

Management of Low Vitamin D Level in Adults (18yrs and over)

Introduction

Vitamin D is essential for musculoskeletal health as it promotes calcium absorption from the bowel, enables mineralisation in bone and plays an important role in muscle function. Severely low levels can lead to osteomalacia or osteoporosis in adults, although there is currently no proven benefit in treating asymptomatic patients. Less severe vitamin D deficiency or insufficiency may lead to secondary hyperparathyroidism, bone loss, muscle weakness, falls and fragility fractures in older people.

Sources of Vitamin D

Over 80% of the body's vitamin D supply is produced from the action of sunlight on the skin. Dietary sources of vitamin D include oily fish, liver, meat, eggs, mushrooms and fortified cereal/milk. Dietary sources can contribute to vitamin D status, but on their own, they are unlikely to sufficiently raise vitamin D level.

Public Health England (PHE) advises that in spring and summer, the majority of the population produce enough vitamin D through sunlight on the skin and a healthy, balanced diet. During autumn and winter, everyone will need to rely on dietary sources of vitamin D. Since it is difficult for people to meet the 10microgram recommendation from consuming foods naturally containing or fortified with vitamin D, people should consider taking a daily supplement containing 10micrograms (400 IU) of vitamin D in autumn and winter (1st October to 31st March inclusive).

Patient's in the 'at risk group' below should also consider taking a daily supplement containing 10micrograms (400 IU) of vitamin D throughout the year.

Vitamin D testing

Vitamin D status is best assessed by measuring **serum 25OHD** (25-hydroxyvitamin D). Serum level of other '**bone health markers**' should also be checked such as Calcium, Alkaline phosphatase (ALP), Phosphate and eGFR (or Creatinine clearance).

It is noted by the specialist that Parathyroid hormone levels would generally be raised with low vitamin D levels and hence testing is not required.

Routine vitamin D screening is not advisable. The following recommendation should be followed:

	Patient Group	Recommendation
1	Patients with bone diseases that - a) may be improved with vitamin D treatment. Such as - Osteomalacia Insufficiency fracture Paget's disease or b) where correcting vitamin D deficiency before starting osteoporosis treatment is necessary. Such as - Unexpectedly low bone mineral density Bone mineral loss while on osteoporosis treatment Treatment with a potent antiresorptive agent such as Zoledronate, Denosumab or Teriparatide Fragility fracture - Correction of calcium and mineral metabolism (e.g. Vitamin D deficiency, hypocalcaemia) should commence before starting treatment with bisphosphonates.	Testing of 25-OHD level is recommended
2	Patients with musculoskeletal symptoms as chronic aches and pains that could be attributed to vitamin D	Testing of 25-OHD level is recommended
3	Asymptomatic individuals at higher risk of developing vitamin D deficiency ('at risk' group)	Routine testing is not recommended
4	Asymptomatic healthy individuals without any risk factor	Testing not recommended

Patients who may be at risk of developing Vitamin D deficiency

An individual who has one or more of the following **risk factor(s)** (**'at risk' group**):

- Age above 65 years
- Institutional care or housebound
- People who have darker skin, for example African, African – Caribbean and South African origin
- Pregnant or breastfeeding woman
- Routine covering of face or body or routine use of sun screen with SPF8 and above
- Vegan or vegetarian diet
- Intestinal malabsorption, liver or renal disease (e.g. after bariatric surgery)
- Patients taking certain drugs, including anticonvulsants, cholestyramine, rifampicin, glucocorticoids, anti-retrovirals
- Patients who due to the global pandemic are unable to leave the home safely.

Signs and symptoms of vitamin D deficiency

- General lethargy, muscle ache and pain
- Muscle weakness, skeletal pain and tenderness
- Pathological fractures
- Osteopenia on plain radiography
- Low bone density on DEXA scan

Treatment for deficiency

Vitamin D status	Treatment recommendation
Vitamin D Deficiency (below 25 nmol/L)	Treatment recommended (<u>Loading dose</u> therapy and <u>Long-term Enhanced dose</u> therapy) (Enhanced dose therapy-should be purchased over the counter*)
Vitamin D Insufficiency (level 25–50 nmol/L)	Treatment is only advised in the following groups of patients: <ul style="list-style-type: none"> • Increased risk of developing vitamin D deficiency in future ('at risk') • Symptoms suggestive of low vitamin D level • Fragility fracture, osteoporosis or high fracture risk. If dietary intake of calcium is less than the required 700mg daily or hypocalcaemia evident on blood tests ,a calcium supplement should also be suggested in line with self-care guidance* e.g. Calcichew tablets - 2 daily • Treatment with antiresorptive medication for bone disease • Raised PTH Treatment recommended (<u>Long-term Enhanced dose</u> therapy ONLY-Purchased over the counter*)
Adequate Vitamin D (Level above 50 nmol/L)	<ul style="list-style-type: none"> • Reassurance and general lifestyle advice.. • Patients in the 'at risk group' may be advised to consider taking a daily supplement containing 10 micrograms (400 IU) of vitamin D daily throughout the year. • The remainder of the UK adult population are advised to consider taking a daily supplement containing 10 micrograms (400 IU) of vitamin D daily during the autumn and winter months (1st October to 31st March inclusive). Treatment recommended Maintenance dose therapy purchased over the counter *. Note: If hypocalcaemia evident on blood tests or inadequate dietary intake prescribe Calci-D® - Chew one tablet daily or Adcal D3® caplets – Take two twice daily.

*Self-care with over the counter preparations is recommended. Please see the Barnsley Self-Care Guidance available at:

http://best.barnsleyccg.nhs.uk/clinical-support/medicines/prescribing-guidelines/Self_Care_Guidance.pdf

Management of low Vitamin D level (1 mcg = 40 IU; 2.5 nmol/l = 1 ng/ml)

Key aims of treatment

- Use adequate doses to ensure correction of vitamin D status (>50 nmol/L)
- Reverse the clinical consequences of low vitamin D level in a timely manner
- Avoid toxicity (rare possibility)

Non-Pharmacological treatment: Lifestyle & General Advice

This information should be made available to all individuals.

- **Diet** provides, at most, 20% of daily requirements.
- **Exposure to sunlight** is the main source of vitamin D in most individuals
 - Aim to spend 20-30 minutes outdoors at least 3 times a week between April and October (this increases to 3-10 times for dark pigmented skin)
 - Face and arms exposed without sunscreen
- **Asymptomatic 'at risk' individuals** (see who is '[at risk](#)' earlier) should be advised to take an OTC Colecalciferol supplement 10 mcg (400 IU) daily or intermittently at higher equivalent dose as a prophylaxis all year round (PHE 2016). Available through the community pharmacy or health food shop.
- **Patient >65years** who are housebound or institutionalised or suffers a fall should be assessed for deficiency and calcium and/or vitamin D prescribed appropriately in line with self-care guidance

Pharmacological treatment

Oral Colecalciferol (Vitamin D3) is the preparation of choice. *Clinicians should prescribe Colecalciferol preparation by brand name as prescribing generically may result in expensive specials being supplied which could cost several hundred pounds per prescription.*

Vitamin D2 (Ergocalciferol) injection should only be used in those who cannot take oral colecalciferol for cultural, dietary, religious or medical reasons.

Treatment Regimes

- Where rapid correction of vitamin D deficiency is required, such as in patients with symptomatic disease or about to start treatment with a potent antiresorptive agent (Zoledronate or Denosumab or Teriparatide), the recommended treatment regimen is based on fixed loading doses followed by regular enhanced dose therapy.
- Where correction of vitamin D deficiency is less urgent and when co-prescribing Calcium and Vitamin D supplements with an oral antiresorptive agent, [enhanced dose](#) therapy may be started without the use of loading doses.

Loading dose therapy (Total of approximately 300,000 IU given over 6-12 weeks)

- Stexerol[®] 25,000 IU tablet. Two tablets weekly for 6 weeks (Suitable for vegetarians; Halal and Kosher certified; Nut, Soya, Gelatine and Gluten-free).
OR
- InVita[®] D3 50,000 IU/1 ml liquid once a week for 6 weeks (Suitable for vegetarians; gelatine, PEG and peanut-oil free).
OR
- Thorens[®] 25,000 IU/2.5 ml liquid twice a week for 6 weeks (Suitable for vegetarians but not for vegan patients. The olive oil excipient has not been certified halal or kosher. Once opened Thorens[®] has a six month expiry date).

The following should be borne in mind:

- Supplements should be taken with food to aid absorption.
- Calcium/vitamin D combinations should not be used as sources of vitamin D for the above regimens, given the resulting high dosing of calcium.
- Re-check vitamin D levels 3 months after initial test.

Enhanced dose therapy (commenced after loading dose therapy course completed) – taken

life long and purchased over the counter in line with the self-care guidance

- A suitable self-care daily vitamin D supplement providing 800-2000 IU daily with good dietary calcium intake.
- OR if poor compliance vitamin D 20,000-25,000 IU monthly with good dietary calcium intake.
- OR combined supplementation with Calcium 1000-1200 mg and vitamin D 20 micrograms (800 IU) daily.

NHS Barnsley CCG in line with NHS England recommendations does not promote the prescribing of vitamin D for maintenance or preventative therapy. Patients requiring maintenance or preventative therapy should be advised to purchase an enhanced dose therapy supplement over the counter preparation in line with the Barnsley self-care guidance: http://best.barnsleyccg.nhs.uk/clinical-support/medicines/prescribing-guidelines/Self_Care_Guidance.pdf NHS England does not classify maintenance or preventative treatment as exceptions.

In the case of surgery resulting in malabsorption of macronutrients and/or micronutrients including vitamin D (e.g. some types of bariatric surgery), patients should be advised to purchase a suitable multivitamin tablet to meet their needs. (If this provides insufficient vitamin D a top up dose of vitamin D may be purchased for a required dose of 20micrograms: (800IU)- 50 micrograms (2000IU)⁸). If the patient develops an actual vitamin/mineral deficiency (confirmed by blood testing), despite taking OTC supplements the patient should be treated to correct the deficiency for the period needed to replenish stores or reverse the deficiency only. Following treatment, once deficiency symptoms are resolved and serum blood concentrations returned to normal levels, patients should be asked to purchase OTC.

If in exceptional circumstances with clinical assessment a prescriber has concerns that a patient might be unable/unwilling to self-care then a prescription (FP10) may be considered. The following brands are appropriate to prescribe in this instance:

- Stexero[®] 25,000 IU tablet, Take one tablet once a month (Cost effective option. Suitable for vegetarians; Halal and Kosher certified; Nut, Soya, Gelatine and Gluten-free).
- Stexero[®] 1000 IU tablet, Take one tablet daily (Suitable for vegetarians; Halal and Kosher certified; Nut, Soya, Gelatine and Gluten-free).
- Thorens[®] 10,000 IU/ml drops. Take 4 drops (800iu) daily (Suitable for vegetarians but not for vegan patients. The olive oil excipient has not been certified halal or kosher. Once opened Thorens[®] has a six month expiry date).
- Thorens[®] 25,000 IU/2.5 ml - Take a 2.5 ml dose vial once a month (Suitable for vegetarians but not for vegan patients. The olive oil excipient has not been certified halal or kosher. Once opened Thorens[®] has a six month expiry date).
- ProD3[®] Vegan (unlicensed) – 800 IU capsule. Take one capsule daily (Reserved only for vegan patients where this is documented in the clinical records).
- ProD3[®] Vegan (unlicensed) – 100 IU/drop. Take 8-10 drops daily (Reserved only for vegan patients where this is documented in the clinical records).

The strategies below have been demonstrated not to work or to have a high risk of being ineffective or causing toxicity, and are therefore not to be recommended:

- Annual depot vitamin D therapy either by intramuscular injection or orally
- Use of activated vitamin D preparations (calcitriol and alfacalcidol).

Treatment monitoring

Aims

- detect those who remain deficient after loading
- detect those who become deficient during [enhanced dose therapy](#)
- detect those in whom vitamin D therapy uncovers sub-clinical primary hyperparathyroidism

Routine monitoring of serum 25OHD is unnecessary but may be appropriate in patients with symptomatic vitamin D deficiency or malabsorption and where poor compliance with medication is suspected.

Tests required

1. **Adjusted serum calcium:** 1 month after completing the loading regimen or after starting lower dose vitamin D supplementation in case primary hyperparathyroidism has been unmasked. The presence of hypercalcaemia ought to lead to cessation of further vitamin D supplementation prior to investigation of the hypercalcaemia
2. **Serum Vitamin D (25OHD) at 6 months.** Routine monitoring is unnecessary but may be appropriate in patients with symptomatic vitamin D deficiency or malabsorption and where poor compliance with medication is suspected.

Vitamin D toxicity

- European Food Safety Authority (EFSA) = upper limit of 100 micrograms (4000 IU) a day (or equivalent) is safe for adults and children over 11 years of age
- Short term (4 months or less)⁸ Vitamin D intake below 10,000 IU/day (or equivalent) is not usually associated with toxicity
- Toxicity as defined by hypercalcaemia should be suspected in vitamin D concentrations of 200 nmol/L or above,
- Yearly high-dose vitamin D is ineffective and may cause increased risk of fracture

Indications for specialist referral

- Atypical clinical manifestations, renal stones, hypercalcaemia
- Lack of clinical response to 2 courses of loading Vitamin D therapy (exclude non-compliance)
- Chronic renal impairment (eGFR <35 ml/min)
- Secondary causes – malabsorption, liver disease, renal disease, lymphoma, metastatic cancer, Parathyroid disorders, sarcoidosis and tuberculosis.

Special situations

Pregnant and breastfeeding women

All pregnant and breastfeeding women are recommended to receive vitamin D 10micrograms (400 IU) per day (PHE 2016). In Barnsley, this is provided through the Health Start Vitamins. Please visit www.healthystart.nhs.uk for further information. Pregnant and breastfeeding women who are eligible for the Government's [Healthy Start](#) scheme should be signposted to their local '[Children's Centre](#)' to receive their supplements. Patients not eligible for vouchers can buy Healthy Start vitamins from all children's centres in Barnsley or be signposted to their local pharmacy who will be able to sell them a suitable supplement. The Barnsley Healthy Start Vitamin D Guidance is available at:

<http://best.barnsleyccg.nhs.uk/clinical-support/medicines-management/APC%20memos%20and%20minutes/Enc%20Healthy%20Start%20Vitamin%20D%20Guidance%202017.pdf>

Vitamin D should be measured ONLY on the basis of risk factor and clinical symptoms. Low level should be treated as in the non-pregnant state. However, maximum dosing of colecalciferol is 4000 IU daily during pregnancy. High intermittent dosing is not advised.

Suggested regime for treatment of Vitamin D deficiency in pregnancy would be:

- Thorens® 10,000 units/1ml (400 IU=2 drops); 20 drops daily for 10 weeks (total 280,000 units) – first line

Drug induced vitamin D deficiency⁷

If the patient is taking drugs that accelerate Vitamin D metabolism or if there are concerns regarding absorption, then, higher doses may be required. The Medicines and Healthcare Regulatory Agency (MHRA) have advised that at-risk patients on long-term anticonvulsant therapy may require vitamin D supplementation 10 micrograms (400 IU) daily as a prophylaxis. A suitable product listed above (at the reduced maintenance dose of 10micrograms 400IU) may be prescribed for example Thorens® 10,000 IU/ml drops. Take 2 drops (400iu) daily in exceptional circumstances only.

Intestinal malabsorption / Chronic liver disease

Vitamin D deficiency in these situations should be treated with 2-3 times higher doses of pharmacological vitamin D. Patient may require injectable preparation.

Patients with renal impairment

1-hydroxylation of Vitamin D is impaired in renal impairment. Hence, patients with eGFR 35-50 ml/min/1.73m² may require higher doses of Vitamin D supplementation. If eGFR is below 35, patient will require Alfacalcidol or Calcitriol (Specialist initiation only).

Primary hyperparathyroidism and Vitamin D deficiency

These patients should be treated as needed and serum calcium should be monitored.

References

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Contact names and details

Contact Details	Telephone number	Email
Dr Z Merza (Consultant Endocrinologist)	01226 730000	z.merza@nhs.net
Dr A Adebajo (Consultant Rheumatologist)	01226 730000	aadebajo@nhs.net
Dr Veronika Szentesi (ortho geriatrics)	01226 730000	Veronika.Szentesi@nhs.net
Dr Catherine Dibden (Consultant Biochemist)	01226 730000	Catherine.Dibden@nhs.net
Medicines Information	01226 432857	gilliansmith2@nhs.net

Updated in April 2021 by Joy Power (Medicines Management Pharmacist in conjunction with Rheumatology, Endocrinology and Biochemistry). Ratified by the Area Prescribing Committee, April 2021. Next review due April 2023