

COVID-19 rapid guideline: vitamin D

NICE guideline

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Your responsibility

The recommendations in this guideline represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, professionals and practitioners are expected to take this guideline fully into account, alongside the individual needs, preferences and values of their patients or the people using their service. It is not mandatory to apply the recommendations, and the guideline does not override the responsibility to make decisions appropriate to the circumstances of the individual, in consultation with them and their families and carers or guardian.

Local commissioners and providers of healthcare have a responsibility to enable the guideline to be applied when individual professionals and people using services wish to use it. They should do so in the context of local and national priorities for funding and developing services, and in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities. Nothing in this guideline should be interpreted in a way that would be inconsistent with complying with those duties.

Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should assess and reduce the environmental impact of implementing NICE recommendations wherever possible.

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Overview

This guideline covers vitamin D use in the context of COVID-19. It is for adults, young people and children in hospitals and community settings. Vitamin D is important for bone and muscle health. It may also have a role in the body's immune response to respiratory viruses.

When using this guideline, follow the usual professional guidelines, standards and laws (including those on equalities, safeguarding, communication and mental capacity), as described in [making decisions using NICE guidelines](#).

See also the NICE guideline on [Vitamin D: supplement use in specific population groups](#).

This guideline is for:

- health and care practitioners
- health and care staff in hospital and community settings
- commissioners

The recommendations bring together:

- evidence from published literature on vitamin D supplementation for preventing or treating COVID-19, associations of vitamin D status with COVID-19, and indirect evidence on vitamin D supplementation for preventing acute respiratory tract infection in the general population (from the updated Scientific Advisory Committee on Nutrition rapid review)
- existing national guidance and policies (including [UK government advice on taking a vitamin D supplement](#))
- advice from specialists working in the NHS from across the UK, including nutritionists, intensive care specialists, public health physicians, microbiologists, general practitioners and pharmacists.

We developed this guideline with the Scientific Advisory Committee on Nutrition and Public Health England using the [interim process and methods for guidelines developed in response to health and social care emergencies](#). We will review and update the recommendations as the knowledge base develops.

Recommendations

1.1 Encourage people to follow [UK government advice on taking a vitamin D supplement](#) to maintain bone and muscle health. The advice is that:

- Adults (including women who are pregnant or breastfeeding), young people and children over 4 years should consider taking a daily supplement containing 10 micrograms (400 units; also called international units [IU]) of vitamin D between October and early March because people do not make enough vitamin D from sunlight in these months.
- Adults, young people and children over 4 years should consider taking a daily supplement containing 10 micrograms (400 units) of vitamin D throughout the year:
 - if they have little or no sunshine exposure including because they:
 - ◇ are not often outdoors, for example, if they are frail, housebound or living in a care home
 - ◇ usually wear clothes that cover up most of their skin when outdoors
 - ◇ are spending most of their time indoors because of the COVID-19 pandemic
 - if they have dark skin, for example, if they are of African, African-Caribbean or south Asian family origin, because they may not make enough vitamin D from sunlight.
- Babies from birth to 1 year should have a daily supplement containing 8.5 micrograms (340 units) to 10 micrograms (400 units) of vitamin D throughout the year if they are:
 - breastfed
 - formula-fed and are having less than 500 ml of infant formula a day (because infant formula is already fortified with vitamin D).
- Children aged 1 year to 4 years should have a daily supplement containing 10 micrograms (400 units) of vitamin D throughout the year.
- Some people have a medical condition that means they cannot take vitamin D or should take a different amount from the general population.

- 1.2 Do not offer a vitamin D supplement to people solely to prevent COVID-19, except as part of a clinical trial.
- 1.3 Do not offer a vitamin D supplement to people solely to treat COVID-19, except as part of a clinical trial.

For a short explanation of why we made these recommendations see the [rationale section on recommendations](#).

Full details of the evidence are in the [evidence review](#).

Recommendation for research

We have made the following recommendation for research.

Treating COVID-19

What is the clinical effectiveness of vitamin D supplements for treating COVID-19 in adults, young people and children? Randomised controlled trials in all care settings with a minimum 8-week follow up are recommended. There should be a particular focus on subgroup analyses including, but not limited to, age (such as over 75 years), ethnicity (for example, black, Asian and minority ethnic groups) and comorbidities (for example, obesity) that are associated with poorer outcomes in people with COVID-19.

Suggested PICO (population, interventions, comparators, outcomes)

Criterion	Explanation
Population	<p>Adults, young people and children with confirmed COVID-19.</p> <p>Evidence specific to the following groups should be obtained:</p> <ul style="list-style-type: none"> • people with more severe COVID-19 or longer duration of COVID-19 • older people (over 75) • black, Asian and minority ethnic groups • people with comorbidities (for example, obesity) • people with low vitamin D status. <p>Effectiveness of vitamin D treatment in these populations should be explored wherever possible using:</p> <ul style="list-style-type: none"> • subgroup analyses • sensitivity analyses. <p>Trials should be adequately powered to assess the effectiveness in these groups.</p>

Criterion	Explanation
Intervention	Vitamin D or vitamin D derivatives (all dosages, formulations and routes of administration). Note: Vitamin D as an adjunctive treatment will be included if other treatments are balanced out in the control arm.
Comparators	Placebo or no treatment (in addition to standard care). Note: for vitamin D supplementation as an adjunctive treatment, the comparator will be the index treatment. For example: vitamin D plus treatment X versus treatment X.
Outcomes	<p>Primary:</p> <ul style="list-style-type: none"> • mortality (including all-cause mortality and COVID-19 related mortality) • intensive care unit admission • hospitalisation. <p>Secondary:</p> <ul style="list-style-type: none"> • use of ventilation (including non-invasive and invasive) • infection cure rates (laboratory, or virologically or radiographically confirmed) • time to clinical cure • duration of hospital or intensive care unit admission • complications (primary or secondary to COVID-19) • reduction in symptoms, symptom severity or both • adverse effects and safety • tolerability • long-term effects of COVID-19.

Preventing COVID-19

The panel discussed the importance of research into the clinical effectiveness of vitamin D for

preventing SARS-CoV-2 infection (and subsequent COVID-19).

For a short explanation of why we made a research recommendation about research into vitamin D for treating COVID-19, and a discussion of research into vitamin D for preventing COVID-19, see the [rationale section on recommendations](#).

Full details of the evidence are in the [evidence review](#).

Rationale

Why the panel made the recommendations

The panel agreed that there was little evidence for using vitamin D supplements to prevent or treat COVID-19. However, they agreed that vitamin D use is well established for maintaining bone and muscle health. They expressed concerns that not everyone is aware of, or is following, UK government advice on taking a vitamin D supplement, so wanted to include a recommendation to emphasise the existing guidance. They stressed that everyone should consider taking a supplement containing 10 micrograms (400 units) of vitamin D daily between October and early March, when people in the UK do not make enough vitamin D from sunlight. They also stressed that this was particularly important during the COVID-19 pandemic, when people may have been indoors more than usual over the spring and summer.

The panel discussed that, for most people, 10 micrograms (400 units) of vitamin D a day will be enough to prevent serum 25(OH)D concentration from falling below 25 nmol/litre. They also noted that taking too high a dose of vitamin D over a long period of time could be harmful because it can cause too much calcium to build up in the body (hypercalcaemia). This can weaken the bones and damage the kidneys and the heart. They were aware that the tolerable upper intake level for adults and young people over 11 years is 100 micrograms (4,000 units) daily, and that this dose should not be exceeded. They discussed monitoring requirements if people have renal impairment or high doses are given, and were aware of cautions for use in people with certain medical conditions, such as sarcoidosis. They agreed that, if people are unsure whether they can take vitamin D, they should discuss this with their healthcare professional. The panel also discussed that vitamin D₃ (colecalciferol) supplements can be derived from an animal source. They noted that people's concerns about using animal products because of a religious or ethical belief need to be considered when discussing vitamin D products.

The panel also noted that it is important for some populations to take a supplement containing 10 micrograms (400 units) of vitamin D daily throughout the year. This includes people who are at a higher risk of not getting enough vitamin D because, for example, of lack of exposure to sunlight during the spring and summer months.

The panel discussed access to vitamin D supplements, and were aware of the [NICE guideline on vitamin D: supplement use in specific population groups](#) and the [NHS service supplying free daily vitamin D supplements](#) for people at high risk (clinically extremely vulnerable) from COVID-19.

This service has been set up because it is particularly important for people who have been indoors more over the spring and summer when shielding to take vitamin D for bone and muscle health.

Preventing COVID-19

The panel were presented with evidence from the [NICE evidence review of vitamin D for COVID-19](#) on using vitamin D supplements to prevent SARS-CoV-2 infection (and subsequent COVID-19), and evidence on vitamin D status and its association with COVID-19.

No evidence relevant to the protocol was found for the prevention question. The panel discussed the evidence for the association of vitamin D status with COVID-19. They agreed that low vitamin D status was associated with more severe outcomes from COVID-19. However, it is not possible to confirm causality because many of the risk factors for severe COVID-19 outcomes are the same as the risk factors for low vitamin D status. Vitamin D is a negative acute phase reactant, meaning its serum concentration falls during a systemic inflammatory response, which may occur during severe COVID-19 illness. Therefore, it is difficult to know if low vitamin D status causes poorer outcomes or vice versa.

The panel discussed the significant limitations in the retrospective association studies. These included historic and inaccurate vitamin D status measurements, lack of generalisability to UK practice, the likelihood of confounding and general low quality of the evidence.

Because COVID-19 mainly affects the respiratory tract, the panel also heard indirect evidence from the updated [Scientific Advisory Committee on Nutrition \(SACN\) rapid review on using vitamin D supplements to prevent acute respiratory tract infections](#). They agreed that a systematic review and meta-analysis by Jolliffe et al. (2020) reported a modest protective effect of vitamin D supplementation compared with placebo. From subgroup analyses, this protection was associated with daily doses of 10 micrograms to 25 micrograms (400 units to 1,000 units) of vitamin D, but not higher doses. Also, from subgroup analysis, the protection was only seen in children and young people aged from 1 year to under 16 years (the panel noted that, for COVID-19, poorer outcomes are more common in an older adult population). Beneficial effects on acute respiratory tract infection prevention were not seen with higher doses of vitamin D supplementation (over 25 micrograms [1,000 units] daily or more), when supplementation was weekly or monthly, or in adults. The SACN rapid review highlighted limitations with the studies included in the meta-analysis by Jolliffe et al. (2020) including:

- inconsistency between study results

- differences between studies in vitamin D supplementation doses and regimens, settings, populations, durations and definitions of outcomes (including type of respiratory infection).

The panel were also aware of the updated SACN recommendations that a vitamin D intake of 10 micrograms (400 units) daily, as currently recommended, may provide some additional benefit in reducing the risk of acute respiratory tract infections. However, they noted that this topic is being kept under review and these recommendations may be updated if findings from robust, high-quality randomised controlled trials provide further clarification.

Based on direct evidence from the NICE evidence review and indirect evidence from the SACN rapid review of vitamin D in acute respiratory tract infection (which did not include COVID-19 as an outcome), the panel agreed that there was not enough evidence to recommend vitamin D supplements solely for preventing COVID-19.

The panel agreed that people should be encouraged to follow the existing UK government advice on vitamin D supplementation. They also agreed that the recommendations in this guideline on vitamin D supplements and COVID-19 prevention should be considered for an update as additional evidence becomes available.

The panel agreed that there is a need for research into vitamin D supplementation for preventing COVID-19. However, they discussed issues around ethics, trial design and comparators, and agreed that it would be more appropriate for the research community to define an appropriate PICO (population, interventions, comparators, outcomes) framework. They were aware that the updated SACN rapid review on using vitamin D supplements to prevent acute respiratory tract infections has a recommendation that research is urgently needed on vitamin D and risk of acute respiratory tract infection in black, Asian and minority ethnic groups, and people living with overweight or obesity. The panel also noted that several randomised controlled trials of vitamin D supplements in preventing COVID-19 are known to be in progress.

Treating COVID-19

The panel were presented with evidence from the [NICE evidence review of vitamin D for COVID-19](#) on using vitamin D supplements for treating COVID-19. This comprised 1 small, very low-quality, randomised controlled trial in secondary care from Spain (Castillo et al. 2020) that used oral calcifediol (25[OH]D), which is the circulating metabolite of vitamin D, and not commonly used in the UK. The panel noted the very high dose used. This was estimated to be equivalent to around 5,000 micrograms (200,000 units) of vitamin D in the first week (about 700 micrograms [28,000 units] daily) and 1,300 micrograms in following weeks for the duration of the study (about 200 micrograms [8,000 units] daily). They also noted the lack of generalisability to UK practice. The

panel had concerns about:

- differences in comorbidities between the 2 comparator groups
- use of 'standard care' including anti-inflammatory medicines that are not considered standard care for COVID-19 in UK practice
- the lack of blinding, which could result in biased estimates.

Based on direct evidence from the NICE evidence review, the panel agreed that there was not enough evidence to recommend using vitamin D for treating COVID-19. They also agreed that the recommendation on vitamin D supplements and treatment should be considered for an update as additional evidence becomes available. Because of the lack of evidence identified, the panel made a research recommendation around the clinical effectiveness of vitamin D supplements for treating COVID-19. They stressed that future studies should be high-quality randomised controlled trials.

As additional evidence becomes available, this guidance will be updated in line with [NICE's interim process and methods for guidelines developed in response to health and social care emergencies](#).

Full details of the evidence are in the [NICE evidence review of vitamin D for COVID-19](#).

[Return to recommendations](#)

Context

Vitamin D is important for bone and muscle health. It may also have a role in the body's immune response to respiratory viruses. Sunlight exposure is the main source of vitamin D for most people in the UK during summer months. But, between October and early March, people in the UK do not make enough vitamin D from sunlight. Vitamin D is also found in a small number of foods and can be obtained from supplements. The 2 key forms of vitamin D, D3 (colecalciferol) and D2 (ergocalciferol), are licensed for preventing and treating vitamin D deficiency. They are not specifically licensed for preventing or treating any infection, including SARS-CoV-2 that causes COVID-19.

Vitamin D status is determined by measuring serum concentrations of 25 hydroxyvitamin D (25[OH]D), the major circulating metabolite of vitamin D. Existing UK government recommendations on vitamin D are based on advice from the Scientific Advisory Committee on Nutrition (SACN). To protect bone and muscle health, the [SACN vitamin D and health report](#) recommends that serum 25(OH)D concentration should not fall below 25 nmol/litre at any time of the year. To achieve this, SACN recommends a reference nutrient intake of 10 micrograms (400 units; also called international units [IU]) of vitamin D daily for the UK population aged 4 years and above. This is the average amount needed by 97.5% of the population to maintain a serum concentration of 25 nmol/litre when UVB sunshine exposure is minimal. [UK government advice on taking a vitamin D supplement](#) includes:

- 10 micrograms (400 units) of vitamin D daily for everyone in the UK aged over 4 years between October and early March, and
- 10 micrograms (400 units) of vitamin D daily throughout the year for people whose serum 25(OH)D concentrations may not reach 25 nmol/litre through sunlight alone.

The dose of vitamin D in units can be calculated by multiplying the number of micrograms by 40; for example, 10 micrograms is equivalent to 400 units. This guideline uses 'units' instead of 'international units' or 'IU' for doses of vitamin D. This is consistent with the [BNF guidance on prescription writing](#), and stems from the preferred convention of using 'units' because of safety concerns about using 'IU' in prescribing.

There are services supplying free vitamin D supplements to some population groups. For example, there is an [NHS service supplying free daily vitamin D supplements](#) for people at high risk (clinically extremely vulnerable) from COVID-19. This service has been set up because it is particularly

important for people who have been indoors more over the spring and summer while shielding to take vitamin D for bone and muscle health. Women and children who qualify for the [Healthy Start scheme](#) can also get free supplements containing vitamin D.

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