

Vitamin D and Immunity

Q&A

What is vitamin D?

Vitamin D is the general name given to two different compounds – ergocalciferol (vitamin D₂) and cholecalciferol (vitamin D₃). Vitamin D₂ is naturally occurring in yeast and can only be obtained from our diet. Most vitamin D supplements available to buy contain the vitamin D₃ form.

We can synthesise vitamin D₃ in our skin, and skin synthesis is our main source of vitamin D. However, in the UK (due to the more northerly latitude) this is only possible in the summer months (between April and September) during the hours around midday (around 11am-3pm), when sunshine contains sufficient UVB light (290-315 nm).

During the winter months (October to March), vitamin D can only be obtained from the diet (and supplements), but only a relatively small number of foods in the diet contain vitamin D (see below).



Vitamin D₂ and D₃ that is made in the skin, or obtained from our diet, is converted to 25-hydroxyvitamin D in the liver, which is the major circulating form used to measure vitamin D status, because it has a long half-life in the blood and reflects both dietary intake and synthesis in the skin. Another conversion step to the biologically active form (1,25-dihydroxyvitamin D) occurs in the kidney, although this form is tightly regulated and short-lived.

Snacks for adults

Vitamin D is needed for maintaining the balance of calcium and phosphorus in the body, and it is essential for keeping bones and muscles healthy. Vitamin D has also been investigated for its potential role in reducing the risk of diseases, including cardiovascular disease and cancer, and for its role in immunity (see below for more information), but the evidence is weaker for these. Government recommendations for vitamin D (see below) are made on the basis of protecting musculoskeletal health.

How much vitamin D do we need?

Following publication of the Scientific Committee on Nutrition (SACN) [Vitamin D and health report](#), UK government advice was updated to recommend the following:

- A reference nutrient intake (RNI) of 10 micrograms (10 µg) per day (equivalent to 400 IU/day) for adults (including pregnant and breastfeeding women) and children aged 4 years and older.
- A 'safe intake' of 8.5 to 10 micrograms per day for infants up to 12 months old.
- A 'safe intake' of 10 micrograms per day for children aged 1 to 4 years.

What are the main dietary sources of vitamin D?



There are relatively few food sources of vitamin D in the UK diet. These include the vitamin D found naturally in oily fish, egg yolks, and the smaller amount in meat, and foods fortified with vitamin D such as some milks and milk products (and some dairy alternative products), some fat spreads and some breakfast cereals (check the label to be sure). Mushrooms that have been irradiated with UV light can also contain vitamin D and are available from some supermarkets. For younger children, formula milk (fortified by law) and other fortified milk products are a major contributor to vitamin D intakes whereas meat and oily fish make a greater contribution to the intakes of adults. National dietary data indicate that average vitamin D intakes are below the RNI (or safe intake level) for all age groups in the UK population (except for non-breastfed infants aged 4-6 months), as shown in Table 1.

Table 1: Mean vitamin D intakes in the UK population by age group and sex (including dietary supplements and infant formula).

Age	Mean vitamin D intake (micrograms/day)			
	Males	Females	Breastfed	Non-breastfed
4-6 months	-	-	3.5	10.0
7-9 months	-	-	3.6	8.9
10-11 months	-	-	3.8	7.7
12-18 months	-	-	2.6	3.9
1.5-3 years		2.9	-	-
4-10 years	2.5	2.8	-	-
11-18 years	2.5	4.6	-	-
19-64 years	4.5	3.9	-	-
65+ years	5.1	6.2	-	-

Sources: National Diet and Nutrition Survey (years 7 and 8; 2014/2015 to 2015/2016) and the Diet and Nutrition Survey of Infants and Young Children (DNSIYC, 2011).

For most of us, our main source of vitamin D is from sun exposure on skin, although as outlined below, many people in the UK have low vitamin D status, which suggests they are not making enough through the action of UVB light on the skin.

What is the difference between vitamin D₂ and D₃?

The overall body of evidence available from vitamin D supplementation trials suggests that, while both vitamin D₂ and D₃ both raise concentrations of 25-hydroxyvitamin D in the blood, vitamin D₃ appears to be the more effective form (Tripkovic *et al.* 2012). Vitamin D₃ is only found naturally in animal-derived foods, such as oily fish and meat, which are not suitable for those following a vegetarian or vegan diet, and egg yolk. It is also provided by fortified foods such as some breakfast cereals, milk (and milk alternative) products and fat spreads (it is best to check the label). Vitamin D supplements typically contain vitamin D₃, which is derived from lanolin (a substance extracted from sheep's wool), and so may not be suitable for vegans. Vitamin D₃ supplements suitable for vegans are also available, which are made from lichen.

What is the government's advice on vitamin D?

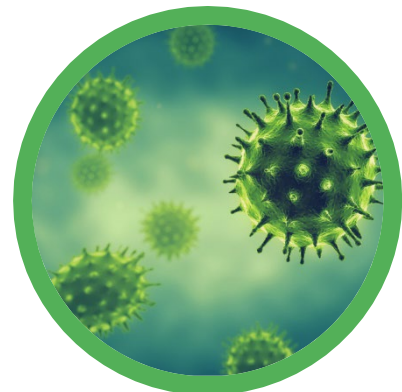
During the autumn and winter months, when vitamin D synthesis in the skin is not possible, it is difficult for people to meet the RNI of 10 micrograms (10 µg) per day, since there are relatively few foods that naturally contain, or that are fortified with, vitamin D. For this reason, Public Health England recommends that people should consider taking a daily supplement containing 10 micrograms of vitamin D throughout the autumn and winter months.

At risk groups, including people who do not often go outdoors, who reside in an institution such as a care home, or those who normally cover most or all of their skin when outdoors, should take a daily 10 microgram vitamin D supplement throughout the year. People with dark skin, including individuals from Black and Minority Ethnic (BAME) groups (e.g. individuals of African, African-Caribbean or South Asian background), should consider taking a vitamin D supplement all year round, as they may not be able to get enough vitamin D from sunlight exposure during spring and summer.

Infants up to 12 months should be given a daily vitamin D supplement containing 8.5 to 10 micrograms, unless they are having more than 500 ml of infant formula per day (this is fortified with vitamin D by law), and children between 1 and 4 years should be given a daily 10 microgram vitamin D supplement throughout the year.

Has government advice on vitamin D changed in response to COVID-19?

No, government advice on vitamin D has not changed as result of the COVID-19 pandemic. However, because restrictions previously imposed as part of the lockdown may have meant people were not able to get outside as often, Public Health England reissued its advice in April 2020 to remind the public of the need to consider vitamin D supplementation, even during the spring and summer months, if time outdoors is limited.



How common is vitamin D deficiency?

Almost 1 in 5 UK adults aged 19 to 64 years have a blood 25-hydroxyvitamin D concentration of less than 25 nmol/L, which is the threshold level considered necessary for protecting musculoskeletal health and reducing the risk of osteomalacia (adults) and nutritional rickets (children). One in ten children aged 4 to 10 years, and a quarter of older children aged 11 to 18 years, have a low vitamin D status (<25 nmol/L), and the proportion below the threshold is highest among adolescent girls (39%). Vitamin D deficiency is also common throughout Europe.

It is estimated that approximately 1 in 8 Europeans are vitamin D deficient, according to a higher threshold for 25-hydroxyvitamin D of 30 nmol/L (set by the US Institute of Medicine [IOM]). The use of different thresholds for defining vitamin D 'deficiency' and 'sufficiency' by expert bodies internationally (e.g. the European Food Safety Authority [EFSA], SACN, and IOM), presents a challenge in interpreting the scientific research on the health effects of vitamin D status, although there is general agreement that a 25-hydroxyvitamin D concentration of less than 25-30 nmol/L should be avoided to protect musculoskeletal health.

Is vitamin D deficiency more common among BAME groups?

Studies from the UK and elsewhere in Europe suggest that vitamin D deficiency is more common among people from BAME (Black, Asian and minority ethnic) backgrounds. For example, a large-scale study of UK South Asians ($n=6433$) published in 2020 (Darling *et al.* 2020), found that 55% had 25-hydroxyvitamin D concentrations below 25 nmol/L and 20% were below 15 nmol/L, while a sizeable proportion of participants ($n=824$) had an undetectable 25-hydroxyvitamin D concentration (<10 nmol/L). Characteristics that were associated with a low vitamin D status in this study population included: being male; Pakistani ethnicity (vs. Indian or Bangladeshi); a higher BMI; 40–59 years old; never consuming oily fish; summer sun exposure <5 h/d; not using a vitamin D-containing supplement; measurement of status in winter or spring; vegetarianism.



A large study conducted as part of a European-wide collaborative project, and which included over 55,000 people from 15 European countries (including the UK), found that dark-skinned ethnic groups had a 3- to 71-fold higher prevalence of low vitamin D status (<30 nmol/L) than for white populations in the study (Cashman *et al.* 2016). This greater prevalence of low vitamin D status among darker-skinned ethnic minority groups was reported for the UK (Black 36%; Asian 60%; White ~20%), Norway (South Asian 65%; White ~1%) and Finland (Somali 28%; Kurdish 50%; White 0.5%).

Although the risk of COVID-19 infection and associated death appears to be higher for people of BAME background, as detailed in a report on [Disparities in the risk and outcomes of COVID-19](#) published by Public Health England, more research is required to test whether low vitamin D status specifically predisposes people with a BAME background to an increased risk of COVID-19 infection or mortality.

Is vitamin D important for immunity?

Laboratory studies have shown that vitamin D receptors are present in cells of the immune system, which has raised the question of whether vitamin D may protect against the risk of autoimmune diseases (such as type 1 diabetes, inflammatory bowel disease, rheumatoid arthritis and asthma), as well as infectious diseases such as colds or flu. However, [in their 2016 report on vitamin D and health](#), SACN concluded that evidence for the proposed health benefits of vitamin D for outcomes other than muscle and bone health was inconsistent, and drawn mainly from observational studies, where it was unclear whether low vitamin D status may be a consequence, rather than a cause, of the illness. For this reason, protection of musculoskeletal health was chosen as the basis for setting dietary reference values for vitamin D.

In 2010, the EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA) [approved a health claim relating to vitamin D and immunity](#) (“*Vitamin D contributes to the normal function of the immune system*”), which can be used on food or drink products which provide a sufficient amount of vitamin D.

Can vitamin D protect against COVID-19 or respiratory tract infections?

There is observational evidence that a lower vitamin D status is associated with acute respiratory tract infections (ARTIs). However, SACN's 2016 Vitamin D and Health report concluded that the evidence from randomised controlled trials on vitamin D supplementation and infection risk (ARTIs and tuberculosis) was inconsistent and generally did not show a beneficial effect on infectious disease risk. Since the COVID-19 outbreak, media reports and some academic publications have suggested that vitamin D supplementation (particularly high doses) could reduce the risk of COVID-19.

In response, three rapid evidence reviews were published in June 2020 by SACN, the National Institute for Health and Care Excellence (NICE), with support from Public Health England (PHE), and separately by the Royal Society, assessing the evidence for a link between vitamin D status and/or supplementation and the risk of COVID-19 or ARTIs. The findings from each review are summarised below:

SACN rapid review

- The purpose of the SACN review was to assess the evidence from randomised controlled trials on vitamin D and the risk of ARTIs, which had been published since the release of SACN's report on vitamin D and health in July 2016, and to consider if this changed SACN's conclusions.
- The review did not consider the evidence on vitamin D and COVID-19 specifically, although this was included in the evidence review conducted by NICE (see below).
- **SACN concluded that the evidence at this time does not support recommending vitamin D supplementation to prevent ARTIs in the general UK population**, and that their conclusion did not affect existing government advice on vitamin D (see above).
- SACN plans to keep this area under urgent review and will consider updating its assessment if emerging evidence from ongoing RCTs on vitamin D and ARTI risk suggests a change to existing conclusions.

NICE rapid evidence summary

- With the support of PHE, NICE reviewed the best available evidence on vitamin D for preventing or treating COVID-19, or for susceptibility to COVID-19 based on vitamin D status.
- They included 5 recently published peer-reviewed studies (other studies that had not been subject to formal peer-review were not considered).
- None of the studies were intervention trials of vitamin D supplementation for the prevention or treatment of COVID-19.
- Although 4 of the 5 studies found an association or correlation between a lower vitamin D status and subsequent development of COVID-19, **no causal relationship between vitamin D status and COVID-19 was found** after adjustment for confounders such as comorbidity, socio-demographics, ethnicity, BMI and other baseline factors.
- **NICE advised that there is no evidence to support taking vitamin D supplements to specifically prevent or treat COVID-19**, although people should continue to follow UK government advice on daily vitamin D supplementation to maintain bone and muscle health during the COVID-19 pandemic.

The Royal Society rapid review

- This rapid review by The Royal Society was intended to add to the understanding of COVID-19.
- The report included recent epidemiological studies on the association between vitamin D status and COVID-19, and laboratory studies of the effect of vitamin D on the immune response to respiratory viruses other than SARS-CoV-2 (the virus responsible for causing COVID-19).
- The review found that, although it is biologically plausible that vitamin D deficiency may contribute to susceptibility to COVID-19 infection, **there is no direct causal link yet between Vitamin D deficiency and increased susceptibility to COVID-19.**
- The authors recommended that more research is required to test the possibility that Vitamin D deficiency predisposes to COVID-19, particularly in groups with a high risk of COVID-19 mortality, such as the institutionalised elderly and people with a BAME background.

Emerging studies of vitamin D and coronavirus

As of November 2020, several observational studies (from various countries) have reported an association between lower vitamin D concentrations and a greater prevalence of worse outcomes among patients hospitalised with COVID-19, including a greater likelihood of developing severe symptoms or death. However, while such studies suggest a possible role for vitamin D in reducing the incidence of coronavirus infection and/or worse health outcomes, they do not provide evidence of causality.



Well-designed, large-scale vitamin D supplementation trials, particularly among those with low baseline concentrations, are the only way to establish a causal relationship between low vitamin D status and a greater risk of COVID-19 infection and mortality risk. Vitamin D supplementation trials are underway, such as the [CORONAVIT study at Queen Mary University of London](#), although it may be some time before the results from clinical trials are available.

Take home messages

- **Vitamin D is essential for maintaining bone and muscle health.**
- Exposure of skin to sunlight during spring and summer is the main source of vitamin D for the UK population.
- Only a few foods in the diet (oily fish, egg yolks, meat, irradiated mushrooms and fortified foods) provide vitamin D.
- **Almost 1 in 5 UK adults has a low vitamin D status (a 25-hydroxyvitamin D concentration below 25 nmol/L).**
- Adults and children aged 4 years and above require 10 micrograms of vitamin D per day (a safe intake of 8.5-10 micrograms per day is recommended for infants under 12 months, and a safe intake of 10 micrograms per day for children between 1 and 4 years).
- Government advice is that adults should consider taking a vitamin D supplement (10 micrograms per day) during the autumn and winter months to protect their bone and muscle health.

- During the ongoing COVID-19 pandemic, Public Health England re-issued its advice that we should all consider taking a daily 10 microgram vitamin D supplement, even in the summer months, if we are not able to be outside in sunlight as much as usual.
- There is no evidence to support recommending vitamin D supplementation to prevent or treat COVID-19 symptoms and more research is needed to explore this relationship further.
- Overall, although some studies suggest an effect, the evidence at this time does not support recommending vitamin D supplementation to prevent ARTIs for the general UK population.
- Following government advice on vitamin D supplementation remains important to ensure healthy bones and muscles.

References

- Cashman KD, Dowling KG, Škrabáková Z et al. (2016) Vitamin D deficiency in Europe: pandemic? *Am J Clin Nutr* **103**: 1033-44.
- Darling AL, Blackbourn DJ, Ahmadi KR et al. (2020) Very high prevalence of 25-hydroxyvitamin D deficiency in 6433 UK South Asian adults: analysis of the UK Biobank Cohort. *British Journal of Nutrition* 1-12.
- Tripkovic L, Lambert H, Hart K et al. (2012) Comparison of vitamin D2 and vitamin D3 supplementation in raising serum 25-hydroxyvitamin D status: a systematic review and meta-analysis. *Am J Clin Nutr* **95**: 1357-64.

Reviewed November 2020.