Guidelines for the Treatment of Vitamin D Deficiency and Insufficiency in Adults
(April 2012)

The prevalence of vitamin D deficiency, in the UK, is 16% whilst around 50% of the UK adult population will have vitamin D insufficiency in winter and spring.† NHS Surrey covers a population of 1.2 million which means there are a potential 150,000 adults who could be deficient. Vitamin D is essential for good bone health and more recently insufficiency has been linked to other health concerns.‡

A consensus statement representing the unified views of the British Association of Dermatologists, Cancer Research UK, Diabetes UK, the Multiple Sclerosis Society, the National Heart Forum, the National Osteoporosis Society and the Primary Care Dermatology Society on the position of Vitamin is D is found below.

Vitamin D is essential for good bone health and for most people sunlight is the most important source of vitamin D. The time required to make sufficient vitamin D varies according to a number of environmental, physical and personal factors, but is typically short and less than the amount of time needed for skin to redder and burn. Enjoying the sun safely, while taking care not to burn, can help to provide the benefits of vitamin D without unduly raising the risk of skin cancer. Vitamin D supplements and specific foods can help to maintain sufficient levels of vitamin D, particularly in people at risk of deficiency. However, there is still a lot of uncertainty around what levels qualify as “optimal” or “sufficient”, how much sunlight different people need to achieve a given level of vitamin D, whether vitamin D protects against chronic diseases such as cancer, heart disease and diabetes, and the benefits and risks of widespread supplementation.

A letter from the Chief Medical Officers for the United Kingdom, published Feb 2012, raises awareness of the risk of vitamin D deficiency amongst certain groups Vitamin D - advice on supplements for at risk groups in particular:

- All pregnant and breastfeeding women
- Infants and young children under 5 years of age
- Older people aged 65 years and over
- People who have low or no exposure to the sun
- People who have darker skin

Nomenclature: The term vitamin D is used for a range of compounds. Vitamin D2 is known as ergocalciferol. Vitamin D3 is known as cholecalciferol when referring to the analyte and colecalficiferol (the recommended International Nonproprietary Name (rINN)) when referring to the drug. (1mcg of colecalficiferol is equivalent to 40units. Units will be used throughout this document)

With acknowledgement to NHS Wandsworth who provided their current guidelines for NHS Surrey to adapt.
**What are the sources of vitamin D?**

The main source of vitamin D for humans is ultraviolet B sunlight exposure. During summer two or three exposures (of at least the face and arms without sunscreen and not behind glass) of 20 to 30 minutes each week, which can be divided, between 10am and 3pm should provide adequate amounts of vitamin D for most individuals. The elderly and those of non-white ethnicity will have higher requirements. Due to the latitude in the UK, from October to April sun exposure is not adequate for synthesis of vitamin D.

Oily fish such as herring, sardines, mackerel, salmon and tuna are the best dietary source of vitamin D. Egg yolks, mushrooms and liver contain small amounts of vitamin D. Liver is also a rich source of vitamin A, therefore consumption should be limited to once a week to avoid toxicity and avoided entirely in pregnancy. There are also some foods such as margarines and cereals that are fortified with vitamin D (check product labels).

**What is the recommended daily intake of vitamin D?**

In the UK, a recommended dietary intake (RDI) has not been set for those leading a normal lifestyle where they are exposed to solar radiation. For adults over 65 years or at risk (e.g. confined indoors, extensively covered), and for pregnant or breastfeeding women the reference nutrient intake (RNI) is 400 units (10 micrograms) per day. The latter recommendation during pregnancy is endorsed by the Department of Health (DoH).

Based on current evidence, however, the consensus is that current governmental guidelines in all countries are too low with respect to how much daily vitamin D is required to maintain bone health and health in general, particularly in the absence of adequate sun exposure.

**How is vitamin D insufficiency and deficiency determined?**

The most reliable way to determine vitamin D deficiency is by assay of serum 25-hydroxyvitamin D (25(OH)D) either by measuring 25-hydroxy vitamin D3 or total 25-hydroxy D2 and D3. Either assay may be used at local institutions. It is important to establish the assay used at the laboratory where the requests are sent as this has implications for assessing treatment response.

There is some consensus that vitamin D deficiency should be defined as 25(OH)D concentration of less than 25 nmol/litre. This is the level below which parathyroid hormone (PTH) starts to rise causing increased bone turnover and hence the symptoms associated with osteomalacia.

<table>
<thead>
<tr>
<th>Serum 25(OH)D concentration</th>
<th>Vitamin D status</th>
<th>Manifestation</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;25 nmol/l</td>
<td>Deficient</td>
<td>Rickets</td>
<td>Treat with high-dose vitamin D</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Osteomalacia</td>
<td></td>
</tr>
<tr>
<td>25-50 nmol/l</td>
<td>Insufficient</td>
<td>Associated with disease risk</td>
<td>Lifestyle advice / Vitamin D supplementation</td>
</tr>
<tr>
<td>50-75 nmol/l</td>
<td>Adequate</td>
<td>Healthy</td>
<td>Lifestyle advice</td>
</tr>
<tr>
<td>&gt;75 nmol/l</td>
<td>Optimal</td>
<td>Healthy</td>
<td>None</td>
</tr>
</tbody>
</table>

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When should vitamin D levels be measured?

Routine testing of vitamin D levels is not recommended given the large proportion of the population who may have insufficient levels. Vitamin D deficiency should be considered and checked for only if:

1. A patient has one or more of the following clinical features: 2,5,6
   - Insidious onset of widespread or localised 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

2. The patient has one or more of the following risk factors: 2,5,6
   - Black and ethnic minority patients with darker skin
   - Elderly patients in residential care or housebound
   - Intestinal malabsorption, for example coeliac disease, crohn’s disease, gastrectomy
   - Routine covering of face or body, for example wearing a veil or habitual sunscreen use
   - Vegan or vegetarian diet
   - Liver or renal disease
   - Medications including anticonvulsants, cholestyramine, rifampicin, glucocorticoids, anti-retrovirals

   AND

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

It is worthwhile encouraging all patients with risk factors – even those not exhibiting symptoms – to make lifestyle changes in order to achieve adequate amounts of vitamin D but it is not necessary to measure their levels.


Pregnant women, women with a baby < 1 year and children from six months to their 4th birthday may be entitled to free Vitamins under the DoH ‘Healthy Start’ scheme. The website for this initiative is http://www.healthystart.nhs.uk/index.html and all patients in these categories should be referred to their nearest distribution centre for supplies which can be found by entering a home postcode on the website.
How should vitamin D status be assessed?

Assessment of vitamin D status should include 25(OH)D (remember levels fluctuate and will be highest after the summer months and lowest early spring), serum calcium (to exclude hypercalcaemia and provide a baseline for monitoring), parathyroid hormone (PTH) (to exclude primary hyperparathyroidism), alkaline phosphatase (ALP) and phosphate. Renal function (to exclude renal failure), liver function tests (to exclude hepatic failure), and full blood count (anaemia may be present if there is malabsorption) are also recommended. The blood test for PTH is unstable therefore phlebotomy needs to take place at the site where the assay is processed.

How should vitamin D deficiency be treated and what products are recommended?

All patients should be reminded of the importance of exposure to sunlight and dietary sources of Vitamin D.

Colecalciferol (vitamin D3) is considered the preferred form of vitamin D for treatment. It has been reported that colecalciferol raises vitamin D levels more effectively than ergocalciferol (vitamin D2), and has a longer duration of action.\(^7\) This may be due to higher affinities of colecalciferol and its metabolites for liver enzymes, plasma vitamin D binding protein, and vitamin D receptors.\(^8\)

Whilst ergocalciferol is effective in treating vitamin D deficiency, the differences in potency suggest that where possible colecalciferol should be used. Furthermore, considering some assays used in the local area may only measure a metabolite of colecalciferol response to treatment may not be detected if ergocalciferol is given.

In the UK there are licensed preparations of vitamin D which contain ergocalciferol (vitamin D2): 10,000unit and 50,000unit tablet, and 300,000unit and 600,000unit injection. However as mentioned above colecalciferol (vitamin D3) is the preferred treatment. Fultium\(^\circledR\)-D3 800iu capsules are a prescription only medicine and the first UK licensed colecalciferol product for prevention and treatment of Vitamin D deficiency and are now included in our guidance. A selection of alternative unlicensed medicinal products containing only colecalciferol and available to prescribe on the NHS and are also listed. Remember - the clinical responsibility for prescribing always lies with the prescriber.

With acknowledgement to NHS Wandsworth who provided their current guidelines for NHS Surrey to adapt.
### Deficiency (25(OH)D less than 25nmol/L) will require high dose colecalciferol only available on prescription

<table>
<thead>
<tr>
<th>Drug options and dose recommended</th>
<th>Preparation &amp; manufacturer</th>
<th>Distributors &amp; Price (Apr 12)</th>
</tr>
</thead>
<tbody>
<tr>
<td>800IU Colecalciferol (equivalent to 20 micrograms vitamin D₃). Four capsules to be taken daily for 12 weeks.</td>
<td>Fultium®-D₃ 800 IU Capsule POM <a href="http://www.medicines.org.uk/EMC/medicine/25664/SPC/Fultium-D3-800IU-capsules">http://www.medicines.org.uk/EMC/medicine/25664/SPC/Fultium- D3-800IU-capsules</a></td>
<td>£3.60 for 30caps (NHS cost price)</td>
</tr>
<tr>
<td>60,000units (3 x 20,000unit capsule) colecalciferol orally once a week for 12 weeks</td>
<td>Dekristol ®20,000unit capsule MIBE, Germany is licensed in Europe. This is the most appropriate option to provide 60,000units once a week orally for patients with deficiency Contains peanut oil, glycerol and gelatin &amp; has Halal certification</td>
<td>Martindale Pharma (0800 137 627) Pack of 50 £18.45 + P&amp;P IDIS (01932 824 000) Pack of 50 £26.10 + P&amp;P</td>
</tr>
<tr>
<td>Two intramuscular (IM) injections of 300,000units colecalciferol given 3 months apart (use this option ONLY if malabsorption present or compliance is problematic)</td>
<td>Colecalciferol 300,000unit injection (Vitamin D₃; Streuli, Switzerland) is licensed in Europe Contains peanut oil, glycerol, gelatin and soya</td>
<td>IDIS (01932 824 000) Pack of 10 x 1ml £49.00 + P&amp;P</td>
</tr>
<tr>
<td>150,000units (50ml of 3,000units/ml liquid or equivalent) colecalciferol once a day for 2 days (use oral liquid option ONLY if capsules or injection are not suitable)</td>
<td>‘Special liquid’ products such as this are not commercially available and need to be extemporaneously prepared and this can be costly. These liquid preparations usually have a short shelf life therefore do not prescribe quantities of more than one month’s supply without confirming a longer expiry. Colecalciferol oral soln 15,000units/5ml is listed in the Drug Tariff Part VIIIIB at £102.70 /100ml (May 2012)</td>
<td></td>
</tr>
</tbody>
</table>

#### Low strength colecalciferol Vitamin D₃ products, which patients can purchase over the counter, for insufficiency or for maintenance therapy are listed in appendix 1.

### Insufficiency (25(OH)D 25 to 50nmol/L).
There is a lack of evidence on the functional outcomes of populations with insufficient levels of Vitamin D. The Surrey Prescribing Clinical Network (June 2012) therefore currently recommends lifestyle advice for these patients with the option for them to purchase “over the counter” high strength colecalciferol preparations 1000-2000units daily – see appendix 1.

### Maintenance therapy
at a dose of 800 to 1,000units of colecalciferol daily may be required once deficiency has been corrected for those patients who were severely deficient and are still considered to be at risk. In some cases this may be lifelong therapy.

- Adcal D3 (calcium carbonate 1.5g & colecalciferol) 400units one tablet twice day. As a UK licensed product, this is the most appropriate option to use for maintenance depending on a patient’s calcium level and dietary intake of calcium.

  OR

- If calcium replete patients should be encouraged to buy a supplement as listed in appendix 1.

As a fat soluble vitamin oral vitamin D products should be taken with food to improve absorption. Avoid taking with orlistat as this reduces absorption.

### Whilst on treatment patients should be advised of signs of hypercalcaemia; nausea, thirst and polyuria.
(Further product choices are available on the East & South East England Specialist Pharmacy Services document which can be accessed on the Prescribing Advisory Database.)

With acknowledgement to NHS Wandsworth who provided their current guidelines for NHS Surrey to adapt.
When is vitamin D supplementation not suitable?
Vitamin D is contraindicated in patients with hypercalcaemia or metastatic calcification. Relative contraindications include primary hyperparathyroidism, renal stones and severe hypercalciuria.

What monitoring should be done?
- In vitamin D deficiency 25(OH)D should be re-checked 12 weeks after commencing high dose replacement treatment in order to monitor response.
- It is not necessary to monitor 25(OH)D in vitamin D insufficiency where low dose treatment is given.
- In patients with renal failure, serum calcium should be checked regularly for a few weeks after starting treatment.
- Once vitamin D deficiency is corrected monitoring every 12 months may be advisable for patients still considered at risk.

Who should be referred to secondary care?
- Patients with the above contra-indications
- Patients with renal impairment (stage 4 Chronic Kidney Disease (CKD) or eGFR less than 30ml/minute)
- Primary hyperparathyroidism
- No response after 12 weeks of treatment

Cost implications
The cost of Vitamin D prescribing in Surrey has been steadily increasing and in particular the use of “Specials” for treatment. The guidelines endeavor to address who is deficient or has an insufficiency in Vitamin D, who to treat and with what medication. The East & South East England Specialist Pharmacy Services produced a document in Jan 2011 and updated in Nov 2011 regarding available products for deficiency and insufficiency in Vitamin D - NHS Surrey has used this document and tailored the choice of products and it is available on the Prescribing Advisory Database. Prescribing Advisory Database.

References:

With acknowledgement to NHS Wandsworth who provided their current guidelines for NHS Surrey to adapt.
Guidelines for Investigation and treatment of Vitamin D deficiency

Does the patient have ≥1 symptom of vitamin deficiency?
- widespread bone pain or tenderness or myalgia
- proximal muscle weakness
- tenderness over pseudo fractures
- Insufficiency fractures

Yes ➔ Vitamin D testing not required
No ➔ Does the patient have ≥1 risk factor for vitamin D deficiency?

Yes ➔ Have other causes for symptoms been excluded?
No ➔ Assessment of vitamin D status required: 25(OH)D, Ca\(^{2+}\), PTH, ALP, PO\(_4\). Also recommended: U+Es, LFTs, FBC

Yes ➔ Refer to appropriate specialist in secondary care.
- Depending on outcome vitamin D treatment may still be required; of which the first treatment course should be prescribed and provided by secondary care before transferring patient with care plan back to primary care.

No ➔ Treatment based on serum 25-hydroxyvitamin D level

Deficiency <25nmol/L
- Fulfium\(^\circ\)-D3 (coleccalciferol 800iu capsules):
  - 4 caps daily for 12 weeks
- OR Dekristol\(^\circ\) (coleccalciferol 20,000unit capsule):
  - Take 3 capsules once a week for 12 weeks
- OR coleccalciferol 300,000unit IM injection:
  - Give one immediately, repeat at 12 weeks
- OR coleccalciferol liquid 3000units/ml:
  - Take 50ml once a day for 2 days

Repeat levels at 12 weeks
- Has patient responded to treatment?

No ➔ Refer to appropriate specialist in secondary care
Yes ➔ Insufficiency 25-50nmol/L
- There is a lack of evidence on the functional outcomes of populations with insufficient levels of Vitamin D hence offer lifestyle advice for these patients with the option for them to purchase “over the counter” high strength coleccalciferol preparations 1000-2000unit daily

Sufficient >50nmol/L
- Lifestyle and dietary advice

Monitor patient every 12 months if patient considered still at risk give lifestyle advice or consider maintenance therapy.
- Adcal D3 (calcium carbonate 1.5g & coleccalciferol) 400units one tablet twice day. -This is the most appropriate option to use for maintenance depending on a patient’s calcium level and dietary intake of calcium.
- OR
- If calcium replete patients should be encouraged to buy a supplement as listed in appendix 1
Appendix 1

*Please note products with soya are not suitable for those with nut allergies

**Colecalciferol health food supplements** (not licensed medicines) are available to purchase over-the-counter (OTC) from retail pharmacies and health food stores – This is not an exhaustive list.

<table>
<thead>
<tr>
<th>Product</th>
<th>Strength And form</th>
<th>Source</th>
<th>Relevant excipients for any dietary/allergy restrictions*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lamberts vitamin D3</td>
<td>400unit tablets</td>
<td>Lamberts</td>
<td>Nil /suitable for vegetarians</td>
</tr>
<tr>
<td>Lamberts vitamin D3</td>
<td>1000unit tablets</td>
<td>Lamberts</td>
<td>Nil / suitable for vegetarians</td>
</tr>
<tr>
<td>Sunvite Vitamin D3</td>
<td>400unit tablets</td>
<td>Holland and Barrett</td>
<td>Soya, gelatine (bovine origin)</td>
</tr>
<tr>
<td></td>
<td>1000unit tablets</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vitamin D</td>
<td>500units</td>
<td>Boots</td>
<td>Free from Glycerin, Gelatin Or Soya Bean Oil.</td>
</tr>
<tr>
<td>Vitamin D</td>
<td>1000unit capsule</td>
<td>Nature’s Remedy</td>
<td>Rice bran oil, gelatine, glycerin</td>
</tr>
<tr>
<td>Vitamin D</td>
<td>1000unit tablet</td>
<td>Nature’s Remedy</td>
<td>Nil / suitable for vegetarians</td>
</tr>
<tr>
<td>Biolife Vitamin D</td>
<td>1000unit tablet</td>
<td>Lifestyle Natural Health</td>
<td>Nil / suitable for vegetarians</td>
</tr>
<tr>
<td>Vitamin D3</td>
<td>1000unit softgel</td>
<td>Solgar</td>
<td>Gelatin, glycerin</td>
</tr>
</tbody>
</table>

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