

GUIDANCE ON THE PREVENTION, DIAGNOSIS AND MANAGEMENT OF VITAMIN D DEFICIENCY IN PRIMARY CARE



Northern Lincolnshire
Area Prescribing Committee

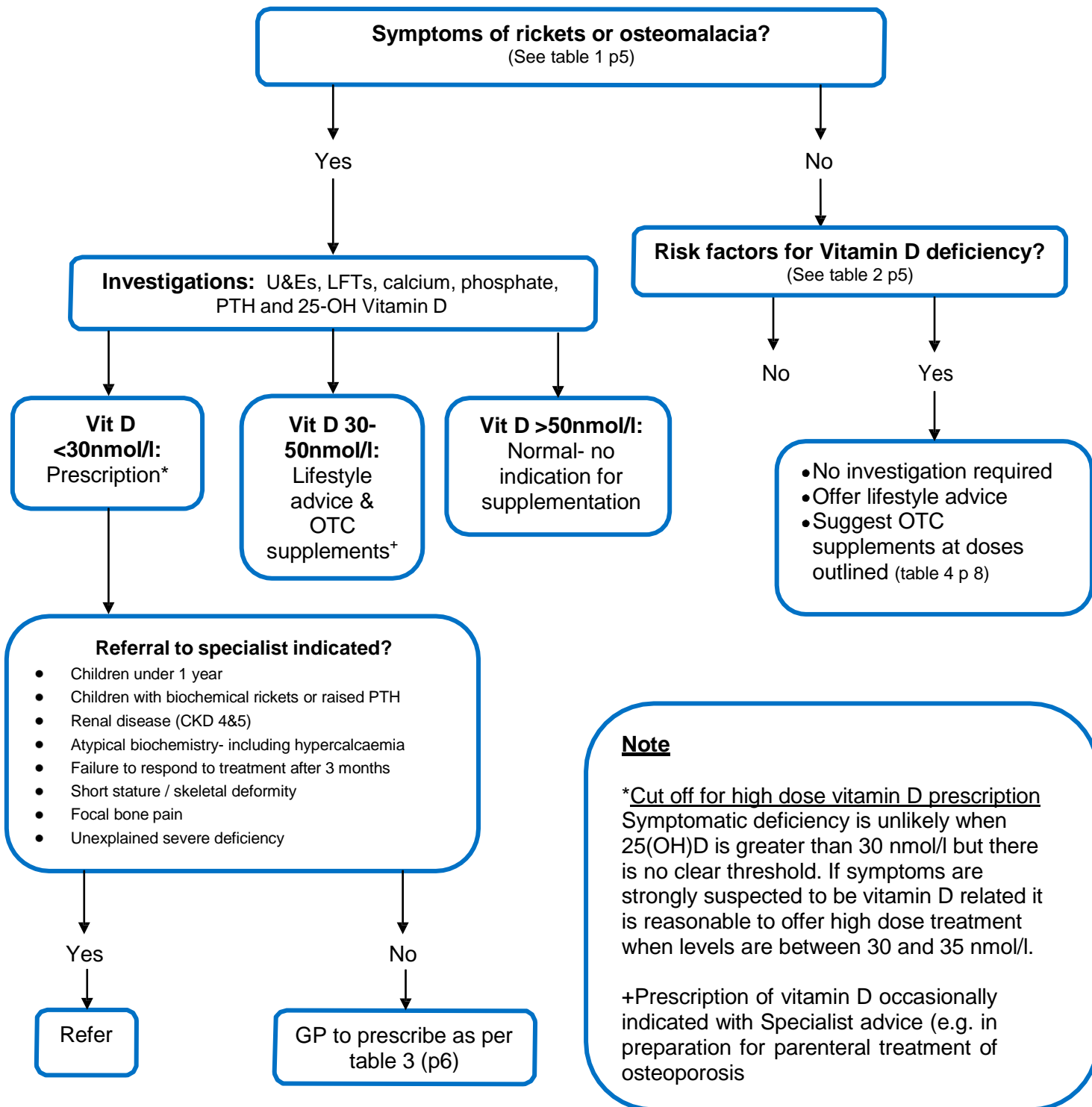
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- Prevention: An estimated 60-70% of the UK population could be vitamin D insufficient.

For this reason:

- Population screening of vitamin D blood levels is not recommended.
 - Lifestyle advice and use of over the counter vitamin D preparations are recommended for prevention. Patient information resources are included in this guideline.
 - The government Healthy Start Scheme offers free vitamin supplements (containing vitamin D) to eligible patients. They can also be purchased cheaply by those not eligible for free supplies.
 - Prescriptions of vitamin D preparations should be reserved for treatment of patients with **symptoms AND low vitamin D** levels and those patients who have an indication for supplementation but are unable to access non-prescription vitamin D supplementation such as the elderly and infirm.
- **Fultium D 3,200 units and InVita D3 25,000 units** are the preferred formulary choice for high dose colecalciferol
 - **Pro D3** is an alternative option for children as it allows flexible dosing and formulations. It may also be an option in patients with swallowing difficulties
 - Vitamin D products should be prescribed by brand name
 - **Fultium D3 800 units, InVita D3 and Desunin 800 units** can be prescribed for maintenance therapy following treatment courses but for supplementation in exceptional cases only.

SUMMARY: Diagnosis and management of Vitamin D deficiency in primary care

Population screening by measuring Vitamin D levels is unnecessary, even in high risk populations.



Diagnosis and management of Vitamin D deficiency in primary care

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Introduction

Vitamin D deficiency is an important public health issue concerning infants, young children, adults & elderly people. Recent evidence estimates that 60-70% of population could be vitamin D insufficient, particularly ethnic minority and the immigrant population.

This guideline has been revised for 2013 following the publication of the National Osteoporosis Society „Vitamin D and Bone Health“ document and new developments in the commercial field of vitamin D supplements. The document provides information on vitamin D, diagnosis and management of deficiency and advice for patients with insufficiency

1: Vitamin D physiology:

What is Vitamin D?

- Vitamin D is a group of fat soluble vitamins that is essential bone formation in all age groups. The 2 main forms are D₂ (ergocalciferol), predominantly from plants and D₃ (colecalciferol), mainly from animal sources. Both have similar actions. Vitamin D is activated in the liver to 25- hydroxycolecalciferol and then in the kidney to 1,25-dihydroxycolecalciferol (active vitamin D). The most well established action of vitamin D is to promote calcium absorption by the GI tract.
- 90% of our daily vitamin requirement is obtained by the action of UVB sunlight on the skin (only during April to September in the United Kingdom)
- 10% is obtained through diet such as oily fish (sardines, salmon), liver, egg yolks, fortified margarine and fortified breakfast cereals)

Does Vitamin D have other functions?

- Research has identified epidemiological links between vitamin D levels and various disease states. It remains unclear whether vitamin D could offer pharmacological benefit for any of these conditions. At the present time the indications for vitamin D treatment relate to maintenance of calcium homeostasis and bone health via the primary mode of action to aid absorption of calcium at the gut.

2: Prevention of Vitamin D deficiency:

All UK Health Departments recently recommended ([CMO letter 2012](#)) that:

- **All pregnant and breastfeeding women** should take a daily supplement containing 400 international units (iu) (10micrograms (µg)) of vitamin D, to fulfil mother's requirements for vitamin D and to build adequate foetal stores
- **All infants and young children aged 6 months to 5 years** should take a daily supplement containing 280-340iu (7-8.5µg) vitamin D in the form of vitamin drops. However, those infants who are fed infant formula will not need vitamin drops until they are receiving less than 500ml of infant formula a day. Breastfed infants may need to receive drops containing vitamin D from one month of age if their mother has not taken vitamin D supplements throughout pregnancy.
- **People aged 65 years and over and people who are not exposed to much sun** should also take a daily supplement containing 400iu (10µg) of vitamin D.

Most of these patients should be offered lifestyle advice as detailed in section 5 (p6) and advised to purchase supplementation over the counter in the first instance (eligible patients can obtain free supplements through the Healthy Start scheme). More information on available products for supplementation and the Healthy Start scheme can be found in appendix 2 (p8). Patients who are unable to access over the counter supplements and are unable to modify lifestyle behaviour adequately should be prescribed the relevant supplement. Relevant groups include patients in Residential and Nursing homes and those unable to afford supplements.

3: Diagnosis:

Vitamin D deficiency is best assessed by measurement of serum 25-OH vitamin D. Measurement of other vitamin D metabolites or sub-fractions adds nothing further and is not recommended.

Population screening is NOT recommended. Vitamin D deficiency should be suspected in patients presenting with clinical features as detailed in table 1 below and the general principle is to test only those individuals who have symptoms or features suggestive of vitamin D deficiency or osteomalacia.

Clinical features of Vitamin D deficiency (Table 1):

Children	Adults
<ul style="list-style-type: none"> • Poor growth, delayed fontanelle closure • Delayed walking or a waddling gait • Tender or swollen joints, classically the wrists or costochondral junctions • Deformed bones (bow legs or knock knees) • Bone pain or tenderness • Muscle pain or proximal myopathy • Delayed eruption of teeth, or enamel hypoplasia • Carpopedal spasm, tetany, seizures or irritability due to hypocalcaemia & requiring urgent treatment 	<ul style="list-style-type: none"> • Gradual onset & persistent bone pain without preceding mechanical injury (frequently in back, ribs or lower limb) • Fragility fracture • Proximal muscle weakness (difficulty with stairs, getting up off the floor or standing after sitting in a low chair, waddling gait) or muscle pain • Carpopedal spasm, tetany, seizures or irritability due to hypocalcaemia & requiring urgent treatment

GPs should consider a diagnosis of vitamin D deficiency in a patient with risk factors (table 2) who presents with chronic musculoskeletal (MSK) pain.

NB. The relationship between chronic MSK pain and vitamin D deficiency is not clear and treatment does not necessarily resolve symptoms.

Risk factors for Vitamin D deficiency (Table 2)

Age Groups	Poor exposure to UVB light	Poor dietary intake	Metabolic risk
≥65years <5 years Pregnant women Breastfeeding women	Pigmented skin Occlusive garments Housebound Use of sun blocking creams	Vegetarian (or fish-free diet) Malabsorption, including bariatric surgery patients Cholestatic liver disease Breast fed infants	Elderly (reduced synthesis) Liver disease (reduced stores) Renal disease (reduced synthesis of active vitamin D) Obese people (excess storage in fat) Drugs: Rifampicin, Antiretroviral drugs, anticonvulsants, cholestyramine, glucocorticoids.

Investigations (to be arranged by primary care):

- U&Es, LFTs, calcium, phosphate and 25-OH Vitamin D
- PTH should be measured when the adjusted calcium is significantly low (<2.15)
- Children: In addition, albumin & PTH should be measured routinely in children (refer if PTH high)
- The findings in osteomalacia are a low/ normal calcium, low/normal phosphate, raised alkaline phosphatase, low vitamin D and raised PTH (secondary hyperparathyroidism)

Vitamin D levels are expressed as nmol/L (ng/ml x 2.5 = nmol/L).

The definition of vitamin D deficiency and insufficiency is based on blood measurements of 25-OH vitamin D:

- >50 nmol/l Satisfactory Vitamin D levels
- 30-50 nmol/l Vitamin D insufficiency
- <30 nmol/l **Vitamin D deficiency**

Note: In patients with a Vitamin D level >30 nmol/l, symptoms are unlikely to be due to Vitamin D deficiency. However, clinicians should use clinical judgment when considering the diagnosis and treatment plan for an individual patient.

4: Management of Vitamin D deficiency:

i.e.: Vitamin D level <30nmol/l

Patients meeting the above criteria should be managed according to the following principles;

For the purposes of this document we define „treatment“ to be high dose therapy to reverse vitamin D deficiency. This is different from lower doses used as long term daily „supplementation“ or as „maintenance“ following high dose treatment.

Symptomatic patients need high dose colecalciferol treatment to reverse deficiency and eradicate symptoms. Asymptomatic patients can usually be commenced on lower doses of colecalciferol (see Maintenance Therapy in section 3 of Table 3) and deficiency will gradually be resolved.

When indicated a single course of high dose therapy should be followed by lifestyle advice and maintenance with lower dose supplementation.

Available evidence suggests that oral colecalciferol offers greater improvements in serum 25-OH Vitamin D compared with oral ergocalciferol or intramuscular preparations at equivalent doses. As such, oral colecalciferol is the first line treatment option.

Alfacalcidol and calcitriol are completely inappropriate for treatment of vitamin D deficiency outside of CKD 4-5, due to high risk of toxicity.

	ADULTS	CHILDREN (>6 months)
Drug	Colecalciferol	Colecalciferol
Dose	20,000iu daily orally Hux D3 is recommended as an available, cost-effective option for symptomatic patients.	6 months – 12 years 6000iu daily orally for 4 – 8 weeks** 12 – 18 years 10,000iu daily orally for 4 – 8 weeks** Pro D3 is recommended in children as it is available in a liquid formulation
Length of course	Standard course 300,000* iu total dose colecalciferol (15 days x 20,000 units) (Consider increase total dose to 400,000-600,000 units if very low baseline or poor absorption anticipated)	4 – 8 weeks Ensure dietary factors improved. Check PTH normalised – indicating deficiency has resolved
Monitoring	6 weeks; Calcium, phosphate, ALP. Repeat vitamin D levels only if symptoms persist.	1 month (or 1 week if symptomatic hypocalcaemia): calcium, phosphate, ALP and PTH. Repeat 3 monthly until treatment stopped. If ALP does not improve, check compliance. Where treatment continues >6months, check early morning urine calcium:creatinine.
Follow up	No further monitoring or follow up needed.	Review and investigate family members. Give prevention advice as a minimum.
Maintenance therapy (This can be used as initial treatment in asymptomatic individuals)	800iu daily. To be continued long term. Fultium D3 is recommended for prescribing as it is a licensed preparation, available as 800iu capsules. Higher doses up to 2400iu daily may be needed in some patients (e.g. malabsorption).	400-800iu daily. To be continued long term. Healthy Start vitamins, Abidec or Dalivit vitamin drops are recommended.
Long term monitoring	No routine monitoring or rechecking of serum 25OHD levels is needed whilst on maintenance therapy. Recheck biochemistry if symptoms return or malabsorption/ poor compliance suspected.	

NB: *Loading regimens for treatment of deficiency up to a total of approximately 300,000 IU given either as weekly or daily split doses. The exact regimen will depend on the local availability of vitamin D.

NB: **The same effect may be achieved by multiplying the dose by seven and giving it weekly if compliance is a concern

NB: Where poor compliance is suspected give supervised stat oral doses (100,000 iu colecalciferol for adults) at weekly intervals

NB: Liquid “specials” of vitamin D (unlicensed) should NOT be routinely prescribed. Cost effective alternatives are available.

NB: Most vitamin D preparations contain gelatin. Hux D3 & Pro D3 are vegetarian and Halal products.

NB: In patients where Fultium D3® is intolerable, or an alternative is required for maintenance, OTC preparations are advised (see Appendix 2).

5: Management of Vitamin D insufficiency:

i.e.: Vitamin D level 30-50nmol/l AND risk factors for Vitamin D deficiency

Patients should be offered lifestyle advice and advised to purchase supplements over the counter (OTC) at doses outlined above for maintenance therapy (see Appendix 2). Healthy start vitamins are available for children <5years. Example patient information leaflets can be found in Appendix 1.

Use of colecalciferol supplements is specifically recommended for patients with 25-OH Vitamin D 30-50 nmol/l and one of the following additional factors;

- fragility fracture, osteoporosis or high fracture risk including patients on antiresorptive medications
- increased risk of future deficiency due to e.g. reduced exposure to sunlight, cultural dress code, dark skin (see Special Circumstances 4. Asian populations)
- raised PTH
- regular prescription for antiepileptic drugs or glucocorticoids
- malabsorption

Lifestyle advice for Vitamin D insufficiency (and deficiency)

Sun exposure: Sun exposure is the main source of vitamin D and should be exploited!

However, this should be balanced with the risks of excessive exposure. Time required in the sun to make sufficient vitamin D is generally short and less than the time needed for skin to burn. This should be adjusted on an individual basis and safe practices adopted. Little and often is best. The following advice was given in the New England Journal of Medicine (2007): *“Exposure of arms and legs for 5 to 30 minutes (depending on time of day, season, latitude, and skin pigmentation) between the hours of 10 a.m. and 3 p.m. twice a week is often adequate”*

Note: Use of creams containing sun protection factors reduces vitamin D synthesis by >95%.

Diet: Dietary sources of Vitamin D include:

- Oily Fish – Salmon, Mackerel, Sardines, Herring, Pilchards, Fresh Tuna etc.
- Cod liver oil & other fish oils
- Red meat & Eggs yolk
- Infant formula milk, powdered milk
- Fortified breakfast cereals
- Soya products, fortified margarines, low fat spreads

It is difficult to obtain enough vitamin D from usual diet alone. The average daily intake from a normal diet is just 80-160iu/day (2-4µg). Where supplementation is indicated, the following doses are recommended (Table 4):

Age and risk group	Daily Requirement
Newborn up to 1 month	300 – 400iu/day (7.5-10µg)
1 month – 18 years	400 – 1000iu/day (10-25µg)
Pregnant and breastfeeding women	400iu/day (10µg)
People aged 65 & over*	400iu/day (10µg)
People not exposed to much sunlight	400iu/day (10µg)

NB: There is no benefit in using preparations of vitamin D combined with calcium in most patients. However calcium & vitamin D 400-800iu/day is appropriate in the elderly, most people aged 60 years or more taking bisphosphonates, and those taking corticosteroids.

OTC supplementation should be continued long term in most patients.

6. Special circumstances

a. Primary hyperparathyroidism/ Hypercalcaemia

Patients with Primary Hyperparathyroidism frequently have vitamin D deficiency. Vitamin D deficiency in primary hyperparathyroidism may exacerbate bone loss in this condition.

Treatment with vitamin D has the potential to exacerbate hypercalcaemia and hypercalciuria but is still often indicated. **Specialist advice (Endocrinology) is recommended prior to vitamin D treatment in this context.** Prescription supplements (eg Fultium D3) are likely to be warranted to ensure accuracy of dosing and avoid toxicity.

b. Development of new hypercalcaemia during Vitamin D replacement

Patients may develop hypercalcaemia during correction of vitamin D deficiency. This can indicate vitamin D toxicity although this would not be expected when using recommended doses. Most other cases are due to underlying and previously undiagnosed Primary Hyperparathyroidism although granulomatous conditions are also relevant (eg Sarcoidosis). The diagnosis can be aided by measurement of PTH- and such cases should be referred to Endocrinology for assessment.

c. Elderly patients

The majority of elderly patients are ambulant and community dwelling. Many will still be at risk of vitamin D deficiency but the principles of management are not different to that presented in the rest of this document. Dual supplementation with calcium and low dose vitamin D (as in numerous commercially available preparations) is more likely to be appropriate in the elderly and infirm where sun exposure is likely to be poor and gastrointestinal calcium absorption reduced.

Occasionally lone vitamin D supplementation may be needed (eg concurrent primary hyperparathyroidism) and in these cases, a prescription vitamin D supplement such as Fultium D3 should be given.

Meta-analysis suggests that Vitamin D supplementation may prevent falls, although this is controversial. Vitamin D supplementation (with or without calcium) will invariably be appropriate in recurrent fallers. In some cases high dose supplementation will be recommended in this context on a case by case basis by the Falls Clinic team (Vitamin D deficiency has been shown by local Audit to be almost ubiquitous in the Falls clinic population so testing of deficiency prior to treatment will not always be needed). Older people with falls should be assessed for their falls risk factors and referred as per local guidelines.

d. Asian populations

A combination of skin type and cultural factors which reduce sun exposure and limit dietary and supplement choices mean that Asian patients are at particular risk of Vitamin D deficiency and have particular barriers to effective treatment.

In fact vitamin D insufficiency is almost ubiquitous in this group and virtually all patients will be appropriate for supplementation. It is known that take up of „Over the Counter“ options is low in this group.

e. Parenteral Osteoporosis treatments

Parenteral treatments for osteoporosis require adequate vitamin D levels in order to be safe and effective. The osteoporosis team will be involved with the care of these patients and will optimise vitamin D prior to initiation of treatment. It is vital that vitamin D levels are adequate prior to each injection to minimise the risk of severe hypocalcaemia. Vitamin D levels should be checked in patients who are not on regular supplements or in those whose compliance is suspected to be poor. The aim is to ensure 25-OH Vitamin D levels are greater than 50 nmol/l prior to treatment.

7: Referral:

The following patients should be referred to secondary care for further investigation:

- Children under 1 year
- Children with biochemical rickets or raised PTH
- Renal disease (CKD 4&5)
- Atypical biochemistry- including hypercalcaemia
- Failure to respond to treatment after 3 months
- Short stature / skeletal deformity
- Focal bone pain
- Unexplained severe deficiency
- Unexplained weight loss

8: References

- Vitamin D and Bone Health: A Practical Clinical Guideline for Patient Management. National Osteoporosis Society. April 2013.
- Diagnosis and management of vitamin D deficiency. Pearce SHS & Cheetham TD. British Medical Journal 2010; 340:b5664.
- Primary vitamin D deficiency in adults. Drug & Therapeutics Bulletin. 2006; 44(4): 25-29.
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- Vitamin D for the treatment of chronic painful conditions in adults (review). The Cochrane Collaboration. 2010. Available from: http://onlinelibrary.wiley.com/o/cochrane/clsysrev/articles/CD007771/pdf_fs.html
- Guide for Vitamin D in Childhood. Royal College of Paediatrics and Child Health. October 2013 (<http://www.rcpch.ac.uk/system/files/protected/page/vitdguidancedraftspreads%20FINAL%20for%20website.pdf>)

Appendix 1: Patient information: National examples

A variety of patient information leaflets are available including:

- [Department of Health: Guide for health professionals](#)
- [NHS Choices Vitamin D PIL](#)
- [Patient.co.uk Vitamin D deficiency](#)
- [National Osteoporosis Society: Healthy bones: Facts about food](#)
- [Royal National Orthopaedic Hospital: FAQs about Vitamin D in childhood](#)
- [National Osteoporosis Society: Children's bone health](#)

Appendix 2: OTC preparations

Healthy Start vitamins: Women and children from families who are eligible for the Government's Healthy Start scheme can get supplements which include vitamin D, in the form of tablets for women and drops for children.

Women qualify for Healthy Start from the 10th week of pregnancy or if they have a child under four years old, **and** if she or her family receive:

- Income Support, or
- Income-based Jobseeker's Allowance, or
- Income-related Employment and Support Allowance, or
- Child Tax Credit (but not Working Tax Credit unless the family is receiving Working Tax Credit run-on only) **and** has an annual family income of £16,190 or less.

Women under 18 and pregnant also qualify even if not on the above benefits.

For further information and application forms, visit <http://www.healthystart.nhs.uk/>

To obtain free supplies, present a Healthy Start voucher (sent to Healthy Start recipients every 8 weeks).

Patients who are not eligible for free supplies can buy Healthy Start vitamins from the local Health Centres listed above, at a cost of £1.80 for 56 tablets or 91p for a 10ml bottle of drops

- **Vitamin drops contain Vitamins A, C & D – dose 5 drops daily**
- **Vitamin tablets contain Vitamins C, D and folic acid – dose 1 tablet daily**

Patients can also buy suitable preparations over the counter from pharmacies and other health food retailers.

NB: Some vitamin D preparations contain soya oil or peanut oil; most vitamin D capsules contain gelatin. Retailers can provide information on the contents and suitability of their products.