

## Vitamin D tests



Vitamin D testing has increased rapidly in the last decade. No benefit has been shown for testing groups who are not at risk of deficiency. Testing should only be ordered in a selected group.

### Key points

- ▶ An MBS review has identified a rapid increase in vitamin D testing. Over the last 10 years, vitamin D testing has increased by 3587%.<sup>1</sup>
- ▶ Guidelines recommend testing people with signs and symptoms of vitamin D deficiency and populations at high-risk of moderate to severe vitamin D deficiency.<sup>2,3</sup> Data from two studies indicate that only 4% of Australians have moderate to severe vitamin D deficiency (serum 25-hydroxyvitamin D levels < 25 nmol/L).<sup>4,5</sup>
- ▶ Use of vitamin D testing for screening in healthy and low-risk populations is not necessary.<sup>2,3</sup> The MBS review of vitamin D testing noted that 98% of vitamin D tests were regularly requested with other MBS items, presumably for the purposes of screening/testing rather than monitoring.<sup>1</sup>
- ▶ In order to encourage the quality use of testing under Medicare, vitamin D testing has been split into two types:
  - 25-hydroxyvitamin D testing for high-risk patient populations to assess overall vitamin D status and diagnose vitamin D deficiency
  - 1,25-dihydroxyvitamin D testing for patients with severe conditions such as renal failure or hypercalcaemia

This decision is evidence-based and supported by the Medical Services Advisory Committee.

### What is the role of vitamin D?

Vitamin D has two main forms: vitamin D<sub>3</sub> (cholecalciferol) and vitamin D<sub>2</sub> (ergocalciferol).<sup>6</sup>

The metabolites of vitamin D are the important forms.

- ▶ 25-hydroxyvitamin D<sub>3</sub> and 25-hydroxyvitamin D<sub>2</sub>, are the major circulating forms of vitamin D measured in most assays and reflect vitamin D status.<sup>6</sup>
- ▶ 1,25-dihydroxyvitamin D<sub>3</sub>, (or calcitriol) and 1,25-dihydroxyvitamin D<sub>2</sub>, are the biologically active forms.<sup>6</sup>

Vitamin D is important to maintain bone health, deficiency leads to osteomalacia and contributes to fragility fractures.<sup>6</sup>

Epidemiological studies have shown an association of low circulating levels to a growing list of conditions, including cancer, cardiovascular disease, autoimmune conditions, diabetes and dementia as well as skeletal conditions.<sup>7,8</sup> It is less clear if many of these associations represent a causative or preventive relationship.<sup>9</sup>

Analysis from a prospective study suggests a harmful association of serum 25-hydroxyvitamin D with cancer mortality in men, although the study was limited by small numbers of cases for subgroup analyses.<sup>10</sup>

## Requesting vitamin D tests

In order to encourage the quality use of testing under Medicare, vitamin D testing items 66608 and 66609 have been deleted and two new items have been created for 25-hydroxyvitamin D and 1,25-dihydroxyvitamin D:

ITEM	ITEM DESCRIPTION	SCHEDULE FEE
66833	<p>25-hydroxyvitamin D, quantification in serum, for the investigation of a patient who:</p> <p>(a) has signs or symptoms of osteoporosis or osteomalacia; or</p> <p>(b) has increased alkaline phosphatase and otherwise normal liver function tests; or</p> <p>(c) has hyperparathyroidism, hypo- or hypercalcaemia, or hypophosphataemia; or</p> <p>(d) is suffering from malabsorption (for example, because the patient has cystic fibrosis, short bowel syndrome, inflammatory bowel disease or untreated coeliac disease, or has had bariatric surgery); or</p> <p>(e) has deeply pigmented skin, or chronic and severe lack of sun exposure for cultural, medical, occupational or residential reasons; or</p> <p>(f) is taking medication known to decrease 25OH-D levels (for example, anticonvulsants); or</p> <p>(g) has chronic renal failure or is a renal transplant recipient; or</p> <p>(h) is less than 16 years of age and has signs or symptoms of rickets; or</p> <p>(i) is an infant whose mother has established vitamin D deficiency; or</p> <p>(j) is an exclusively breastfed baby and has at least one other risk factor mentioned in a paragraph in this item; or</p> <p>(k) has a sibling who is less than 16 years of age and has vitamin D deficiency</p>	\$30.05
66834	<p>A test described in item 66833 if rendered by a receiving Approved Pathology Practitioner (Item is subject to Rule 18*)</p>	\$30.05

66835	1, 25-dihydroxyvitamin D - quantification in serum, if the request for the test is made by, or on advice of, the specialist or consultant physician managing the treatment of the patient	\$39.05
66836	<p>1, 25-dihydroxyvitamin D— quantification in serum, if:</p> <p>(a) the patient has hypercalcaemia; and</p> <p>(b) the request for the test is made by a general practitioner managing the treatment of the patient</p>	\$39.05
66837	<p>A test described in item 66835 or 66836 if rendered by a receiving Approved Pathology Practitioner (Item is subject to Rule 18*)</p>	\$39.05

\* Rule 18: an arrangement under which Medicare benefits payable in a patient episode for a set of pathology services, containing more than three items, ordered by a general practitioner for a non-hospitalised patient, will be equivalent to the sum of the benefits for the three items with the highest Schedule fees.<sup>1</sup>

### What does vitamin D testing involve?

A vitamin D test measures only one of the two metabolites to assess serum vitamin D levels:<sup>2</sup>

- ▶ 25-hydroxyvitamin D (25-OHD) (routine Vitamin D status)<sup>2</sup>
- ▶ 1,25-dihydroxyvitamin D (only in rare circumstances such as hypercalcaemia with suppressed parathyroid hormone).<sup>2,11</sup>

There are two different assays for measuring serum levels of 25-OHD:<sup>12,13</sup>

- ▶ Liquid chromatography-tandem mass spectrometry. Sensitive and specific method that is referred to as a 'gold standard' test. Can be slow and requires expensive equipment and skilled staff.
- ▶ Commercial immunoassays either using radioactive or chemical markers. Less specific and sensitive as these may not distinguish between the metabolites of vitamin D. Cheaper and quicker to conduct (about half the cost of liquid chromatography).

## Limitations of vitamin D immunoassays

In the past, different immunoassays yielded vastly different results, with inter-assay variation up to 25% at low serum 25-OHD levels (15 nmol/L).<sup>14</sup>

The accuracy of different immunoassays for measuring 25-OHD is becoming more consistent with new reference standards. However, the bias and imprecision of many automated methods may still be problematic at the lower, clinically important range (< 50 nmol/L) of the assay.<sup>15</sup>

It is recommended to monitor serum 25OH-D levels in the same laboratory after treatment.<sup>2</sup>

## Optimal vitamin D levels

There is debate about the optimal level of serum 25-OHD. Values anywhere between 50 and 110 nmol/L are advocated.

Levels of 50 nmol/L or higher are recommended at the end of winter (Table 1). During summer levels are expected to be 10–20 nmol/L higher (60–70 nmol/L).<sup>2,4</sup>

**Table 1. Recommended serum concentrations of 25-OHD<sup>15</sup>**

VITAMIN D STATUS	SERUM 25-OHD CONCENTRATIONS (NMOL/L)
Adequate	≥ 50
Mild deficiency	30–49
Moderate deficiency	12.5–29
Severe deficiency	< 12.5

## Clinical indications for vitamin D testing

Only patients listed in the MBS item descriptors should be tested.

No benefit has been shown for testing groups who are not at risk of deficiency.<sup>1</sup> Therefore do not routinely screen for vitamin D status.<sup>2,3</sup> Even though a large proportion of Australians (between 31% and 58%) are estimated to have vitamin D levels below 50 nmol/L depending on the season, moderate to severe deficiency (25-OHD level < 25 nmol/L) is uncommon and only present in around 4% of the population.<sup>4,5</sup>

The clinical significance of mild or moderate deficiency is not fully determined and the optimal serum concentration of vitamin D is not established.<sup>15</sup>

## Supplementation without testing

Supplementation without testing may be appropriate in some high-risk groups including housebound, older and/or disabled people, those in residential care and people with dark-skin tones.<sup>15</sup>

## Practice points

Note the indication for testing on the request form.

- ▶ Signs and symptoms to suggest moderate to severe deficiency (osteomalacia, osteoporosis, rickets, bone pain or tenderness, muscle weakness or pain, fracture increased alkaline phosphatase with otherwise normal liver function tests, hyperparathyroidism, hypo- or hypercalcaemia, hypophosphataemia)<sup>1,2</sup>
- ▶ Risk factors associated with moderate to severe deficiency (see MBS item indicators).

## Further information

For further detail see the MBS review, Vitamin D testing report (at [www.msac.gov.au/internet/msac/publishing.nsf/Content/0014r-public](http://www.msac.gov.au/internet/msac/publishing.nsf/Content/0014r-public)).

For more information on vitamin D refer to:

- ▶ When is vitamin D testing appropriate? (at [www.nps.org.au/vitamin-d-deficiency-tests](http://www.nps.org.au/vitamin-d-deficiency-tests)).
- ▶ Vitamin D: cause or effect? (at [www.nps.org.au/health-news-evidence](http://www.nps.org.au/health-news-evidence)).

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