

# Vitamin D Deficiency

## Health conditions, signs and supplement considerations



Dr Emma Derbyshire PhD, Freelance  
Nutritionist and Health Writer

It is widely accepted by scientists that vitamin D deficiency is a prominent health problem in the UK, impacting on health and wellbeing. Although the causes underpinning vitamin D deficiency are multi-faceted, inadequate skin synthesis, limited food fortification and availability of vitamin D from natural food sources are contributing factors. This article explains how certain health conditions can further exacerbate the risk of vitamin D deficiency, describes the signs of vitamin D deficiency and discusses potential ways forward.

### Introduction

There have been rising concerns about the high prevalence of low vitamin D intakes and deficiency in Europe.<sup>1</sup> In the UK, Reference Nutrient Intakes (RNI) for vitamin D are currently only set for children aged 1.5-3 years and adults aged 65 years and over. Using these, data from the latest UK National Diet and Nutrition Survey (NDNS) shows that mean intakes of vitamin D from food sources are just 27% of the RNI for young children and 33% of the RNI for those 65 years and over, indicating a limited intake from foods alone.<sup>2</sup>

Blood biomarkers, however, are the gold standard in terms of evaluating vitamin D status accurately. While there are more than 50 different vitamin D metabolites, 5-hydroxyvitamin D (25(OH)D) is regarded as the best single measure of vitamin D status.<sup>3</sup> When it comes to

identifying vitamin D deficiency there are some disparities in the cut-offs used. Those used by the National Osteoporosis Society (2016)<sup>4</sup> are summarised in **Table One**. However, it should be considered that the UK NDNS used a plasma vitamin D levels of <25 nmol/L to identify vitamin D deficiency.<sup>5</sup>

Based on this it was identified that, on average, 19.7% of boys and 24.4% of girls aged 4-10 years had 25(OH)D levels <25 nmol/L, indicating deficiency.<sup>2</sup> Furthermore, 24% of men and 21.7% of women aged 19-64 years had plasma vitamin D levels below these thresholds.<sup>2</sup> These figures, however, are averaged out across the year. When looking at seasonal variations in vitamin D status, the UK NDNS found that 40% of young people and adults were deficient between the months January to March.<sup>6</sup>

**Table One: Vitamin D Thresholds in Respect to Bone Health**

Serum 25(OH)D <30 nmol/L	Deficient
Serum 25(OH)D 30-50 nmol/L	May be inadequate in some people
Serum 25(OH)D >50 nmol/L	Sufficient for almost the whole population

Source: National Osteoporosis Society (2016)<sup>4</sup>

Vitamin D deficiency is also highly prevalent amongst UK South Asians. A study of 1105 South Asian males recruited from Birmingham health practices found that 42% were vitamin D deficient.<sup>7</sup> Other work with South Asian women of childbearing age (n=35) living in Surrey showed that 81% had vitamin D levels <25 nmol/L during the winter and 79.2% during the autumn.<sup>8</sup> Averaging these figures out, it has been reported that vitamin D deficiency rates vary between 40% and 60% in the healthy general adult European population.<sup>9</sup> Unfortunately, certain health conditions, particularly malabsorption syndromes can result in a very high prevalence of vitamin D deficiency.<sup>10</sup> This article looks at these aspects in more detail, along with common signs of vitamin D deficiency and potential ways forward.

### Health conditions

As mentioned, particular health conditions including malabsorption syndromes, such as coeliac disease, cystic fibrosis, short bowel syndrome and inflammatory bowel disease (IBD), can increase the prevalence of vitamin D deficiency to levels exceeding that of the general population.<sup>10</sup>

A PubMed search identified seven key studies evaluating the prevalence of vitamin D deficiency amongst adolescents and adults with malabsorption syndromes (see **Table Two**). One Canadian study showed that up to 26% of children and young people had inadequate 25(OH)D levels.<sup>11</sup> Another study conducted on patients with acute intestinal failure, aged 3-22 years, showed that 39.8% had low serum vitamin D levels, indicating deficiency, and 12.5% had a low bone mineral density.<sup>12</sup>

Amongst adults, an Irish study involving 81 patients with Crohn's disease (CD) found that 63% were vitamin D deficient using a 50 nmol/L cut-off.<sup>13</sup> In a cross-sectional study of Iranian patients with CD there was found to be a higher frequency of low vitamin D levels amongst those with the active form of the disease compared to those in remission (80% versus 50%).<sup>14</sup> A pooled analysis of patients with CD and ulcerative colitis in the U.S showed that 49.8% were vitamin D deficient and 10.9% had severe deficiency.<sup>15</sup> Finally, with regard to coeliac disease, a U.S. study identified that 25% of patients had vitamin D deficiency.<sup>16</sup>

Overall, these studies show that vitamin D deficiency is highly prevalent amongst patients with malabsorption syndromes. Clearly, international uniformity is needed to

align biochemical cut-offs used to identify vitamin D deficiency. On a separate note it should be considered that particular medications, such as antiresorptive medications for bone disease, antiepileptic drugs, or oral glucocorticoids, can also increase the need to treat vitamin D deficiency.<sup>4</sup>

### Symptoms

Symptoms of vitamin D deficiency vary across the lifespan and according to the level of deficiency (see **Table Three**). Amongst adolescents, severe vitamin D deficiency has been associated with muscle cramps, pain in weight-bearing joints, back and/or calves, problems walking, running and/or climbing the stairs.<sup>17</sup>

In adults, those with a mild lack of vitamin D may be asymptomatic, perhaps only feeling tired or having general aches and pains.<sup>18</sup> In severe cases of vitamin D deficiency this can lead to more serious health problems, including osteomalacia and increased fracture risk post menopause.<sup>18</sup>

Vitamin D deficiency has been linked to increased symptoms of faecal incontinence

amongst women attending urogynaecology clinics.<sup>19</sup> Whilst suboptimal vitamin D status (<50 nmol/L) has been associated with an increased risk of severe infections and sepsis amongst those that are critically ill.<sup>20</sup>

### Considerations

#### Objective

Firstly, it is important to identify the main objective when considering vitamin D supplementation. For example, is it to maintain and prevent deficiency, or is it to treat diagnosed vitamin D deficiency? For the former, the European Food Safety Authority (EFSA) have recently proposed an Adequate Intake of 15 µg/day (600 IU) for adults.<sup>21</sup> At this level of intake it is thought that most of the population could achieve a serum 25(OH)D concentration near, or above, the target of 50 nmol/L.<sup>21</sup> In the UK, RNIs have not been available for vitamin D for adults. However, an RNI of 10 µg/day (400 IU) has been suggested for the UK population aged 11-65 years.<sup>22</sup> This is regarded as the amount needed to achieve a serum 25(OH)D levels ≥25 nmol/L during winter in 97.5% of the population.<sup>22</sup>

**Table Two: Malabsorption Conditions and Vitamin D Deficiency**

Reference	Disease	Deficiency Prevalence
Ubesie <i>et al.</i> (2013) U.S.	Intestinal failure (3-22 years)	39.8%
Norton <i>et al.</i> (2015) Canada	Cystic fibrosis (1-18 years)	23-26%
Tavakkoli <i>et al.</i> (2013) U.S.	Coeliac disease (adults)	25%
Suibhne <i>et al.</i> (2012) Ireland	Crohn's disease (adults)	63-68% in winter 50% in summer
Torki <i>et al.</i> (2015) Iran	Crohn's disease (adults)	18%
Ulitsky <i>et al.</i> (2011) U.S.	Inflammatory bowel disease* (adults)	49.8% deficient 10.9% severe deficiency
Torki <i>et al.</i> (2015) Iran	Ulcerative colitis (adults)	39%

Key: \* Data pooled for Crohn's disease and ulcerative colitis.

**Table Three: Symptoms of Vitamin D Deficiency**

Reference	Symptoms	Population
Soliman <i>et al.</i> (2014)	Pain in weight-bearing joints, back, thighs and/or calves, difficulty in walking and/or climbing stairs, or running and muscle cramps.	Teenagers
Parker-Autry <i>et al.</i> (2014)	Faecal incontinence	Women
Galesanu & Mocanu (2015)	Tiredness, general aches and pains	General population with mild deficiency
Galesanu & Mocanu (2015)	Rickets, osteomalacia	General population with severe deficiency
De Haan <i>et al.</i> (2014)	Increased risk of infections	Adults (critically ill)

In cases of severe vitamin D deficiency, for example, patients with diagnosed bone diseases or who are using antiresorptive medications, loading regimens may be required.<sup>4</sup> The intention of these is to correct vitamin D status rapidly. Loading doses of up to 7,500 µg (300,000 IU) have been advised by the National Osteoporosis Society (2016), given as weekly or daily split doses. So, for example, taking 20 µg/day (800 IU) capsules, five a day given for 10 weeks (total of 280,000 IU), could be used in the rapid correction of vitamin D deficiency<sup>4</sup> without exceeding the EFSA Upper Limit.<sup>23</sup> It should be considered, however, that supplements are best taken with food to aid absorption.<sup>4</sup>

Following on from this, a maintenance period should be considered one month after the loading period with doses equivalent to 20 µg/day (800 IU) to 50 µg/day (2000 IU) daily (occasionally up to 4,000 IU daily), given either daily or intermittently at a higher equivalent dose.<sup>4</sup> The National Osteoporosis Society also advises that adjusted serum calcium levels should be measured one month after completing the loading regime, or after commencing vitamin D supplementation, in case primary hyperparathyroidism has been unmasked.<sup>4</sup>

### Patient preference

With regard to the form of vitamin D to be taken, systematic and meta-analytical evidence indicates that vitamin D<sub>3</sub> (cholecalciferol) is more effective at raising 25(OH)D levels than D<sub>2</sub> (ergocalciferol).<sup>24</sup> Vitamin D<sub>3</sub> supplementation in doses of 25µg (1000IU) daily for 25 weeks beginning at the end of summer has been found to be more effective at maintaining 25(OH)D levels through the winter than D<sub>2</sub>.<sup>25</sup> In terms of half-life, vitamin D<sub>3</sub> also appears to be more effective at sustaining 25(OH)D levels in the longer-term.<sup>26</sup>

Depending on patient preferences and in order to improve adherence to vitamin D supplementation programmes, there is potential to adapt the dosing protocol. For example, a study of 48 women aged 81 years who had undergone surgery to repair hip fractures either daily, weekly and monthly vitamin D dosing after two months achieved serum 25(OH)D improvements equally well.<sup>27</sup>

It should be recognised that some patients may find capsules hard to swallow. In these cases smaller tablets can be prescribed, or crushed and mixed with texture modified food and drinks. For individuals who are vegetarian, licensed vitamin D<sub>3</sub> products can be found that do not contain animal derived ingredients. Equally, there are also products available that do not contain peanut oil or soya, which can be tolerated by patients at risk of peanut or soya allergies.

### Licensing

Given the fact that unlicensed products are uncontrolled, this means that they are not guaranteed to contain the correct dose of vitamin D. As well as being more expensive, these products also have the potential to expose patients to risk. Consequently, the best way forward is to use licensed vitamin D<sub>3</sub> products authorised by the UK Medicines Healthcare Products Regulatory Authority (MHRA) for efficacy, safety and quality.<sup>28</sup> Typically, these are available by prescription, rather than an over-the-counter/supermarket purchase.

### Upper limits

With regard to Upper Limits (UL), the EFSA have set this at 100 µg (4000 IU) per day for vitamin D. This applies to adults in general, including pregnant and lactating

women. Given that rapid growth and bone formation takes place during late childhood, a similar UL has also been set for 11-17 year olds.<sup>23</sup> Similarly, an UL of 100 µg per day for adults has also been established by the Institute of Medicine, along with an adequate circulating level of 50 to 125 nmol/L 25(OH)D.<sup>29</sup>

With regard to toxicity effects, the U.S. Food and Nutrition Board of the Institute of Medicine concluded that vitamin D intakes below 250 µg (10,000 IU) per day are typically not associated with toxicity effects. Doses equal to or above 50,000 IU/day, taken for several weeks or months have been associated with some toxicity effects, including hypercalcaemia.<sup>29</sup> Subsequently, as previously mentioned, it is advisable that serum calcium levels should be checked one month after loading regimes have been used and completed.<sup>4</sup>

## Conclusions

Vitamin D deficiency is highly prevalent in the UK, especially during the winter months and amongst vulnerable populations, including those who have darker skin or malabsorption conditions. Certainly, signs of vitamin D deficiency can be difficult to identify but can include tiredness and general fatigue. Individuals reporting these symptoms, especially those with malabsorption conditions, should be encouraged to have their serum 25(OH)D levels measured by a medical practitioner.

Given that few foods naturally contain vitamin D (although some may be fortified) these levels are unlikely to plug the gap between deficiency and optimal vitamin D status. Subsequently, supplementation seems to be a sensible way forward with specialised regimes using licenced vitamin D<sub>3</sub> products most worthy of use.

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