

Information for Clinicians

VITAMIN D DEFICIENCY IN ADULTS

Background

- Vitamin D (calciferol) is the collective name for a group of related steroid-like molecules, which includes vitamin D2 (ergocalciferol) and vitamin D3 (cholecalciferol). It is a fat soluble vitamin and is stored in liver and adipose tissue.
- Vitamin D regulates the absorption of calcium and phosphate, and is essential for skeletal growth and bone health. It also has several non-skeletal roles in the body, such as regulating cell proliferation and differentiation and maintaining a healthy immune system.
- Around 20% adults may have low vitamin D status. Severe deficiency of vitamin D can result in rickets in children and osteomalacia in adults.
- The principle source of vitamin D for humans is from synthesis in the skin following exposure to UV light. In the northern hemisphere, the intensity of sunlight required to generate vitamin D in this way is only present during the summer months.
- Dietary vitamin D is available in foods such as oily fish, cod liver oil, red meat, fortified cereals, fortified margarine/spreads and egg yolks. In the UK, milk is not fortified with vitamin D, so dairy products contain only small amounts of vitamin D.
- The biologically active form of vitamin D is synthesised in the body by hydroxylation in the liver, and then the kidneys, to make 1,25-dihydroxyvitamin D (calcitriol).
- Routine laboratory testing measures 25-hydroxyvitamin D, which is the most stable form of the vitamin circulating in the plasma, and reflects both cutaneous synthesis and dietary intake.

Risk factors for Vitamin D deficiency

Table 1 summarises the main risk factors for vitamin D deficiency in the UK population¹:

Table 1: Risk factors for Vitamin D deficiency

| Inadequate UVB light exposure | Inadequate dietary intake or absorption | Metabolic factors |
|--|---|--|
| Pigmented skin (non-white ethnicity) | Vegetarian/vegan (or other fish-free diet) | People aged ≥65 years (reduced synthesis in the skin) |
| Lack of sunlight exposure or atmospheric pollution | Malabsorption (e.g. coeliac disease, cystic fibrosis, Crohn's disease etc.) | Pregnant/breastfeeding women |
| Latitude | Short bowel syndrome | Drug interactions, e.g. rifampicin, anticonvulsants (carbamazepine, oxcarbazepine, phenobarbital, phenytoin, primidone, valproate), isoniazid, cholestyramine, sucralfate, glucocorticoids, highly active antiretroviral treatment (HAART) |
| Skin concealing garments or routine use of sun protection factor 15 or above | Cholestatic liver disease, jaundice | Chronic liver disease |
| Housebound or indoor living (e.g. care homes) | | Chronic kidney disease |
| Seasonal | | Nephrotic syndrome |

Prevention of Vitamin D deficiency/insufficiency

The Scientific Advisory Committee on Nutrition (SACN) report on Vitamin D and Health² and NICE Clinical Knowledge Summary (2018)³ recommend the following for the UK population to prevent vitamin D deficiency/insufficiency:

- **People in higher risk groups (see Table 1) are advised to take a daily supplement of 400 IU (10 µg) vitamin D throughout the year.**
- In winter months (October to early March), ALL adults (and children >4 years old) should consider taking a daily supplement of 400 IU (10 µg) vitamin D
- In summer months, the majority of the population will get enough vitamin D through exposure to sunlight and a healthy, balanced diet.

NOTE: Supplements are widely available as over the counter preparations and SHOULD NOT be prescribed.

Vitamin D and COVID-19

In December 2020, in response to the global pandemic, NICE published a rapid guideline⁴ on the use of vitamin D supplements to either prevent or treat COVID-19. While acknowledging there is insufficient evidence at present to advocate use of supplements for this purpose, the panel strongly reiterated current UK government advice regarding year round supplementation in high risk groups and in the whole population over the age of 4 years old during the winter months. This is considered to be particularly important during the pandemic because people have been confined indoors more than usual during the spring and summer months⁵.

Vitamin D supplements should not be offered solely to prevent or treat COVID-19, except as part of a clinical trial.

When should vitamin D be measured?

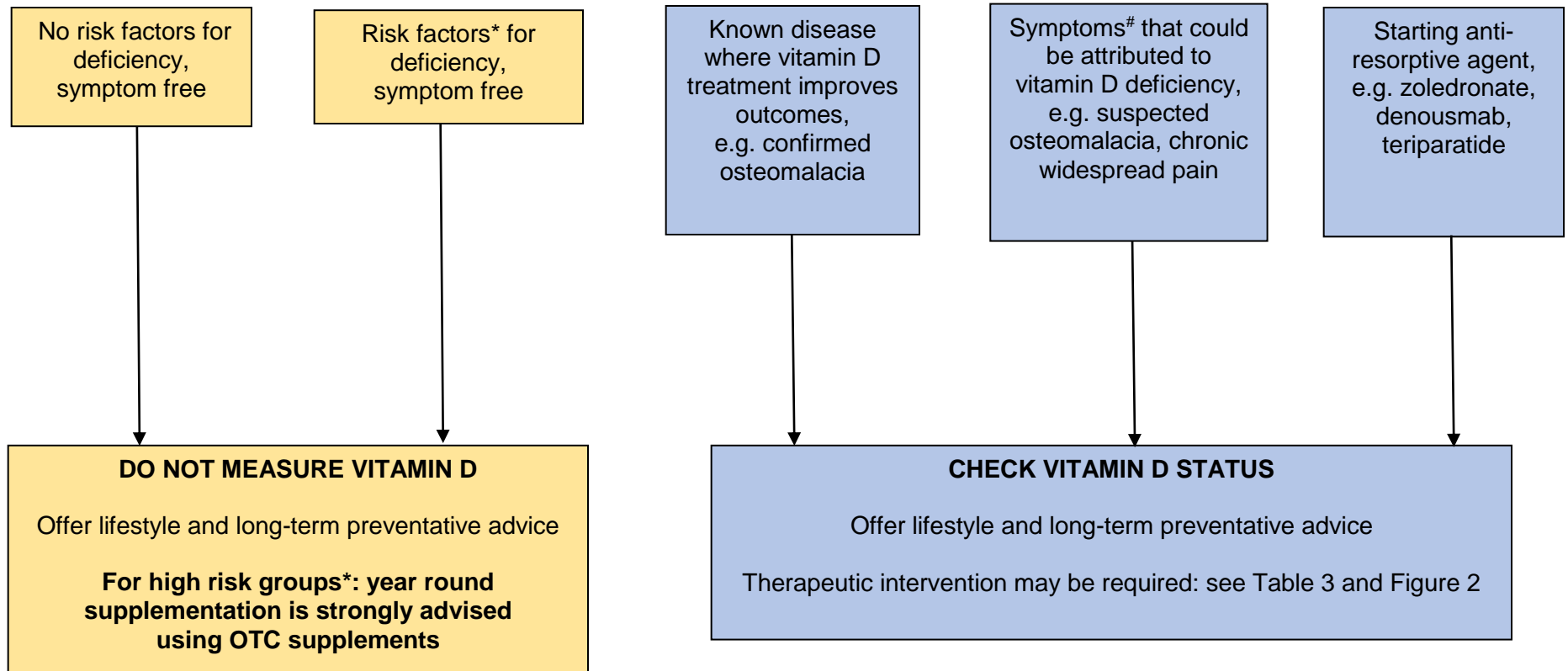
Routine testing for vitamin D deficiency is NOT necessary.

Vitamin D (25-hydroxyvitamin D) measurement is only indicated:

- for patients with diseases with outcomes that may be improved with vitamin D treatment, e.g. confirmed osteomalacia, osteoporosis. (NB: measurement is **not necessary** if patient is co-prescribed vitamin D with their anti-resorptive treatment)
- for patients with symptoms that could be attributed to vitamin D deficiency, e.g. suspected osteomalacia, chronic widespread pain with other features of osteomalacia
- before starting patients on a potent antiresorptive agent (zoledronate, denosumab, teriparatide)⁶.

See Figure 1 for a summary of the guidance from the Royal Osteoporosis Society (Vitamin D and Bone Health: a practical clinical guideline for patient management, 2018).⁶

Figure 1: When should vitamin D be measured?



***Risk factors, e.g. lack of sunlight exposure, darker skin, housebound, malabsorption, pregnant/breastfeeding (see Table 1 for full details)**

#Symptoms can include muscle aches and weakness, especially in quadriceps and glutei, waddling gait, chronic widespread pain or bone pain in lower back, pelvis and foot.

Interpretation of vitamin D results

The Royal Osteoporosis Society guideline⁶, Vitamin D and Bone Health: a practical clinical guideline for patient management, recommends the following interpretation of vitamin D results with respect to bone health (see Table 3).

Table 3: Interpretation of vitamin D results

| Vitamin D concentration | Vitamin D status | Management |
|-------------------------|---|---|
| <25 nmol/L | Deficient | High dose cholecalciferol, then maintenance treatment Further investigations generally not required, but may be helpful to identify treatable causes of vitamin D deficiency |
| 25-50 nmol/L | May be inadequate for some people | Review modifiable risk factors Lifestyle advice. Maintenance vitamin D supplements |
| >50 nmol/L | Adequate: sufficient for bone health in most people | Lifestyle advice, including supplements as advised for general population |

Further investigations

The major causes of vitamin D deficiency are lack of sun exposure and/or poor dietary intake. Further investigations are therefore generally NOT required.

Other common causes are malabsorption and underlying disease such as kidney or liver dysfunction, for which specific investigations may be appropriate. These could include FBC, U&E/eGFR, LFTs, calcium/phosphate, PTH (if hypercalcaemic). **However, these tests are not routinely indicated in vitamin D deficiency.**

For further advice about individual patients, please contact the duty biochemist to discuss appropriate investigations (tel: 01225 824050).

Management

- A summary of the BSW CCG treatment guidelines for vitamin D deficiency is shown in Figure 2. For more detailed information, please refer to the full guideline.⁷
- If there is severe vitamin D deficiency (<25 nmol/L), a **treatment** (loading) dose followed by long-term **maintenance** vitamin D is recommended (maintenance vitamin D should be over the counter medication and not prescribed)
- If serum vitamin D is between 25-50 nmol/L, treatment **may** be indicated if high risk.

- If serum vitamin D is >50 nmol/L, vitamin D replacement is NOT necessary, unless there are specific clinical indications.
- Routine monitoring of serum vitamin D is usually unnecessary; it may be appropriate in patients with symptomatic vitamin D deficiency, malabsorption, or if poor compliance is suspected.
- Whilst on maintenance dose, re-check bone profile and vitamin D if there are symptoms suggestive of vitamin D toxicosis or hypercalcaemia (confusion, polyuria, polydipsia, anorexia, vomiting, constipation or muscle weakness).
- If taking potent anti-resorptive agents (e.g. zoledronate, denosumab, teriparatide), check vitamin D before starting treatment, then annually (to prevent hypocalcaemia developing).

References

1. Nottinghamshire Area Prescribing Committee: Vitamin D Management in Adults (2021)
<https://www.nottsapc.nhs.uk/media/1248/vitamin-d-guidelines-adults.pdf> (accessed 21.05.21)
2. Scientific Advisory Committee on Nutrition: Vitamin D and Health (2016)
https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/537616/SACN_Vitamin_D_and_Health_report.pdf (accessed 21.05.21)
3. NICE Clinical Knowledge Summary (last revised December 2020): Vitamin D deficiency in adults – treatment and prevention
<https://cks.nice.org.uk/topics/vitamin-d-deficiency-in-adults-treatment-prevention/> (accessed 21.05.21)
4. NICE guideline 187: COVID-19 rapid guideline: vitamin D (2020)
<https://www.nice.org.uk/guidance/ng187/resources/covid19-rapid-guideline-vitamin-d-pdf-66142026720709> (accessed 24.05.21)
5. Vitamin D supplementation during winter (November 2020): PHE and NICE statement
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6. Royal Osteoporosis Society 2018: Vitamin D and Bone Health: a practical clinical guideline for patient management
<https://strwebprdmedia.blob.core.windows.net/media/ef2ideu2/ros-vitamin-d-and-bone-health-in-adults-february-2020.pdf> (accessed 21.05.21)
7. BSW CCG Treatment of Vitamin D deficiency in adults (March 2021)
<http://bswformulary.nhs.uk/chaptersSubDetails.asp?FormularySectionID=9&SubSectionRef=09.06.04&SubSectionID=A100> (accessed 21.05.21)

Figure 2: Treatment guidelines for vitamin D deficiency⁷ (BSW CCG March 2021)

