evidence for an association with outcomes such as cancer, cardiovascular outcomes, diabetes, poor immunity and all-cause mortality is either inconsistent or absent, and often derived from retrospective analyses of poor quality.[1,4,7,8] High quality systematic reviews have concluded that there is no high or even moderate quality evidence that vitamin D supplementation is effective in reducing the incidence of these outcomes. Until large prospective studies provide consistent evidence that supplementation reduces the risk of non-bone health diseases, no specific conclusions can be drawn.[3]

Figure 1: Metabolism of vitamin D [9]



4.4 *What is vitamin D deficiency?*

There is still scientific debate regarding what is the optimal serum concentration of vitamin D. Further, it is suggested that the optimal level may vary at different stages of life.

The existing evidence only supports definitions of vitamin D deficiency and insufficiency in relation to bone health.[1,4] There is considerable consensus that 25-OHD levels < 25 nmol/l indicate deficiency, since rickets and osteomalacia are rare in people with higher concentrations. There is no robust evidence that adverse health effects are associated with vitamin D levels > 50 nmol/L (except at toxic levels). On this basis along with laboratory findings (plateau of PTH levels) several high quality reviews have proposed a target of > 50 nmol/L to define vitamin D sufficiency (Table 2).[2,3,4]

Table 2: Serum 25-hydroxyvitamin D concentrations, health and disease

Vitamin D level	Vitamin D status
<25 nmol/L	Deficient
25-50 nmol/L	Insufficient
>50 nmol/L	Adequate

4.5 Who is at risk of vitamin D deficiency?

Three situations place people at higher risk of vitamin D deficiency – inadequate exposure to sunlight, poor gastrointestinal intake and metabolic abnormalities (Table 3).[10]

Table 3: People at risk of vitamin D deficiency

<table>
<tr><th>Inadequate UV light exposure</th><th>Poor oral intake or gastrointestinal absorption</th><th>Metabolic risk</th></tr>
<tr><td rowspan="3">• Northern latitude
• Pigmented skin
• Occlusive garments
• Habitual sunscreen use
• Institutionalised or housebound</td><td rowspan="3">• Vegetarian or fish-free diet
• Malabsorption, short bowel, or cholestatic liver disease
• Cholestyramine use
• Breast fed infant</td><td>Reduced synthesis
• Elderly</td></tr>
<tr><td>Increased Breakdown
• Drugs (Rifampicin, anticonvulsants,
• HAART therapy, glucocorticoids).</td></tr>
<tr><td>Reduced stores
• Liver disease
• Multiple, short interval pregnancies</td></tr>
</table>

The amount of UVB in sunlight changes substantially with season, latitude and time of day. These factors greatly affect vitamin D production, which is greatest around two hours either side of solar noon and during summer months. Physical characteristics can also affect vitamin D production, with darker skin requiring longer UV exposures to produce the same amount of vitamin D as those with light skin.

4.6 What are the clinical features of vitamin D deficiency?

Evidence suggests that low vitamin D status is implicated in a range of diseases including osteoporosis, several forms of cancer, cardiovascular disease, tuberculosis, multiple sclerosis and type 1 diabetes.[10]

Rickets and osteomalacia are clinical illnesses which present with some combination of the symptoms and signs listed in Table 4. Vitamin D deficiency and insufficiency may also predispose to adverse bone outcomes for which there are no clinical features prior to the event.

Table 4: Clinical features of Vitamin D deficiency

SYMPTOM, SIGN, BIOCHEMISTRY	CHILDREN	ADULT
Seizures	✓	✓
Tetany	✓	✓
Hypocalcaemia	✓	✓
Irritability	✓	✕
Leg bowing	✓	
Knock knees	✓	
Impaired linear growth	✓	
Delayed walking	✓	
Limb girdle pain	✓	✓
Muscle pain	✓	✓
Proximal myopathy /	✓	✓
Cardiomyopathy	✓	

4.7 What tests are indicated for suspected vitamin D deficiency?

Table 5: Tests for assessing vitamin D status[11]

Test	Reason
25-OHD Vitamin D levels	Best measure of vitamin D status
Renal function Liver function (albumin)	To exclude renal and liver disease as causes and/or to modify treatment regime
Calcium Phosphate Alkaline phosphatase	To assess if calcium deficiency and markers of bone disease present
Parathyroid hormone	Not always necessary
FBC	Iron deficiency commonly co-exists
1-25-OHD Vitamin D levels	ONLY if granulomatous disease suspected
24h urine calcium	ONLY where Vitamin D excess suspected

5. Management of Vitamin D Deficiency / Insufficiency

5.1 National Guidance

Population screening of Vitamin D levels is not currently recommended, even in high risk populations. This is because there is no evidence that supplementation based on testing of asymptomatic people reduces the incidence of diseases associated with vitamin D deficiency, or that testing increases adherence to recommendations for increasing intake of vitamin D.[9] Table 6 summarises recommendations from the Department of Health (letter from the Chief Medical Officer).

Table 6: Department of Health treatment guidance for at risk groups

Adult groups at risk of vitamin D deficiency:
• All pregnant and breastfeeding women, especially teenagers and young women
• Older people, aged 65 years and over
• People who have low or no exposure to the sun, for example those who cover their skin for cultural reasons, who are housebound or who are confined indoors for long periods
• People who have darker skin, for example African, African-Caribbean or South Asian origin, because their bodies are not able to make as much vitamin D
Recommendations
• All pregnant and breastfeeding women should take a daily supplement containing 10 micrograms (400 units) of vitamin D, to ensure the mothers requirement for vitamin D are met to build adequate foetal stores for early infancy
• People aged 65 years and over and people not exposed to much sun should also take a daily supplement containing 10 micrograms (400 units) of vitamin D

Purely based on the evidence, high risk populations who do not have symptoms should simply be targeted for lifestyle advice (sun and diet) as well as advice on obtaining over the counter (OTC) supplements.

5.1.1 Vitamin D and surgery

There is a high prevalence of low serum levels of vitamin D within the adult orthopaedic surgery population.[12] Extremely low vitamin D levels have been associated with osteomalacia and impaired muscle function.[13] Spine-related disability has also been observed as higher in patients with low levels of vitamin D due to facture pseudo-arthrosis and suboptimal surgical outcome.[14]

5.1.2 Vitamin D and osteoporosis

In all studies investigating the use of treatments for osteoporosis it was necessary for patients to be calcium and vitamin D replete (i.e. have normal serum concentrations of calcium and vitamin D levels) to avoid the development of hypocalcaemia. As such, the NICE guidance on the secondary prevention of osteoporotic fragility fractures in postmenopausal women specifies that adequate levels of vitamin D are required prior to use of disease-modifying treatments for osteoporosis.[15]

5.2 RNOH Guidance

All patients should, where appropriate, be encouraged to improve their dietary intake of vitamin D and where possible regularly expose at least one third of their skin to sunlight for short periods, especially during the summer months.

All patients with vitamin D deficiency or insufficiency should be identified prior to admission. Supply of medication should therefore be brought into hospital with the patient as 'Patient Own Drug.'

- ***See Appendix 1 & 2 for a summary of investigations and treatments for adults.***
- ***See Appendix 3 & 4 for a summary of investigations and treatments for children.***
- ***Prescriptions for vitamin D should comply with the RNOH Formulary (Appendix 5).***

5.2.1 Who should be tested?

The need for a vitamin D level should be determined by the Consultant. For patients who are scheduled for elective admission, the Consultant should request on the blood form that a vitamin D level is required when the patient is seen in pre-admission clinic.

Note: the nursing staff within pre-admission clinic are not responsible for determining if a vitamin D level is required.

Unless patients are being investigated for the treatment or prevention of postmenopausal osteoporosis (where vitamin D level must be replete prior to initiation of therapy in accordance with NICE Technology Appraisal 161; October 2008) requests for vitamin D levels should be limited to patients with ***signs and symptoms*** suggestive of vitamin D deficiency only [see below for further detail].

Vitamin D deficiency should be considered and checked (excluding part of spinal cord injury or osteoporosis management) if the following criteria are met:

- **A patient has one or more of the following clinical features:**
  - Insidious onset of widespread or localized bone pain and tenderness (especially lower back and hip pain, but may include rib, thigh or foot pain)
  - Proximal muscle weakness i.e. in quadriceps and glutei. This may cause difficulty rising from a chair and/or a waddling gait
  - Swelling, tenderness and redness at pseudo-fracture sites
  - Fractures, typically femoral neck, scapula, pubic rami, ribs or vertebrae
  - Non-specific myalgia especially with a raised creatine kinase (CK)
  - Myalgia on prescription of a statin

AND

- **The patient has one or more of the following risk factors:**
  - Black and ethnic minority patients with darker skin
  - Elderly patients in residential care (institutionalised) or housebound
  - Patients with significant physical disability affecting mobility
  - Intestinal malabsorption, for example Coeliac and Crohn's disease, gastrectomy
  - Routine covering of face or body, e.g. wearing a veil or habitual sunscreen use
  - Vegan or vegetarian diet
  - Liver or renal disease
  - Medications including anticonvulsants, cholestyramine, rifampicin, glucocorticoids, anti-retrovirals

AND

- Other causes for symptoms have been excluded, for example myeloma, rheumatoid arthritis, polymyalgia rheumatica and hypothyroidism

5.2.2 How should the vitamin D level be taken?

For a vitamin D level, the gold colour (SST II) tube should be used as part of clinical biochemistry and a level of vitamin D specified. As samples are sent to Royal Free Hospital the turnaround time may take up to 48 hours.

5.2.3 How should vitamin D deficiency / insufficiency be managed?

Results of the blood test should be marked for the attention of the consultant who will review and interpret. If there is no evidence of deficiency / insufficiency, no action will be taken. If the blood results indicate deficiency / insufficiency the following actions will then be followed:

5.2.3.1 Patient is on the ward at RNOH: Treatment will be prescribed and supplied via RNOH Pharmacy.

5.2.3.2 Emergency admission OR elective-admission within 4 weeks: Treatment will be prescribed and supplied via RNOH Pharmacy.

5.2.3.3 Elective-admission greater than 4 weeks: The Consultant will write to the patients GP recommended that treatment for vitamin D deficiency / insufficiency be prescribed and initiated in primary care ahead of patient admission.* The patient should be advised to bring in supply of their own medication on return for their elective admission.

* As per recommendations within the National Osteoporosis Society Guideline on vitamin D management, the choice of products on the RNOH Formulary have been made on the basis that they are readily accessible, appropriately priced, made to a high quality and comply with patient specific requirements (e.g. gelatin-free)

A proposed approach to deciding whether to test vitamin D status is shown in Table 7.

Table 7: Advice and management on vitamin D for different groups

Patient characteristics	Advice and management
Healthy people not in high risk group, symptom free	No investigations required Lifestyle advice Consider preventative therapies
People at high risk (see above)	Lifestyle advice Consider long term preventative therapies
People at high risk **AND** symptoms/signs	Lifestyle advice Investigations Therapeutic intervention Long term preventative treatment
Women with osteoporosis	Investigations Therapeutic intervention Long term preventative treatment
People with spinal cord injury (SCI)	Investigations Therapeutic intervention Long term preventative treatment

Due to unpredictable bioavailability, slower onset of repletion, and administration burden associated with intramuscular injection of vitamin D, oral delivery (capsules, liquid) is the preferred route of administration. Refer to Appendix 1-4 for dosing schedule and Appendix 5 for products available on the RNOH Formulary.

RNOH Clinicians are only expected to prescribe, and RNOH Pharmacy required to supply, only in the following circumstances:

- In-patients as continuous therapy who are unable to obtain further supply from home / their GP
- In-patients who are non-elective
- Patients seen in pre-admission with a date of admission within the next 2 weeks
- Long stay patients

Supplementation should not be prescribed until vitamin D levels have been determined unless the clinician feels that the patient falls into a group which is at ***high risk of adverse bone outcomes*** from vitamin D deficiency – principally children not provided with supplements (particularly those with darker skin pigmentation), post-menopausal women and older men and women.

Colecalciferol is the preferred form of vitamin D for treatment since it raises levels of 25-OHD more effectively than ergocalciferol.

5.2.4 How should vitamin D deficiency / insufficiency be monitored?

Patients receiving therapy for vitamin D deficiency should be monitored as follows:

Month 1	check plasma calcium concentration
Month 3	25-OHD, plasma calcium, phosphate, ALP and parathyroid hormone checked (and possibly every 3 months depending on the circumstances).

Note: these checks may be performed by the patients' GP or their local hospital if the patient has already been discharged from RNOH.

Once levels have returned to normal, long-term maintenance supplementation should be prescribed for adults i.e. 2 tablets of Adcal D_3 daily (each tablet contains calcium carbonate 1.5g and colecalciferol 400 units). Such supplementation is not routinely recommended for children unless as part of osteoporosis management.

Avoid supplementation in patients with hypercalcaemia resulting from myeloma, bone metastases or other malignant bone disease, sarcoidosis, co-existing primary hyperparathyroidism. If a combined calcium and vitamin D preparation is not appropriate, consider maintenance dosing with a vitamin D preparation that gives up to 1,000 units vitamin D daily.

NB: All patients receiving calcium supplementation for hypocalcaemia in addition to vitamin D need more frequent monitoring of plasma-calcium every 1-2 weeks in the first months of treatment to determine length of time calcium supplementation is needed and to avoid hypercalcaemia. Patients or carers should be informed about the symptoms of hypercalcaemia e.g. weight loss, sickness, vomiting, headache, abdominal pain, apathy, polyuria.

Appendix 1: Investigation and treatment of Vitamin D deficiency / insufficiency in adults

Does the adult patient have ≥1 clinical feature of vitamin D deficiency?

- Insidious onset of widespread or localised bone pain and tenderness (especially lower back and hip, but also rib, thigh or foot)
- proximal muscle weakness i.e. quadriceps and glutei
- Swelling, tenderness and redness at pseudo-fracture sites
- Insufficiency fractures, typically femoral neck, scapula, pubic rami, ribs or vertebrae
- Non-specific myalgia especially with raised creatinine kinase (CK)
- Myalgia on prescription of a statin
- Pre-assessment for osteoporosis management

NO → Vitamin D testing not required

YES

Does the adult patient have ≥1 risk factor for vitamin D deficiency?

- black or ethnic minority with darker skin
- elderly and housebound or institutionalised
- intestinal malabsorption
- routine covering of skin on face or body
- vegan/vegetarian
- liver or renal disease
- anticonvulsants, cholestyramine, rifampicin or anti-retrovirals

NO → Vitamin D testing not required at this stage.

First exclude other causes for symptoms e.g. myeloma, rheumatoid arthritis, polymyalgia rheumatic or hypothyroidism

YES

Carry out tests for suspected vitamin D deficiency: 25-OHD, Ca^{2+}, ALP, PO_4, U+Es, LFTs, FBC

Do any of the following apply?

- atypical clinical manifestations
- unexplained weight loss
- renal stones
- secondary causes- renal disease, liver disease, lymphoma, metastatic cancer, parathyroid disorders, sarcoidosis, TB
- Pregnancy or breastfeeding

YES → **<u>Refer</u> to appropriate secondary care specialist(s).**

If patient is admitted at RNOH and treatment is necessary, initiate treatment as advised.

Further supply of vitamin D may be obtained from primary care on discharge provided a **treatment plan is in place.**

NO

Assess need for treatment based on serum 25-OHD level, whether symptomatic or not and other patient factors

25-OHD < 25nmol/L and symptomatic

1. PO colecalciferol 300,000 units STAT or 40,000 units daily for 7 days **OR**
2. IM 300,000 units colecalciferol or ergocalciferol every 3-4 months

25-OHD < 25nmol/L no symptoms

1. OTC high strength vitamin D at 1,000 to 2,500 units daily

If patient is 'high risk' or has very low levels:
2. PO colecalciferol 60,000 units once a week for 6-8 weeks **OR**
3. IM 300,000 units colecalciferol or ergocalciferol every 3-4 months

25-OHD 25-49 nmol/L (including maintenance)

1. OTC high-strength vitamin D at 1,000 or 2,500 units daily **OR**
2. Diet + sunshine advice

If patient is 'high risk' or has levels towards lower end of range:
3. PO colecalciferol 40,000 units monthly for 2 months only **OR**
4. IM 300,000 units colecalciferol or ergocalciferol every 6-12 months **OR**
5. Ca^{2+} + vit D prep providing 800 units per day may be sufficient

- Check plasma calcium levels monthly
- Repeat 25-OHD, Ca^{2+}, ALP, PO_4 and PTH (if possible) at 3 months.

If patient fails to respond to treatment after 3 months (consider non-compliance) discuss case with specialist.

Once 25-OHD levels return to normal, consider maintenance supplementation (e.g. combined Ca^{2+} + vit D prep providing 800 units / day) if patient still at risk (& lifestyle advice)

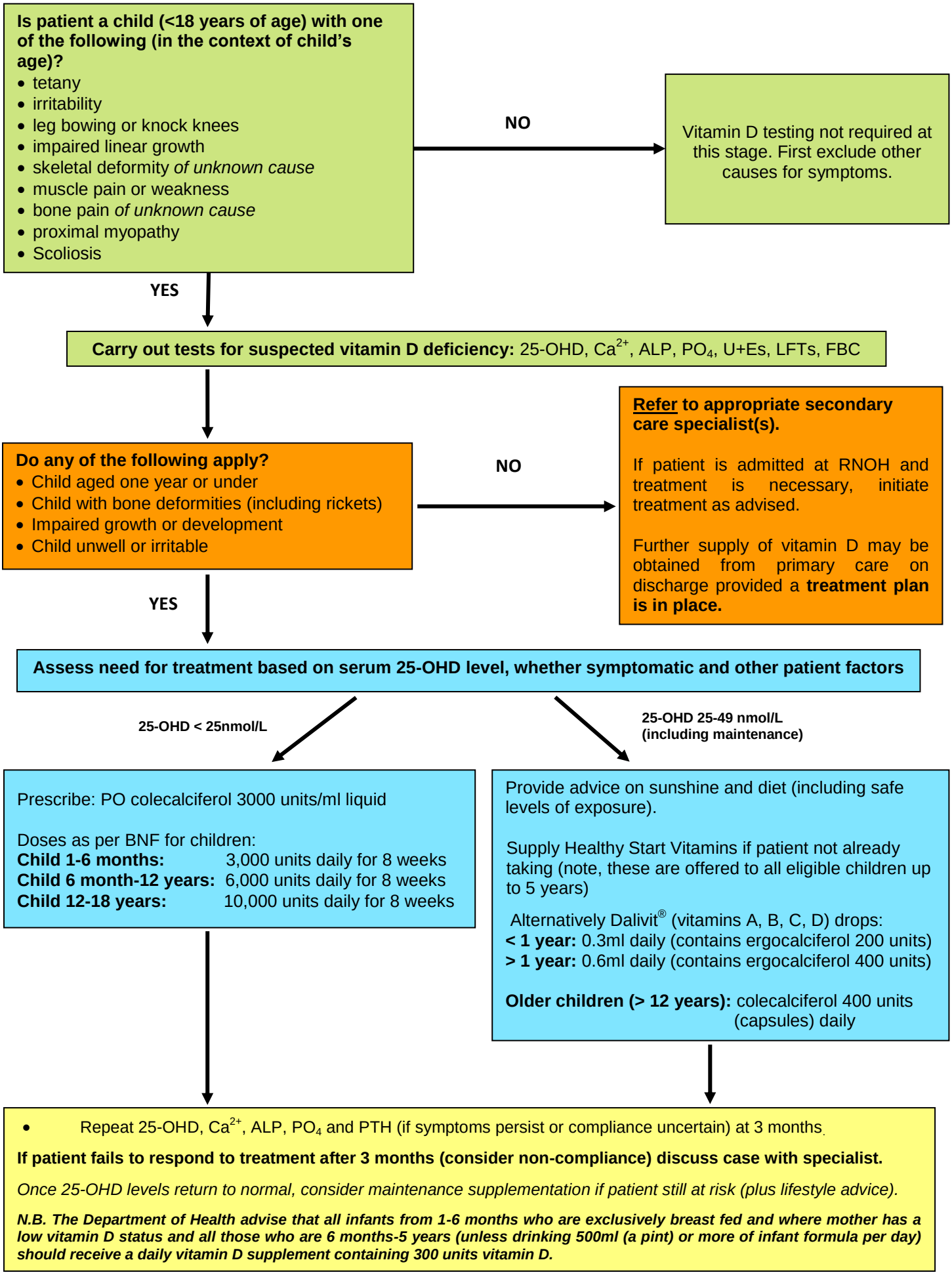
Key
Testing Criteria, Referral Criteria; Management; Monitoring

Appendix 2: Summary of Treatment Recommendations in Adults

PATIENT CHARACTERISTICS	ADVICE AND MANAGEMENT
ADULTS	
Deficiency	
25-OHD levels < 25 nmol/L with **symptoms**	**1.** PO colecalciferol 300,000 units (capsules) STAT or 40,000 units (capsules) daily for 7 days i.e. total of 280,000 units **OR** **2.** IM colecalciferol or ergocalciferol 300,000 units (injection) every 3 to 4 months *Once levels returned to normal, consider long term maintenance supplementation if clinically justified*
25-OHD levels < 25 nmol/L with **no symptoms**	**1.** Advise self-treatment with 'over the counter' high strength vitamin D preparations 1,000 to 2,500 units (capsules) daily. **If patient is considered 'high risk' or has very low vitamin D level:** **2.** PO colecalciferol 60,000 units (capsules) once a week for 6-8 weeks **OR** **3.** IM colecalciferol or ergocalciferol 300,000 units (injection) every 3 to 4 months. *Once levels returned to normal, consider long term maintenance supplementation if clinically justified*
Insufficiency or Maintenance	
25-OHD levels 25-49 nmol/L	**1.** Advise self-treatment with 'over the counter' high strength vitamin D preparations 1,000 to 2,500 units (capsules) daily. **2.** Advice on diet + exposure to safe levels of sun. **If patient is considered 'high risk' or has vitamin D level towards lower end of range:** **3.** PO colecalciferol 40,000 units (capsules) once a month for 2 months only **OR** **4.** IM colecalciferol or ergocalciferol 300,000 units (injection) every 6-12 months **OR** **5.** Depending on patient needs and 25-OHD levels, maintenance therapy with combination calcium and vitamin D may be sufficient (daily dose of 800 units vitamin D daily) - avoid in patients with co-existing primary hyperparathyroidism *Once levels returned to normal, consider long term maintenance supplementation if clinically justified*
Adequate	
25-OHD levels > 50 nmol/L	Advise on diet + exposure to safe levels of sun

(Refer to appendix 5 for details of products that can be used to give the doses recommended below)

Appendix 3: Investigation and treatment of vitamin D deficiency / insufficiency in children



Appendix 4: Summary of Treatment Recommendations in Children

PATIENT CHARACTERISTICS	ADVICE AND MANAGEMENT
CHILDREN	
Deficiency:	
25-OHD levels < 25 nmol/L with **symptoms**	Age 1 to 6 months: 3,000 units (liquid) daily for 8 weeks Age 6 month to 12 years: 6,000 units (liquid) daily for 8 weeks Age 12 years to 18 years: 10,000 units (capsules) daily for 8 weeks *Once levels returned to normal, consider long term maintenance supplementation if clinically justified*
25-OHD levels < 25 nmol/L with **no symptoms**	Advice on diet and exposure to safe levels of sunshine. For patients up to 5 years of age from low income families, supply Healthy Start Vitamins. Further supply can be obtained from primary care free of charge. For all other patients, prescribe Dalivit® (vitamin A, B, C, D) drops: Age < 1 year: 0.3 ml daily (contains Ergocalciferol 200 units) Age > 1 year: 0.6 ml daily (contains Ergocalciferol 400 units) Age > 12 years: Colecalciferol 400 units (capsules) daily *Once levels returned to normal, ensure long term maintenance supplementation if clinically justified*
Maintenance	
Supplementation	Age < 1 year: Dalivit 0.3 ml daily (contains Ergocalciferol 200 units) Age > 1 year: Dalivit 0.6 ml daily (contains Ergocalciferol 400 units), or 400 units (capsules) daily Age > 12 years: Colecalciferol 400 units (capsules) daily

(Refer to appendix 5 for details of products that can be used to give the doses recommended below)

Appendix 5: Products on the RNOH Formulary for treatment of vitamin D deficiency, insufficiency or maintenance supplementation

Table 1: Colecalciferol preparations

Drug Name + Strength + Form	Manufacturer + Licensing Status	Active Ingredients and Excipients	Suitable for vegetarians?	Suitable for vegans?	Suitable for peanut allergy sufferers?
Colecalciferol (D_3) preparations*					
Healthy Start vitamin drops 300 units / 5 drops x 25 ml bottle oral solution	Available from NHS organisations i.e. PCTs *Vitamin*	Colecalciferol (source not confirmed) Excipients: Water, glycerol, polysorbate 80, banana flavour	Manufacturer does NOT recommend	☒	☑
Colecalciferol 400 units x 30 capsules [Pro-D3®]	Synergy Biologics (via AAH Pharmaceuticals) *Vitamin (Food Supplement)*	Colecalciferol (vegetarian certified derivative from sheep wool fat) Excipients: Microcrystalline cellulose, magnesium stearate Capsule shell: HPMC (Hydroxypropyl Methylcellulose)	☑	☑	☑
Colecalciferol 1,000 units x 30 capsules [Pro-D3®]	Synergy Biologics (via AAH Pharmaceuticals) *Vitamin (Food Supplement)*	Colecalciferol (vegetarian certified derivative from sheep wool fat) Excipients: Microcrystalline cellulose, magnesium stearate Capsule shell: HPMC (Hydroxypropyl Methylcellulose)	☑	☑	☑
Colecalciferol 2,500 units x 30 capsules [Pro-D3®] x 30	Synergy Biologics (via AAH Pharmaceuticals) *Vitamin (Food Supplement)*	Colecalciferol (vegetarian certified derivative from sheep wool fat) Excipients: Microcrystalline cellulose, magnesium stearate Capsule shell: HPMC (Hydroxypropyl Methylcellulose)	☑	☑	☑
Colecalciferol 10,000 units x 30 capsules [Pro-D3®]	Synergy Biologics (via AAH Pharmaceuticals) *Vitamin (Food Supplement)*	Colecalciferol (vegetarian certified derivative from sheep wool fat) Excipients: Microcrystalline cellulose, magnesium stearate Capsule shell: HPMC (Hydroxypropyl Methylcellulose)	☑	☑	☑
Colecalciferol 20,000 units x 30 capsules [Pro-D3®]	Synergy Biologics (via AAH Pharmaceuticals) *Vitamin (Food Supplement)*	Colecalciferol (vegetarian certified derivative from sheep wool fat) Excipients: Microcrystalline cellulose, magnesium stearate Capsule shell: HPMC (Hydroxypropyl Methylcellulose)	☑	☑	☑
Colecalciferol 30,000 units x 10 capsules [Pro-D3®]	Synergy Biologics (via AAH Pharmaceuticals) *Vitamin (Food Supplement)*	Colecalciferol (vegetarian certified derivative from sheep wool fat) Excipients: Microcrystalline cellulose, magnesium stearate Capsule shell: HPMC (Hydroxypropyl Methylcellulose)	☑	☑	☑

POM = prescription only medicine (available from pharmacies only via prescription)

**** Quality Assurance of Pro-D3 products***

- Raw materials compliance with USP and EP.
- USP, EP and BP test procedures in place including identification (UV spectrometric analysis), assay & microbiology
- All Pro-D3 products are suitable for vegetarians, gelatine-free, halal, kosher, alcohol-free, PEG-free, soya-free, lactose-free, gluten-free, preservative-free, salt-free, yeast-free and do NOT contain peanut oil.
- Manufactured within the UK; packaging and patient information leaflet in ENGLISH language.

Table 1 (continued): Colecalciferol preparations

Drug Name + Strength + Form	Manufacturer + Licensing Status	Active Ingredients and Excipients	Suitable for vegetarians?	Suitable for vegans?	Suitable for peanut allergy sufferers?
Colecalciferol (D_3) preparations*					
Colecalciferol 3,000 units/ml x 50 ml bottle oral solution [Pro-D3®]	Synergy Biologics (via AAH Pharmaceuticals) *Vitamin (Food Supplement)*	Colecalciferol (vegetarian certified derivative from sheep wool fat) Excipients: Sunflower seed oil, orange flavour, medium chain triglycerides, DL-alpha tocopherol	☑	☑	☑
Colecalciferol 300,000 units/ml x 10 ampoules for injection	Streuli Pharma, Switzerland (via IDIS) *POM – Unlicensed*	Colecalciferol (derived from sheep wool fat) Excipients: Ethanol 49% v/v, mediocatenal triglyceride	☒	☒	**TBC**

Table 2: Ergocalciferol preparations

Drug Name + Strength + Form	Manufacturer + Licensing Status	Active Ingredients and Excipients	Suitable for vegetarians?	Suitable for vegans?	Suitable for peanut allergy sufferers?
Ergocalciferol (D_2) preparations [non animal derived]					
Ergocalciferol 3,000 units/ml x 20 ml bottle oral solution	Nova Labs *POM – Vitamin*	Ergocalciferol (derived from non-animal sources) Excipients: Arachis oil	☑	☑	☒
Ergocalciferol 600,000 units / 1.5 ml x 1 ampoule for injection [Sterogyl® 15-H]	DB Pharma, France (via IDIS) *POM – Unlicensed*	Ergocalciferol (derived from non-animal sources) Excipients: Groundnut oil	☑	☑	☒
Dalivit® multivitamins 400 units / 0.6 ml x 25 ml bottle oral solution	LPC Pharmaceuticals Ltd. (via normal wholesaler route) *Vitamin*	Ergocalciferol (source not confirmed) Excipients: Sodium hydroxide, polysorbate 80 BP, sucrose BP, E219 sodium methylhydroxybenzoate BP, deionized water	☑	☑	☑

POM = prescription only medicine (available from pharmacies only via prescription)

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