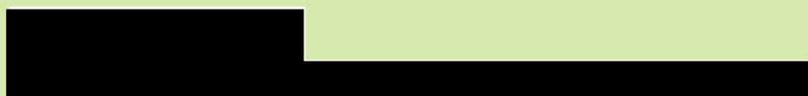# Classification of Vitamin D

Review of Classifications for Dietary Supplements

October 2025

Contents

Overview

In 2016, a series of submissions were made to the Medicines Classification Committee proposing the reclassification of several substances commonly used in dietary supplements. These substances were to be considered as part of the Natural Health Products Bill at the time. Following the removal of the Natural Health Products Bill from the legislative programme, and the recent repeal of the Therapeutic Products Act, the reclassification of these substances is yet to be considered.

One substance to be considered was vitamin D. Vitamin D has essential roles in calcium, phosphorus, and bone metabolism, as well as a range of functions in other body systems. Despite its importance, deficiency in vitamin D remains a significant global public health issue. Vitamin D deficiency is estimated to affect over half the global population and is linked to a range of chronic health conditions, including type 2 diabetes mellitus, cancer, cardiovascular conditions, and immune disorders. As such, vitamin D supplementation is an area of considerable interest. However, overdosing of vitamin D may lead to adverse effects, with the most documented being hypercalcemia, hypercalciuria, and nephrolithiasis.

The submission made to the Medicines Classification Committee in 2016 proposed that the limit for vitamin D in medicines for internal use be increased from **25 micrograms** to **75 micrograms** per recommended daily dose. This report summarises this submission, provides an overview of the risk-benefit balance of this proposal, and makes recommendations regarding the classification of vitamin D.

Classification of Vitamin D

History of the Classification of Vitamin D

Vitamin D was first discussed by the Medicines Classification Committee (MCC) at the 37th meeting held in May 2007. In this meeting, the National Drugs and Poisons Schedule Committee (NDPSC) in Australia recommended that New Zealand should harmonise the wording of the vitamin D classification statement by making the recommended maximum daily dose of 25 micrograms applicable only to products for internal use. The MCC agreed with this recommendation.

Vitamin D was next discussed at the 44th MCC meeting held in November 2010, where an MCC member suggested it may be appropriate to reclassify vitamin D in tablets containing 1.25 mg of colecalciferol from a prescription to a restricted medicine for the prevention and treatment of vitamin D deficiency. At that time, the MCC recommended Medsafe make a submission proposing the reclassification of vitamin D. This submission was constructed and later discussed at the 47th MCC meeting held in May 2012. The MCC agreed that there was not enough evidence to support a reclassification to restricted medicine at that time.

Vitamin D was again discussed at the 49th MCC meeting held in June 2013, where it was discussed as an Australian harmonization item. It was proposed to create a new restricted medicine entry to enable a weekly dose of vitamin D up to 175 micrograms per recommended daily dose. The MCC agreed that, on the basis of recent discussions at previous meetings and the data presented, there was not enough benefit data to outweigh the risks associated with reclassifying vitamin D at this dose.

Vitamin D, along with several other dietary supplements, was to be discussed at the 56th MCC meeting in 2016, pending the third reading of the Natural Health Products (NHP) Bill. However, attempts to better regulate natural health products through this legislation never came to fruition. Despite this, the recently repealed Therapeutic Products Act did set the framework to enable new regulatory

requirements and the ability to make evidence-based therapeutic claims for products, including those containing vitamin D. However, with the repeal of this Act, these products continue to be regulated under the Dietary Supplements Regulations 1985.

A recent submission from an individual regarding vitamin D was made at the 74th MCC meeting held on 23 July 2025. This submission proposed that the classification of vitamin D be amended to increase the recommended daily dose limit from 25 micrograms to 75 micrograms. This is the same proposal made at the 56th MCC meeting. The MCC noted that much of the content in this submission is duplicated from the MCC56 submission, and queried whether the information provided was up to date. The MCC recommended against reclassification at that time.

Current Classification

At the time of writing, vitamin D is classified as:

*Prescription; for internal use in medicines containing more than 25 micrograms per recommended daily dose **except** in parenteral nutrition replacement preparations.*

General sale; for external use; for internal use in medicines containing 25 micrograms or less per recommended daily dose; in parenteral nutrition replacement preparations.

Classification of Vitamin D Overseas

Australia

The classification of vitamin D in Australia is:

*Schedule 4 (prescription); for internal human therapeutic use **except** in preparations containing 25 micrograms or less of vitamin D per recommended daily dose; **except** when included in Schedule 3.*

*Schedule 3 (restricted); for human internal therapeutic use in preparations containing 175 micrograms or less of vitamin D per recommended single weekly dose **except** in preparations containing 25 micrograms or less of vitamin D per recommended daily dose.*

As such, vitamin D is unscheduled when in products for external use, and when in products for internal use containing 25 micrograms or less per recommended daily dose.

United Kingdom

In the United Kingdom (UK), there is no national legislation setting maximum levels for vitamins and minerals that may be used in the manufacture of food supplements. However, the Expert Working Group on Vitamins and Minerals in the UK estimate that a level of 25 micrograms per day of vitamin D would not be expected to cause adverse effects in the general population.

However, vitamin D is classified as a pharmacy medicine above 10 micrograms. Below this, vitamin D is unscheduled.

Canada

Vitamin D (cholecalciferol and ergocalciferol) is classified as a non-natural health product as it is listed in the Canadian Prescription Drug List as:

Prescription; in oral dosage form containing more than 62.5 micrograms or 2,500 International Units of vitamin D per dosage form, or where the largest recommended daily dosage shown on the label would result in the daily intake by that person of more than 62.5 micrograms of 2,500 International Units of vitamin D.

United States

The National Institutes of Health (NIH) Office of Dietary Supplement defines an upper intake level of 100 micrograms (4000 IU) per day of vitamin D for individuals aged 9 years and older. The upper intake levels for other groups are listed in the table below:

Age	Upper Limit
Birth to 6 months	25 micrograms
Infants 7-12 months	38 micrograms
Children 1-3 years	63 micrograms
Children 4-8 years	75 micrograms

The recommended daily intake of vitamin D for all groups is 15 micrograms (600 IU), except in 0-6 month olds (10 micrograms).

In the US, many vitamin D products are marketed as dietary supplements, and they do not have to undergo a pre-approval process. The vitamin D content of these products ranges from 10-125 micrograms.

European Union

The European Food Safety Authority (EFSA) has indicated a tolerable upper intake level of 100 micrograms per day of vitamin D for adults aged 18 years and older. The upper intake levels for other groups are listed in the table below:

Age	Upper Limit
4-6 months	25 micrograms
7-11 months	35 micrograms
1-3 years	50 micrograms
4-6 years	50 micrograms
7-10 years	50 micrograms
11-14 years	100 micrograms
15-17 years	100 micrograms
Adults	100 micrograms
Pregnancy	100 micrograms
Lactation	100 micrograms

Overview of the MCC56 Submission for Vitamin D

Background

Vitamin D occurs in two forms: cholecalciferol and ergocalciferol. Cholecalciferol (vitamin D3) is produced by the action of solar ultraviolet B radiation from sunlight on skin, and ergocalciferol (vitamin D2) is found in a limited range of foods. Vitamin D in foods is fat soluble and is biologically less active. Its metabolite, 1,25-dihydroxyvitamin D (calcitriol) is the biologically active hormone responsible for its physiological actions. In the circulation, vitamin D appears as 25-hydroxyvitamin D (25-(OH)D), which is five times more potent than cholecalciferol (NRV, 2006). Cholecalciferol and ergocalciferol are transferred to the liver where they are converted to 25-hydroxyvitamin D, which is then transferred to the kidneys and converted to the active 1,25-dihydroxyvitamin D (Martindale, 2011). Regardless of the source of origin the body stores excess vitamin D to release it in the hydroxylated form gradually.

Vitamin D has essential roles in calcium, phosphorus, and bone metabolism, as well as a range of functions in other body systems. Its active metabolite calcitriol exerts pleiotropic effects through vitamin D receptor (VDR)-mediated genomic and non-genomic pathways. It is generally acknowledged that skin synthesis as the sole source of cholecalciferol does not guarantee the maintenance even of a minimal recommended serum calcitriol levels throughout the year. In internationally accepted clinical guidelines cholecalciferol is the preferred form of vitamin D of choice for the management of osteoporosis. Cholecalciferol, unlike calcifediol, guarantees an exact dosage in IU of vitamin D and has pharmacokinetic properties that allow daily, weekly, fortnightly, or monthly administration in its equivalent doses, which can facilitate adherence to treatment.

Despite its importance, deficiency in vitamin D remains a significant global public health issue. Vitamin D deficiency is estimated to affect over half the global population and is linked to a range of chronic health conditions, including type 2 diabetes mellitus, cancer, cardiovascular conditions, and immune disorders. While optimal 25-hydroxyvitamin D (25(OH)D) levels remain debated, its circulating levels are influenced by both the environment and genetics (Glustina 2024; Gruber-Bzura 2025). Despite the lack of consensus on what levels within the bloodstream are optimal, vitamin D deficiency has historically been defined as serum 25(OH)D concentrations below 20 ng/mL (Holick 2011). Total serum 25(OH)D, the sum of $25(OH)D_3$ and $25(OH)D_2$, is the accepted biomarker of vitamin D status.

In 2010, the Institute of Medicine (IOM) in the US defined the target value of supplementation as the serum 25(OH)D concentration above 20 ng/ml which corresponds to 400 IU – 800 IU. This definition was based only on the calcemic role of vitamin D. The Endocrine Society in the US have recognized the minimum level of 30 ng/ml (400 IU – 2,000 IU/day), for the healthy population depending on the age group, body weight and race (Pludowski 2018). At the same time, it was recognized that for people with a BMI > 30 kg/m^2 (already classified as obese), the daily dose of vitamin D should be two times higher than the dose recommended for people with normal body weight (Gruber-Bzura 2025).

These guidelines, however, are contested (Heaney 2011; Rosen 2012; Balvers 2015). Critics suggest that theIOM recommendations were mainly based on white individuals, whereas other investigations suggest that there may be much higher intakes required in individuals from other ethnicities (Correia 2014; Cashman 2022). Vitamin D requirements may also vary considerably between different regions or continents. A study in Britain found deficiencies were more likely in vegetarians and vegans than in meat and fish eaters, and that diet was in fact an important source (Crowe 2011). These findings suggest that some populations may require higher doses than previously estimated.

Vitamin D guidelines issued by other major organizations worldwide now recommend optimal 25(OH)D levels to be in the range of 50 to 75 nmol/L (20-30 ng/mL) (Ross 2011; Holick 2011; Cashman

2016). A pooled analysis of 308 studies involving 7.9 million participants from different countries recently estimated that 45% of people globally had vitamin D deficiency (Cui 2023), with a prevalence in winter-spring being 1.7 times that in summer-autumn. People living in high latitude areas, and females, had a higher prevalence (Cui 2023).

Few foods are a rich natural source of vitamin D, with main dietary sources including fatty fish, egg yolks, cheese, mushrooms, and dark chocolate. In New Zealand, as with many other countries, voluntary fortification of foods with vitamin D occurs, including in foods such as milk, yoghurt, fat spreads, orange juice, breakfast grains, and plant-based beverages. Vitamin D may be added to specific foods in New Zealand as regulated in Standard 1.3.2 Vitamins and Minerals, of the Australia New Zealand Food Standards Code (the Code). In Australia, it is mandatory for edible oil spreads and margarines to contain no less than 55 µg/kg of vitamin D. This mandatory requirement does not apply to these foods for sale in New Zealand (Standard 2.4.2, the Code). Vitamin D may also be added to supplemented foods as regulated in the New Zealand Food (Supplemented Food) Standard (New Zealand Food Safety Authority, 2010). Vitamin D permissions are higher for supplemented foods compared to foods for sale under the Code.

A Technical Paper prepared by ESR for MPI in 2014 reviewed the subject of Vitamin D and its fortification in foods In New Zealand, and provides extensive data concerning food sources of this Vitamin (Thomson 2014). In this report, preliminary intake assessments using the 2009 New Zealand Total Diet Study (NZTDS) simulated diets, vitamin D concentrations from the NZ Food Composition Database (NZFCD, for unfortified foods), and Manufactured Food Database (MFD, for potentially fortified foods) were undertaken to identify key contributing foods.

Based on voluntary notifications, New Zealand food products fortified with vitamin D included baby foods, margarines, dairy desserts, food drinks and meal replacements, skim and reduced fat milks, protein beverages derived from legumes, yoghurts, and cereal bars. Dried milks, cheese and cheese products, analogues of cheese, and butter, which are approved for vitamin D fortification, were not identified in the Manufactured Food Database (MFD). Cereal and orange juice that may be fortified overseas, particularly in the United States (US), are not approved for vitamin D fortification in New Zealand.

Fortification can be achieved in multiple ways with varying efficiency. Most New Zealand companies stated no technological issues were experienced when fortifying with vitamin D. At least two companies had in 2009 been fortifying for over 20 years, with a stable vitamin supplier and a prescribed level of fortification. Most companies contacted (7/9) were adding vitamin D in the form of vitamin D3 (cholecalciferol). Six companies were undertaking some analytical testing, although two companies commented on the variability of results and the lack of confidence in single results, leading one company to cease fortification of a product line with vitamin D.

The report found that at that time, there was very limited New Zealand derived vitamin D concentration data in the New Zealand Food Composition Database (NZFCD), with single brands of bread, butter, cheese, yoghurt, milk, sausage roll and one fish species (salmon). Results for two egg and margarine samples only were available. Additional validated data are available (but not included in the NZFCD) for a fortified infant formula, three fortified food drinks, a fortified fruit drink, eight fortified margarines, and five fortified milk products.

The report concluded that from an intake based approach, that is targeting those foods likely to have the greatest impact on vitamin D status, the priority foods to analyse to fill vitamin D concentration data gaps in New Zealand are: butter, milk, cheese, ice-cream, yoghurt, salad dressing, fish (fresh and canned), oysters, lambs' liver, meat pie, bread (wheatmeal and mixed grain), cake, biscuits (plain), pasta, pizza and brewed coffee (Thomson 2014).

As stated in the Medsafe submission at the 47th MCC meeting, in the nutrient reference values (NRV) for Australia and New Zealand's monograph for vitamin D it is reported that, with current food supplies and patterns of eating, it is almost impossible to obtain sufficient vitamin D from the diet alone. Similar conclusions have been made in other countries such as in Germany, where studies indicate that only 10 to 20 percent of the vitamin D3 requirement is met through food sources (Falk 2024). In Europe, the adequate daily intake of vitamin D of 15 µg/day set by the European Food Safety Authority is also acknowledged as being hard to achieve through diet alone, meaning that dietary supplements of vitamin D are usually recommended (Benedik 2022; Falk 2024).

Concentrations of 25-(OH)D or calcidiol, the most commonly measured metabolite, vary markedly around the world and are influenced by many factors including sun exposure, skin pigmentation, covering, season, and supplement use. Whilst overt vitamin D deficiency with biochemical consequences presents an increased risk of rickets, osteomalacia, or cardiomyopathy, the role of vitamin D supplementation in the population presents a different set of considerations (Harvey 2024).

Another key consideration is the natural age-dependent decline of 7-dehydrocholesterol (7-DHC) in the epidermis, which directly impacts vitamin D_3 synthesis (Wacker 2013). Levels of 7-DHC concentrations in the epidermis in older adults decline significantly with age, leading to a significant reduction in the skin's ability to produce vitamin D (Holick 1989). This factor combined with less sun exposure due to more time being spent indoors, may be contributory to vitamin D deficiency being on the rise, at a population level (Cashman 2016).

Proposed Classification
The submission made to the 56th MCC meeting proposed that vitamin D is reclassified as follows:

Prescription; for internal use in medicines containing more than 75 micrograms per recommended daily dose except in parenteral nutrition replacement preparations; except in products for external use.

General sale; for external use; for internal use in medicines containing 75 micrograms or less per recommended daily dose; in parenteral nutrition replacement preparations.

Proposed Warning Labels
When used as an active ingredient in oral or sublingual products, the submission recommended that the following warning statements be included:

"Vitamins can only be of assistance if the dietary vitamin intake is inadequate" or

"Vitamin supplements should not replace a balanced diet"

Products Affected
A list of approved medicines containing vitamin D that are known to Medsafe is shown below.

File Number	Medicine	Classification
TT50-10908	Elevit, Film coated tablet Bayer UI 1613794	Pharmacy only
TT50-4970/3a	Fosamax Plus, Tablet 70/140	Prescription

TT50-6234	Cernevit, Powder for injection	General sale
TT50-6706/1	Elevit, Film coated tablet New formulation	Pharmacy only
TT50-6706/2	Elevit, Film coated tablet Vitamin D 5 microgram	Pharmacy only
TT50-9427	Vit.D3, Soft gelatin capsule 1.25 mg	Prescription
TT50-4175	Vitalipid N Adult, Emulsion for injection	General sale
TT50-4175/1	Vitalipid N Infant, Emulsion for injection	General sale

A wide range of dietary supplements containing vitamin D are available in New Zealand, most of which contain vitamin D3. Most are in capsule or soft-gel form, although liquid forms are also available. Several of these dietary supplements are available through online commerce channels or local online dietary supplement retailers. Such products can contain amounts of vitamin D significantly greater than the current 1000 IU daily recommended dose limit, with some products containing as much as 10,000 IU per day. If the proposed change to the classification of vitamin D is made, several sponsors manufacturing dietary supplements may opt to reformulate their products to contain higher levels of Vitamin D.

It should also be noted that all dietary supplement products were to be regulated under the Natural Health Products Bill and most recently, the Therapeutic Products Act. Under these regulations, products would have been required to be manufactured according to a Code of Manufacturing Practice in order to make therapeutic claims, permitting products to be classified as a natural health product rather than a dietary supplement.

It should also be noted that a maximum daily dose of 25 mcg for vitamin D is specified in the Dietary Supplement Regulations 1985.

Review of Comments

Fifteen comments were received on the proposed amendment to the classification of vitamin D. Of these, nine were in favour of the proposed change, and five against. Of those supporting the proposed amendment, four were from natural health industry companies, two were from general practitioners, and three were individuals. A reasonable amount of evidence was provided by three parties supporting the proposal. These emphasised the extent of vitamin D deficiency as being at least 20%, and cited studies showing a low risk of adverse effects. While acknowledging a risk from supplementation, the risk of vitamin D toxicity was stated to be exceedingly rare, and the risk from deficiency was felt to be the greater risk.

Five submitters were opposed to the proposal. They included the Pharmacy Guild, the NZ Food and Grocery Council, the Australian Self Medication Industry, one pharmaceutical company, and the Ministry of Primary Industries (MPI). The lack of information in the submission concerning evidence of benefit for increasing the level of vitamin D from 25 μg to 75 μg was commented upon. The main benefit appeared to be the opportunity to make a health claim on a natural health product around maintenance of healthy teeth and bones. One commented that it was likely that daily dietary supplement doses of 75 μg would result in a dietary intake that is close to or exceeds the current upper limit. Another concern was the risk of chronic toxicity over time, due to storage of active vitamin D.

The risk of people taking high doses of vitamin D long term without medical supervision was raised by the Pharmacy Guild. The Guild pointed out that, as previous MCC meeting minutes showed, there had been unsuccessful proposals to reclassify the current prescription only strengths of vitamin D to be restricted (pharmacy only) medicines in the past. These objections were based around vitamin D deficiencies not being able to be diagnosed or managed in a pharmacy setting. Therefore, it is considered even less likely that the general consumer will be able to effectively diagnose or manage a vitamin D deficiency. A patient's dose of vitamin D to treat a deficiency should be based upon plasma tests to determine vitamin D and calcium levels, rather than a blanket uniform dosage being taken. The risk that consumers would be less likely to adhere to dosage recommendations for medications or products available on general sale, where there was no discussion with either a doctor or pharmacist, was a concern expressed by others opposed to the proposal.

While they declined to comment on the vitamin D or any other individual proposal, the Royal New Zealand College of General Practitioners urged the MCC to place considerable weight on the opinions of experts working from a scientific evidence-based perspective, who have public safety as their primary motivation, and who are independent of commercial interests.

One submitter from the pharmaceutical industry queried a statement in the submission 'when the NHP Bill is passed, natural health products will have to meet a Code of Manufacturing Practice'. This submitter noted that, whilst this is clearly a beneficial step, it is unclear how this manufacturing-related information supported the proposed increase in amounts of vitamins and minerals in natural health products.

The desirability of maintaining a classification system that is harmonised or consistent with that of Australia, given the fact that New Zealand had worked for many years to achieve classification harmonisation with Australia where practical, was also cited as a concern.

Risk – Benefit Assessment

Benefits of the Proposal

As summarised in the submission from the postponed 56th MCC meeting, multi-ingredient supplements such as trace elements and essential nutrient formulations are usually taken to complement dietary intake of essential vitamins and minerals. Such products are generally regarded as dietary supplements. At the present time, under the current Dietary Supplements Regulations 1985, therapeutic claims are not permitted for dietary supplements, and products cannot provide advice on their labels on how they should be used.

The Natural Health Products (NHP) Bill that was proposed at the time, followed by the recently repealed Therapeutic Products Act, aimed to address this problem. However, neither have progressed to the development of updated regulations in relation to natural health products. As previously noted, the ability to make claims for allowed health conditions, provided the manufacturer of the natural health product holds evidence to support the claim(s) being made, is not yet in existence. The main benefit outlined in the submission was that the proposed changes would enable easier implementation of the NHP system by allowing the essential vitamin or mineral to be present in effective quantities/doses in natural health products and/or dietary supplements. Given the fact that the NHP Bill and the Therapeutic Products Act did not progress, this benefit is no longer valid.

The above issues notwithstanding, I agree with the content of the submission statement of the benefits to both the consumer and to the public expected from the proposed change. A major biologic function of vitamin D is to maintain normal blood levels of calcium and phosphorus. Vitamin D aids

in the absorption of calcium, promoting bone mineralization in concert with a number of other vitamins, minerals, and hormones. Without vitamin D, bones can become thin, brittle, soft, or misshapen. Vitamin D is known to prevent rickets in children and osteomalacia in adults.

Aside from the above, relatively little material was provided in the submission on the benefits expected from the proposed classification change. However, as previously mentioned, the subject of vitamin D classification has been extensively investigated by Medsafe and discussed in previous MCC meetings. The 15-page submission for reclassification of vitamin D report prepared by Medsafe in December 2011 provides a comprehensive review, and was considered by the MCC at its 47th meeting in 2012. This is included as Appendix 1 of the 56th MCC submission.

In addition to its association with bone and muscle health, an adequate vitamin D status has been increasingly linked to a wide range of chronic diseases. Several observational studies have demonstrated inverse associations between vitamin D status and the risk of type 2 diabetes, cardiovascular disease (CVD), immune disorders and cancer. Considerable research into these and a wide range of other human health conditions that may be influenced by this vitamin has taken place, and more is underway. Results from these observational studies and some but not all randomized clinical trials indicate that vitamin D supplementation is a promising strategy with long-term preventive effects on multiple chronic diseases and thus has the potential to decrease all-cause mortality.

However, findings from Mendelian randomization (MR) studies have been less supportive of such benefits (Liu 2021; Chen 2025; Fang 2025). These types of studies aim to identify and monitor genetic risk variants with altered function, which are randomized at conception and remain fixed throughout one's lifetime. They are less susceptible to confounding bias such as dietary, lifestyle, or socio-economic factors, and reverse causality, all of which tend to be weaknesses of observational studies and many clinical trials (Roberts 2018).

Additionally, increasing evidence suggests that genetic variation may impact the physiological effects of calcium, as well as Vitamin D, and thus variable results reported in the case of vitamin D supplementation in various trials (Yang 2018; Weinstein 2024; Gariballa 2024; Molani-Gol 2025). The influence of vitamin D receptor genetic polymorphisms on disease risk and outcomes is not well understood, but is theorised to be important. A recent meta-analysis of 133 Mendelian randomization studies found genetically high levels of 25(OH)D were associated with reduced risks of a wide range of conditions, but increased risk of a small number of others (Fang 2024).

Future randomized clinical trials should consider interindividual differences and identify whether certain subgroups of individuals may benefit from vitamin D supplementation in the context of disease outcomes. A focus on personalized interventions for diseases involving considerations of genetic variations in combination with low vitamin D concentrations is likely to enhance our knowledge on the benefits of supplementation. The current understanding of the potential benefits of vitamin D are summarized below.

Comments on Dose

In a review aimed at fostering consensus and harmonizing vitamin D guidelines, a European research team recently argued against a general screening for vitamin D deficiency, but suggested 25-hydroxyvitamin D (25(OH)D) testing in certain risk groups (Pludowski 2024). In the discussion on vitamin D dosage recommendations, one major scientific debate is whether serum 25(OH)D ≥ 50 nmol/L (20 ng/mL) or ≥75nmol/L (30 ng/mL) should be the target of general vitamin D supplementation. As 25(OH)D concentrations below 20 ng/mL have the strongest correlations with adverse health outcomes, raising 25(OH)D concentrations above 20–30 ng/mL can be expected to

have very significant health benefits (Grant 2025). However, others have advocated for serum 25(OH)D levels of ≥75 nmol/L (30 ng/mL) as being more appropriate and better aligned with protective effects against chronic disease (Grant 2025; Pludowski 2024).

In order to achieve these levels, higher supplementation doses than current recommendations are being advocated. A daily dosage of at least 2000 IU has been suggested as the minimum appropriate dose for many people in order to achieve around 30–40 ng/mL, with minimal safety concerns (Pludowski 2024; Grant 2025). Data from controlled trials suggests that daily supplementation with 2000 IU is likely to improve health outcomes and is sufficient to raise and maintain serum 25(OH)D concentrations above 50 nmol/L (20 ng/mL) and above 75 nmol/L (30 ng/mL) in >99% and >90% of the general adult population, respectively (Cui 2023).

As is always the case however, different individuals will require different dosages in order to achieve optimal plasma levels. As summarized previously, darker-skinned individuals, particularly when residing at higher latitudes, are likely to require higher supplementation doses. This consideration is especially important in a New Zealand public health context, given the increasing ethnic diversity of our population. Other groups at increased risk of deficiency include the elderly, vegetarians and vegans, and those with obesity. People living in polar regions also face an increased need due to limited solar radiation, diet, and environmental stressors.

In a supplementation protocol within a practitioner setting, treatment success may be evaluated after at least 6 to 12 weeks in certain risk groups (e.g., patients with malabsorption syndromes) by measurement of serum 25(OH)D (Pludowski 2022).

Musculoskeletal Benefits

Increasing serum vitamin D levels via supplementation combined with calcium is generally associated with improved bone mineral density and a reduced risk of falls and fractures, particularly in the elderly (Manoj 2023; Giustana 2023). A recent meta-analysis found daily oral supplementation of 800 IU of vitamin D3 plus 1200mg of calcium was significantly more effective than 800 IU of Vitamin D3 plus 1000mg of calcium in reducing hip fractures (Manoj 2023).

However, the extent to which vitamin D either alone or with calcium reduces the fracture risk in the elderly has recently been queried. A 2019 systematic review and meta-analysis of eleven observational studies and eleven clinical trials found no association of standard doses of 400-800 IU per day of vitamin D with a reduced risk of fracture, although a 6% reduced risk of any fracture, and a 16% reduced risk of hip fracture, was associated with combined Vitamin D and calcium supplementation (Yao 2019).

Another recent meta-analysis of eighteen clinical trials involving the fracture risk with administration in people aged 60 or over found no reduction in the incidence of vertebral or any other fracture, even following subgroup analysis which looked at dosage or serum 25(OH)D levels (Khatri 2023). A recent review of fracture risk in postmenopausal women without osteoporosis also found no vitamin D associated reduction despite improvement in 25(OH)D levels and bone remodeling (Reis 2023).

These recent studies would seem to raise doubt on the findings of earlier meta-analyses such as those by Bischoff-Ferrari (2009a, 2009b) cited in the submission. These suggested that doses between 700 and 1000 IU of vitamin D are associated with a 19% reduction in risk of falling in people older than 65 years of age in stable health, within 2-5 months of treatment initiation (Bischoff-Ferrari et al 2009a).

Another meta-analysis by Bischoff-Ferrari et al (2009b) indicated that vitamin D doses of 482-770 IU/daily resulted in a 20% reduction in the relative risk of non-vertebral fractures and an 18%

reduction in the relative risk of hip fractures. These benefits were dose dependent, and were not seen with lower doses of vitamin D. Maintaining a serum vitamin D concentration at or above 60 nmol/L has been associated with a 23% reduction in falls, and this level has been calculated as required for fall prevention (Bischoff-Ferrari et al, 2009a).

The 2011 Medsafe submission noted that these studies found evidence of improvement at vitamin D quantities that are currently unscheduled (i.e. up to 1000 IU or 25 µg per day), although the authors indicated that higher doses of vitamin D should be explored to optimise the benefit.

More recently, higher levels of serum 25(OH)D of at least 30 ng/mL (75 nmol/L) have been advocated for patients with rheumatic diseases to prevent osteomalacia, secondary osteoporosis, and fracture, and possibly 40-60 ng/mL (100-150 nmol/L) to achieve maximal benefit from vitamin D for immune health and overall health (Charoenngam 2021).

Cardiovascular Disease

Systematic reviews and meta-analyses of randomized clinical trials have indicated that vitamin D supplementation improves several cardiovascular risk factors, including a significant increase in HDL cholesterol and reductions in triglycerides and systolic blood pressure (Mirhosseini 2018). Other studies have suggested supplementation may help heart failure patients (Camici 2013). A 2019 meta-analysis, however, found no evidence from clinical trials that vitamin D supplementation reduces the risk of cardiovascular disease (Barbarawi 2019).

The D-Health randomized controlled trial conducted in Australia (2014 to 2020) found a marginally significant reduction in major cardiovascular events when 60,000 IU of vitamin D was given each month for up to five years (Thompson 2023). While the reduction for the entire set of participants with vitamin D supplementation was marginal (HR = 0.91) it was significant for participants who were taking concomitant cardiovascular drugs (HR = 0.84). The higher compliance rate and longer follow-up duration might partly account for an increased statistical power to demonstrate the effects of vitamin D supplementation.

A retrospective, observational, nested case–control study in the US evaluated the effects of vitamin D supplementation on the risk of myocardial infarction and all-cause mortality for patients with vitamin D deficiency who received care at the Veterans Health Administration from 1999 to 2018 (Acharya 2021). This compared 10,014 treated subjects who achieved 25(OH)D concentrations > 30 ng/mL, to 2,942 untreated subjects with 25(OH)D concentrations < 20 ng/mL. A Hazard Ratio (HR) for all-cause mortality rate of 0.61 was measured for the Vitamin D supplemented group, and a HR for myocardial infarction of 0.73.

Observational studies have also reported that the incidence of stroke is inversely correlated with serum 25(OH)D concentration (Grant 2024). While these are encouraging findings, methodological variability including inconsistent dosing regimens, baseline vitamin D status, and heterogeneous populations, are likely to have influenced results from several of these clinical trials (Zhao 2024). As emerging evidence indicates a potential threshold effect of vitamin D, future well-designed studies focused on specific populations with vitamin D deficiency or insufficiency have been recommended (Zhao 2024).

Immune System Support

Vitamin D is reported to support immune function by enhancing innate and adaptive immunity in many different ways (Gmobart 2005; Tabsh 2025; Mehta 2025). Chronic vitamin D deficiency causes immune system dysfunction, which increases susceptibility to pathogens such as bacteria,

especially intracellular parasites, and viruses (Liu 2024). A 2019 meta-analysis found an association between inadequate vitamin D status and an increased risk of community acquired pneumonia (Zhou 2019) and Covid-19 (Kaufman 2020; Oristrell 2022).

Evidence from randomized trials and observational studies supports a role of vitamin D supplementation in reducing the incidence and severity of influenza (Pandey 2025). Supplementation of young children with vitamin D at a dose of 1200 IU/day over the winter months was shown to reduce the incidence of influenza type A, in a Japanese placebo controlled clinical trial. Eighteen out of 167 children given vitamin D contracted influenza A, compared to thirty one out of 167 children in the placebo group. The rate of secondary asthma attacks was also markedly reduced in those receiving vitamin D supplementation, with only two children developing this versus twelve children from the placebo group (Urashima 2010).

Spanish patients on cholecalciferol treatment and achieving 25(OH)D levels ≥ 30 ng/ml were shown to have a lower risk of SARS-CoV2 infection and a lower risk of developing severe Covid-19 and a lower mortality from Covid-19 than unsupplemented 25(OH)D-deficient patients (Oristrell 2022).

A meta-analysis of thirteen studies which pooled data from 2,933 Covid-19 patients, also found supplementation to reduce Covid-19 severity and death (Pal 2022). Subgroup analysis showed supplementation was associated with improved clinical outcomes only in patients who took it post-Covid-19 diagnosis, and not in those who had received vitamin D before diagnosis. Other studies have provided support for vitamin D supplementation reducing hospitalization rates and improving outcomes in Covid-19 infected patients (Bikle 2022).

Vitamin D deficiency has also been implicated as a risk factor for *Chlamydia trachomatis* infection and treatment failure, and adjunctive therapy alongside antibiotic therapy, suggested to improve treatment outcomes (Liu 2024).

Low levels of serum 25(OH)D) have also been associated with an increased risk of developing autoimmune conditions such as psoriasis, type 1 diabetes, and multiple sclerosis (Feige 2020; Giustina 2024). Various clinical trials describe the efficacy of supplementation of vitamin D and its metabolites for treating these diseases, although others have found no benefits (Sirbe 2022; Formisano 2023; Giustina 2024).

The role of vitamin D deficiency in the development of multiple sclerosis has been investigated by multiple studies (Scazzone 2021; Fang 2024). Variants in some genes encoding proteins involved in vitamin D metabolism, transport, and function have been related to the susceptibility of this autoimmune condition. However, to what extent these variants can influence the risk of multiple sclerosis remains unknown (Scazzone 2021).

Chronic Respiratory Disease

There is mounting evidence that higher serum 25(OH)D concentrations are associated with a lower risk of chronic obstructive pulmonary disease (COPD). Analysis of data from the UK Biobank study reported an association between serum 25(OH)D concentrations and the incidence of COPD (Zhu 2023). A recent Mendelian randomization analysis based on European data also found an inverse causal association between genetically predicted 25(OH)D concentration and the risk of COPD (Lu 2023). Significantly, each standard deviation of 25(OH)D concentration increase was associated with a 57% reduced risk of COPD (OR = 0.43; 95% CI, 0.28–0.66). This suggests improved protection with higher supplementation doses.

A 2021 meta-analysis of randomised controlled trials of vitamin D supplementation for prevention of acute respiratory infections revealed a small but statistically significant protective effect (Jolliffe

2021). Another meta-analysis of twelve trials, however, failed to reveal a significant effect of vitamin D supplementation on the risk of acute respiratory infections among older adults, although benefits in those with a low baseline 25(OH)D concentration and in those living in low- and middle-income countries were implicated (Jia 2024). A further recent systematic review found no statistically significant protection regardless of baseline vitamin D status, dosing frequency, or dose size (Jollife 2025).

The vitamin D status of dark-skinned individuals is generally regarded as being less assured than for white-skinned people due to a reduced ability to absorb UVB. While some studies have reported an inverse association and the incidence of acute respiratory tract infections in black and indigenous groups, a recent review of eighteen studies limited to non-white ethnic groups failed to find conclusive evidence of an association between vitamin D supplementation and the incidence of acute upper respiratory tract infections in dark-skinned individuals (Bournot 2024).

Cancer

Meta-analyses of observational studies have reported inverse correlations of serum 25(OH)D with the incidence of twelve types of cancer. These include colorectal, bladder, breast, liver, lung, ovarian, head and neck, pancreatic, renal and thyroid cancer, and multiple myeloma (Moukayed 2017; Munoz 2022; Ismail 2023). A recent narrative review also provided convincing evidence in support of a global protective action of vitamin D against several important types of cancer (Munoz 2022). Vitamin D deficiency was found to be common and significant among head and neck cancer patients in a recent review, implicating a possible role in cancer risk, prognosis, survival, treatment-related side effects, malnutrition, and post-surgical complications (Mot 2025). Another study on Kenyan breast cancer patients reported deficient or insufficient vitamin D levels in 81% of patients (Wasike 2025). Polymorphisms in the vitamin D receptor and related genes have been associated with cancer risk, including breast, colorectal, and lung cancer (Gnagnarella 2020; Latacz 2021; Li 2024).

Inverse correlations have also been made between solar UVB radiation dose indices and incidence or mortality rates for over twenty types of cancer (Munoz 2022). Epidemiological studies from the UK and Sweden also link sun exposure with reduced all-cause, cardiovascular, and cancer mortality (Weller 2024).

This protective relationship between sun exposure and cancer risk has been reported despite simultaneously excessive solar UVB exposure being known to increase the risk of non-melanoma and melanoma skin cancers through mechanisms involving DNA damage and oxidative stress (Uçar 2025). Given the high UV index and associated skin cancer risk here in New Zealand, and the reasonably good awareness to therefore avoid excessive sun exposure, more research and public education regarding the benefits of moderate sun exposure on vitamin D status has been called for (von Hurst 2023).

A 2019 meta-analysis pooled data from 17 prospective cohort studies to evaluate colorectal cancer incidence in relation to serum 25(OH)D levels in 5,706 colorectal cancer case participants and in 7,107 control participants. This calculated that for each 10 ng/mL increase in 25(OH)D concentration, the risk of colorectal cancer was 19% lower in women (RR = 0.81) and 7% lower in men (RR = 0.93) (McCullough 2019). However, clinical trials in which vitamin D doses from 400 to 1100 IU/day have been taken with or without calcium, have suggested no significant benefit in cancer incidence but significant improvements in cancer mortality (Keum 2014; Bjelakovic 2014). The possibility of reverse causation has also been raised by some researchers, in which the existence of certain diseases or conditions themselves may lead to reduced 25(OH)D concentrations (Autier 2014; Bilezikian 2023; Bouillon 2023).

The New Zealand Vitamin D Assessment (ViDA) study was a double-blind placebo controlled trial in which 5,110 adults aged 50 to 84 years from Auckland were randomised to receive vitamin D3 in monthly doses of 100,000 IU or placebo for a median of 3.3 years. This study found similar rates of cancer in both groups (Scragg 2018). However, the relatively short duration, relatively small number of non-European participants (17%), and intermittent bolus rather than daily oral supplementation regimen, may have contributed to the lack of a reported benefit.

Another clinical trial involved 2,303 healthy postmenopausal women in Nebraska who took a higher dosage of 2000 IU of vitamin D plus 1500 mg of calcium or placebo daily for four years. This study found a suggestive but nonsignificant 30% reduction in a new diagnosis of cancer (Lappe 2017).

The largest randomized clinical trial to study the effects of vitamin D supplementation on the risk of cancer and cardiovascular disease was the VITAL study. This study enrolled over 25,000 US participants in 2012–2014, half of whom took 2000 IU/day of vitamin D3, and the other half placebo. No significant effect of vitamin D supplementation on cancer risk reduction was seen, despite a median follow up period of 5.3 years (Manson 2019). However, subgroup analysis suggested that participants with a BMI of less than 25 kg/m^3, or those with a p53 protein mutation, did benefit from a significantly reduced risk of cancer (Kanno 2023).

Vitamin D supplementation has also been reported to help reduce chemoradiation side effects like mucositis, skin toxicity, dysphagia, and pain, ultimately improving patients' quality of life during treatment (Mot 2025). A recent systematic review of vitamin D supplementation during cancer treatment with chemotherapy or radiotherapy found it attenuated some chemotherapy adverse events in patients with non-small-cell lung cancer. Vitamin D deficiency was also associated with an increased risk of peripheral neuropathy induced by chemotherapy in breast cancer patients. Supplementation was found to be both safe and effective (Afonso 2025).

Other Potential Benefits

Type 2 Diabetes Mellitus

Animal studies have implicated a possible protective role for maternal vitamin D supplementation against metabolic disturbances such as insulin resistance that can occur later in life (Lorenzon 2021). Other findings highlight a potential contribution of vitamin D deficiency to outcomes in pediatric type 2 diabetic patients (Barot 2025). However, despite observational studies showing lower serum 25(OH)D concentrations in patients with type 2 diabetes (Bouillon 2019), most Mendelian randomisation studies have not supported these conclusions (Bouillon 2022). A large five-year trial in Finland, in which healthy older adults were given placebo, 1,600 IU/day or 3,200 IU/day of vitamin D3 for five years, found no preventative effect for either dosage against the risk of developing type 2 diabetes (Virtanen 2025).

Several studies have identified a correlation between vitamin D deficiency and childhood obesity, although the mechanism behind these associations implicating vitamin D as a causal factor remains overall unclear (Aldana 2025).

Neurological Effects

Vitamin D also has many effects on the brain, mediated through various mechanisms (Farghali 2020), and evidence is emerging to support a therapeutic potential for vitamin D across various mental and neurological disorders (Al Noman 2025; Khatoon 2025). Lower serum vitamin D levels may be associated with higher motor symptom severity in Parkinson's disease. While a recent meta-analysis

found no impact of supplementation Vitamin D on the Unified Parkinson's Disease Rating Scale part 3 score, improvements were seen in the 6-Minute walking test distance and some other motor symptoms (Xu 2025). A systematic review of four studies on Parkinson's disease found evidence of some symptom improvement, although studies were variable in patient populations and primary outcomes, and treatment durations were mostly short (Homann 2024).

A recent trial studied eighty-three children aged 4 to 15 years diagnosed with chronic tic disorder who were randomly assigned to receive either high-dose (5,000 IU/day) or low-dose (1,000 IU/day) vitamin D for three months. Both groups showed significant improvements in tic severity and increases in serum 25(OH)D levels, but improvements were more pronounced in the high-dose group (Mohamed 2025).

Several studies suggest the potential involvement of vitamin D in the pathophysiology of depression. A recent systematic review of 50 articles published between 2008 and 2024 found that most cross-sectional and cohort studies indicated an inverse relationship between serum 25(OH)D levels and the risk of depression, as well as the severity of depressive symptoms. Increased serum 25(OH)D concentration was associated with an improvement in depression test scores, with vitamin D supplementation exerting a beneficial effect on both the incidence and the prognosis of depression (Rosian 2025). Several studies have reported improved clinical outcomes in depressed patients receiving vitamin D either alone or alongside antidepressants (Vellekkatt 2019; Kaviani 2022; Zhao 2024). A 2022 meta-analysis of 29 studies with 4,504 participants found the use of vitamin D had beneficial impacts on both the incidence and the prognosis of depression (Xie 2022). A 2022 review of trials also found evidence of improved sleep quality following vitamin D supplementation, although its effect on sleep quantity and sleep disorders requires further investigation (Abboud 2022).

Involvement in various neurodevelopmental and neuropsychiatric conditions has also been implicated. An inverse association has been reported for serum 25(OH)D and young patients with ADHD, with ADHD children having significantly lower levels than healthy controls (Kotsi 2019; Massoodi 2023).

Emerging evidence indicates that vitamin D can ameliorate neurodegeneration by regulating pertinent molecules and signaling pathways including maintaining calcium homeostasis, reducing oxidative stress, inhibiting inflammation, and suppressing the formation and aggregation of pathogenic proteins (Wang 2023). Chronic vitamin D deficiency has been associated with neurodegeneration and leading to cognitive decline in Alzheimer's disease and dementia (Gezen-Ak 2023). However, despite many studies implicating a role for vitamin D in cognition, further research is necessary to better understand this association (Roy 2021; Beauchet 2021).

Pregnancy
Vitamin D supplementation during pregnancy in women with low vitamin D status has been shown to have many potential benefits. These include improved foetal growth and lower risks for small-for-gestational-age, preeclampsia, preterm birth, and gestational diabetes (Perez-Lopez 2020; Gallo 2020). Convincing data associates vitamin D deficiency during pregnancy with a greater risk of preterm birth. Maternal 25(OH)D concentrations ≥40 ng/mL were associated with a substantial reduction in preterm birth risk in a large, diverse population of American women (McDonnell 2017).

Current New Zealand guidelines include the recommendation of vitamin D supplementation for pregnant people at risk of deficiency, and in all exclusively and partly breast-fed infants up to the age of one year.

A recent update of a 2017 systematic review and meta-analysis of clinical trials involving vitamin D supplementation during pregnancy concluded that further trials specifically focused on populations

with low vitamin D status or at greater risk of key outcomes such as gestational diabetes are needed. The authors concluded that many benefits of supplementation in pregnancy remain uncertain because current evidence has high heterogeneity, including variation in study context, baseline and achieved end-line 25(OH)D levels, and studies with high risk of bias (Yang 2025).

Potential Risk of Harm from the Proposal

I agree with most of the content of this section of the submission, although further consideration of this important area is needed. While vitamin D supplementation is generally safe within recommended limits, excessive intake may cause harm.

As outlined in the submission, consuming too much vitamin D through diet alone is not likely, but is much more likely to occur from high intakes of vitamin D in supplements. The NZ Ministry of Health (National Health and Medical Research Council, 2006) considers a daily intake of 25 mcg (1,000 IU) for infants up to 12 months of age and 80 mcg (3,200 IU) for children, adults, pregnant, and lactating women to be the tolerable upper intake level (UL). Upper limit recommendations from the National Institutes of Health Office of Dietary Supplements in the U.S., are somewhat higher, with 100µg (4,000 IU) being recommended (ODS, 2016).

The submission cites the fact that some researchers argue that the UL has been set too low, and that adverse events are likely only with serum 25(OH)D concentrations >140 nmol/L. Some researchers also that these levels are likely to require daily amounts of vitamin D of 10,000 to 20,000 IU to attain (Vieth 2001; 2007; Pilz 2018). The fact that sunshine can provide an adult with vitamin D in an amount equivalent to daily oral consumption of 250 µg (10,000 IU)/day, also seems supportive of higher supplemental doses and the current proposal. Intuitively however, the physiological processes involved in metabolism of vitamin D via UV exposure to the skin, and the body's ability to deal with the manufacture of relatively high levels in some cases through this natural process, may involve additional safety mechanisms or factors that ameliorate risk of toxicity more so than achievable through dietary supplementation.

As stated in the 2011 Medsafe MCC submission, vitamin D has a wide margin of safety, and intoxication (intentional or unintentional) is extremely rare. The submission also references several clinical trials in which participants took supplementation dosages of 25 to 100 µg (1000 to 4000 IU) per day for prolonged periods, with no adverse events being reported. The safety and efficacy of vitamin D supplementation at doses of 1200 IU during pregnancy and breastfeeding, has also been supported by various trials (Roth 2018; O'Callaghan 2018). However, since the submission to the 56th MCC, additional safety data has become available.

Data collected from Northern Germany suggests that target serum levels are not achieved even during the summer months, despite the replenishment of vitamin D stores for the winter months. Therefore, it can be reasonably and safely assumed that supplementation at least in amounts typically used in Germany, which are not dissimilar to those currently used in New Zealand, is appropriate and safe even during the summer months (Falk 2024).

However, overdosing of vitamin D, particularly over a prolonged period of time, may lead to adverse effects, with the most documented in the literature being hypercalcemia, hypercalciuria, and nephrolithiasis.

Hypercalcaemia & Hypercalciuria

Hypercalcaemia is one of the principal concerns associated with excess vitamin D intake. This may cause a variety of symptoms including loss of appetite, confusion, kidney problems including kidney

stones, nausea, vomiting and weakness. However, the extent of this risk may have been over-estimated in previous reports. No cases of hypercalcemia (total serum calcium > 2.63mmol/L) were reported in a study on 75 healthy but vitamin D deficient adults who took cholecalciferol in three different dosages up to 10,000 IU per day for 8 weeks, followed by 1000 IU per day for four weeks (Fassio 2020). Another study involving 69 healthy adults and a supplemental dose of 2500 IU/day over a 60-day period was not associated with hypercalcaemia or other adverse events (Solnier 2024). While reassuring, these participant numbers are relatively low when it comes to being sufficiently statistically powered to detect adverse events, and the studies were relatively short term in their duration.

While most clinical trials involving long term vitamin D supplementation have reported a low incidence of adverse events, interpreting their findings is sometimes difficult due to calcium being taken concomitantly (Malihi 2017). Recent trials have found no effects on serum calcium or calciuria unless very high doses were used, such as 4000 to 10,000 IU per day in the large Calgary study (Burt 2019). Vitamin D supplementation was not found to increase the risk of hypercalcemia in a meta-analysis of eleven clinical trials in 906 chronic kidney disease patients (Yeung 2023).

Another recent meta-analysis of 22 clinical trials including 12,952 participants found that long term administration of supplemental vitamin D in doses of 3200-4000 IU daily did increase the risk of hypercalcemia and other adverse events in a small proportion of individuals (Zitterman 2023). This suggests that these higher doses are not completely safe. Higher rates of possible hypercalciuria were also reported following supplementation with high doses of vitamin D from mid pregnancy until 26 weeks postpartum in a trial involving women in Bangladesh (Roth 2018).

Treatment of healthy adults with vitamin D for 3 years in the Calgary trial at a dose of 4000 IU per day or 10 000 IU per day resulted in statistically significant lower radial bone mineral density, and for the 10,000 IU dose only, also in tibial bone mineral density. While no significant differences were measured in bone strength at either the radius or tibia, these findings suggest potential harmful effects from such high-doses of vitamin D supplementation on bone health (Burt 2019). This pattern of apparent bone loss was dose-dependent and greatest in the 10,000 IU group, and was seen more in females than in males (Burt 2020; Billington 2020; Burt 2021). Hypercalciuria was more common than hypercalcemia, and both occurred more frequently with higher doses (Billington 2020).

Other potential adverse effects have been revealed for high doses of supplemental vitamin D through various studies during the past five years. These include an increased risk of falls, which has been reported in several trials (Bischoff-Ferrari 2016; Mazess 2021; Michos 2022; Zittermann 2023; Gallagher 2023).

A systematic review and meta-analysis of twenty-two trials which reported safety data (Zittermann 2023) found that at supplemental doses of 3200-4000 IU per day, vitamin D appeared to increase the risk of hypercalcemia and the risk of falls and hospitalization, with a RR of 1.25 and 1.16 respectively. Mean baseline 25(OH)D values were < 50 nmol/l in eleven trials and ≥ 50 nmol/l in the other eleven trials. Of the twenty-two trials, eight were performed in apparently healthy individuals with three studies including pregnant women, and fourteen trials included different groups of patients.

While only four of the twenty-two studies reported data on the risk of falls, any association with an increased risk of falls and hospitalization, particularly in elderly patients, is of some concern. Further and long-term studies are needed. Results from these studies indicate an increased risk of falls at circulating 25(OH)D of between 40nmol/l and 100 nmol/l and above (Bischoff-Ferrari 2016; Michos 2022), and particularly in those taking 4000 IU daily. Higher plasma calcium concentrations in patients receiving these doses of vitamin D may also affect neuromuscular activity and thus the risk of falls.

While a review by Vieth in 2007 concluded that the clinical trial evidence then available showed that a prolonged intake of 10,000 IU per day of vitamin D(3) is unlikely to pose any risk of adverse effects in almost all individuals in the general population, this view has been put under doubt by various subsequent authors. Furthermore, dose response studies involving vitamin D remain largely lacking, and controversy remains amongst researchers concerning optimal treatment doses in many instances.

The elderly, children, and infants are more vulnerable to adverse events following vitamin D supplementation. Mild hypercalcemia and hypervitaminosis using currently recommended doses have been reported in infants with rickets (Vanstone 2012). A 2018 Lithuanian study reported rates of vitamin D deficiency, sufficiency, and hypervitaminosis in 67%, 21%, and 12% of cases, respectively. Most cases with hypervitaminosis were in the group of children up to 2 years of age (Bleizgys 2018).

Other Potential Risks

A recent Polish study involving a group of 1,400 geriatric patients reported that, within five years, vitamin D_3 concentrations exceeding the recommended level were recorded in seven patients, including three with toxic levels. All abnormal results occurred in women, most above 74 years of age. The most frequently reported symptoms included general weakness, lower limb and joint pain, sleep disorders and a low mood. People with toxic concentrations reported dizziness (Żórawska 2024). Vitamin D toxicity was shown to be relatively rare, although the clinicians involved concluded that doses >4000 IU daily should not be used in seniors, and that individual 25(OH)D status and all dietary supplements being taken should be assessed to prevent such toxicity (Zorawska 2024).

A recent case report of an elderly woman who exhibited progressive lower limb weakness, delirium, and abdominal distension over a 3-day period with significant electrolyte imbalances, was found to have consumed an excessive amount of liquid vitamin D3 over the preceding 3 weeks (Yu 2024). Another case report of a 76 year-old British man who developed acute renal failure and hypercalcaemia from overconsumption of vitamin D is noted (Khan 2024). The patient had been taking high doses of vitamin D supplements (10,000-20,000 IU daily, increased to 50,000 IU when feeling unwell) for several years without medical supervision (Khan 2024).

A number of recent clinical trials have provided additional safety data for doses of 2000 IU (50 µg) of vitamin D per day when administered for long periods in relatively unselected general adult populations (Luttmann-Gibson 2019; Manson 2019; Adebayo 2021). These include the VITamin D and OmegA-3 Trial (VITAL), in which 2000 IU (50 µg) of vitamin D or placebo were taken by 25,871 older men and women from the US with an intervention period of 5.3 years. This study showed no significant signs of vitamin D toxicity in the intervention group (Manson 2019). After one year, 99.4% of participants allocated to vitamin D achieved serum 25(OH)D concentrations of ≥50 nmol/L (20 ng/mL), yet few safety concerns were reported from long term use of a daily dose of 2000 IU (50 µg) (Luttmann-Gibson 2019).

A meta-analysis of fifteen trials involving vitamin D supplementation at ≥2800 IU (70 µg) for at least one year also showed no increase in overall total adverse events. Reassuringly, this meta-analysis also included clinical trials in different populations, including, amongst others, patients with heart failure, epilepsy, multiple sclerosis, chronic obstructive pulmonary disease, or lung transplantation (Malihi 2019).

However, the fact that some would benefit more from lower amounts, and some from higher amounts, should be acknowledged. Supplementation regimens selected based upon the individual person, and in some cases, pre-treatment serum levels of 25(OH)D is preferable. Also, while rare, genetic mutations that predispose to hypercalcemia in individuals who are supplemented with

vitamin D, should be considered (Cappellani 2021). Potential risks can be ameliorated through adopting personalized treatment strategies.

The extent of food fortification with vitamin D, and New Zealand's policy on this, is also likely to influence the risk of overdosage or toxicity through excessive intakes, and should be considered. Finland began to add vitamin D to fat spreads at a concentration of 10 µg/100 g and fluid milk products at 0.5 µg/100 g, in 2003. These values were doubled in 2010. As a result, the mean serum 25(OH)D concentrations among non-supplement users increased by 20 nmol/L between 2000 and 2011 for daily fluid milk consumers and by about 15 nmol/L for fat spread consumption (Jaaskelainen 2017).

<u>Product Stability</u>

With liquid forms of vitamin D, considerations of stability tend to become more important. The literature reports the potential applicability of several methods for encapsulating vitamin D in beverages, including spray drying, micro/nanoemulsions, nanostructured lipid carriers, liposomes, and complexation to polymers. However, while some of these delivery systems have been assessed regarding vitamin D stability, there is a lack of kinetic data that allow for the prediction of its stability under industrial processing conditions (Vieira 2022).

Importantly, several cases of intoxication presenting as severe hypercalcemia, hypercalciuria, or nephrocalcinosis have been reported. Such cases were related to errors in manufacturing, formulation, or prescription (Vogiatzi 2014).

An evaluation and analysis of unlicensed vitamin D preparations (food supplements) in the UK published in 2021 found that these accounted for 7% of vitamin D prescriptions in 2018. Testing found that the eleven food supplement products selected showed vitamin D content ranging from 41.2 ± 10.6% to 165.3 ± 17.8% of the labelled claim, with eight of the preparations failing to comply with the food supplement specification (80-150% of labelled claim) (Wan 2021). In contrast, the two licensed vitamin D preparations tested showed a mean vitamin D content of 90.9 ± 0.7% and 90.5 ± 3.9% of the labelled claimed amount, meeting the BP specification for licensed medicines (90-125% of labelled claim).

While dietary supplement products sold in New Zealand are generally manufactured to a high standard, this UK study suggests another risk not discussed within the submission. Specifically, this is how amounts of this unstable vitamin in products that are not subject to appropriate quality standards and adequate regulatory oversight can be disturbingly different from amounts stated on the product packaging.

Adverse Events

Adverse events have previously been reviewed in the 2011 Medsafe submission. They include chronic vitamin D-induced hypercalcemia, and kidney stone formation, particularly when taken in combination with calcium. Growth arrest has been reported in children after prolonged administration of large doses of cholecalciferol daily, and death (as a result of renal or cardiovascular failure caused by vitamin D toxicity). The NZ Pharmacovigilance Centre had eight reports of suspected adverse reactions in which cholecalciferol was listed as a suspect medicine, to 31 September 2011 Reported reactions assessed by CARM as causally related (i.e. possible, probable or certain) were: face oedema, oedema genital, pruritus, skin dry, nail disorder, rash erythematous, prothrombin decreased, drug interaction, rash purpuric, choking, and dysphagia.

Long term use of 4,000 to 10,000 IU per day of vitamin D has been associated with lower radial bone mineral density, and doses of 10,000 IU with lower tibial bone mineral density. High bolus doses have

also been associated with an increased risk of falls, by various authors (Bischoff-Ferrari 2016; Mazess 2021; Michos 2022; Zittermann 2023; Gallagher 2023).

Interactions with Other Medicines

As per the submission, the National Institutes of Health Office of Dietary Supplements in the US states that vitamin D has the potential to interact with several medicines, including corticosteroids and weight-loss drugs such as orlistat and cholestyramine (ODS, 2016).

Those taking anticonvulsant medications such as carbamazepine, phenobarbitone, phenytoin, and primidone may also have a greater vitamin D requirement. Vitamin D can interact with thiazide diuretic drugs, as well as calcium, to increase the risk of hypercalcemia, particularly in the elderly. Concurrent vitamin D supplementation has also been reported to reduce plasma levels of atorvastatin (Robien 2013). Potential additional benefits on bone health through combining vitamin K with vitamin D supplementation have been reported (Aaseth 2024).

Contraindications and Precautions

While no information on contraindications and precautions was provided by the applicant, as per section 13 of the 2011 Medsafe report, vitamin D supplementation is contraindicated in hypercalcemia, hypervitaminosis D, and renal osteodystrophy with hyperphosphatemia. Caution should also be applied, and a risk-benefit assessment considered when various medical conditions are present, such as cardiac or renal function impairment, or granulomatous conditions such as sarcoidosis or tuberculosis (Doyle 2023; Tebben 2016; Gluba-Brzozka 2018). Those who are taking certain medications such as thiazide diuretics or calcium supplements, particularly where elderly, should also have their need for vitamin D supplementation assessed by a trained clinician or pharmacist, in conjunction with blood tests where required.

Summary

Vitamin D is a critical component of the human body, with far-reaching effects on health. It is an essential nutrient through the entire human lifespan, from prenatal to end-of-life stages, and an important precursor of 1,25-dihydroxyvitamin D (1,25(OH)2D), with regulatory actions in calcium homeostasis and other endocrine systems. It has an established role in skeletal diseases such as osteoporosis and bone fractures, and its supplementation has been used in the elderly and other high-risk groups for many years.

Vitamin D deficiency is increasingly considered a public health problem due to its worldwide high prevalence and many adverse clinical consequences. Most foods contain small amounts of this nutrient, and apart from its manufacture by the body following exposure to sunshine, supplementation is regarded as necessary to prevent levels of 25-hydroxyvitamin D (25(OH)D) falling below a certain level in order to prevent various chronic diseases.

Research into the functions of vitamin D in human health has provided significant new findings in recent years, and this is likely to continue. A wide range of potentially important contributions made by this essential substance to both the prevention and prognosis of a number of chronic and acute conditions are emerging. Associations between vitamin D deficiency and the risk of mortality, cardiovascular events, autoimmune diseases, diabetes and cancer, have been shown (Zhao 2024; Israel 2025). However, despite decades of intensive scientific research, several knowledge gaps

remain regarding the precise definition of vitamin D deficiency and sufficiency, the health benefits of improving vitamin D status, and optimal vitamin D intakes. Consequently, recommendations on the dosages for vitamin D supplementation are variable.

Current doses recommended by official agencies are increasingly regarded as conservative. The recommended 600 international units (IU) daily dosage for children aged 1 year and older and adults up to age 75 is often inadequate in raising circulating concentrations of 25(OH)D above 30 ng/mL. There is now compelling data to suggest that some people will gain more benefit from a daily supplemental dose of 75 µg (3,000 IU) of vitamin D than a 25 µg dose. The current NHMRC UL for Australia and NZ is 80 µg (3,200 IU) per day in adults aged 19 and over (NRV 2006). This is well within the suggested tolerated upper limit of 10,000 IU per day.

According to data from randomized controlled trials, a daily vitamin D supplementation dose of 2,000 IU (50 µg) may improve some health outcomes and is sufficient to raise and maintain serum 25(OH)D concentrations above 50 nmol/L (20 ng/mL) and above 75 nmol/L (30 ng/mL) in >99% and >90% of the general adult population, respectively. Findings from clinical trials also indicate that there are no significant safety concerns in supplementing such a dose for several years, even in individuals with an already sufficient vitamin D status at baseline.

However, despite compelling evidence to support the above, vitamin D supplementation at these doses and at higher doses has potential for adverse effects. While rare, the risk of these depends on the dose and the dosing schedule, and is greater in infants and children, the elderly, and in those with medical conditions such as heart disease, renal impairment, hypercalcemia, or hyperphosphataemia. As such, involvement of a health practitioner trained to anticipate these, and able to pursue appropriate testing, prescribing and/or monitoring practices to try and prevent any adverse event or contraindication, would enable the use of doses as high as the 3,000 IU (75 µg) proposed to be safely used where necessary.

Previous MCC meetings have discussed the concept of vitamin D in amounts greater than 25 µg doses being reclassified (from a prescription medicine to a pharmacy only medicine). As mentioned in page 10 of the submission, and as with the NDPSC in Australia, this was decided against on the basis that vitamin D deficiency cannot be diagnosed and managed in a pharmacy setting. It was deemed that a patient's medical practitioner would need to get involved as the diagnosis and ongoing management would require clinical laboratory monitoring of serum 25(OH)D levels.

However, clinical pharmacy service capability within New Zealand community pharmacies has increased since 2009, and particularly since the Covid-19 pandemic. Most pharmacies are likely to have this capability now, subject to suitable training and resource provision, as was provided during the Covid-19 pandemic. Additionally, the concept of higher amounts than available through general sale being made available to patients of natural health practitioners or nutritionists who have received comprehensive training in the usage of vitamins and dietary supplements has much merit.

Given that many of the diseases for which vitamin D status is being associated are serious and often life threatening, and the potential benefits of much higher doses than usual for some of these, the case for practitioner involvement in the prescribing or dispensing of these is strong (Feige 2020). In a supplemental protocol within a practitioner setting, treatment success may be evaluated after at least 6 to 12 weeks in certain risk groups by measurement of serum 25(OH)D levels and dosage adjustment if necessary.

From a public health perspective, the benefits likely to be achieved through individuals being able to take higher doses (2000 IU per day) of vitamin D appear to outweigh the additional risk of adverse events associated with this higher dose, which are rare and relatively mild.

However, despite the compelling rationale to increase limits for vitamin D in products for general sale to enable a recommended daily dose of 2,000 IU, it is considered less safe and therefore not recommendable to do so for 3,000 IU, based on current knowledge. A three-fold increase in current levels, unless available through a practitioner prescription or adopted by other reputable regulatory agencies in other jurisdictions, is regarded as excessive.

Finally, given the substantial amount of ongoing research underway into this vitamin globally, I recommend close attention is given to any updates in international guidance on vitamin D supplementation, as these are likely to have future implications for practice in New Zealand.

Recommendations

That the proposal to increase the recommended daily dose of vitamin D in unscheduled medicines for internal use from 25 micrograms (1,000 IU) to 75 micrograms (3,000 IU) is **not supported**. However, I do support an increase to **50 micrograms** (2,000 IU) per day.

References

Avenell A, Gillespie WJ, Gillespie LD and O'Connell D. Vitamin D and vitamin D analogues for preventing fractures associated with involutional and post-menopausal osteoporosis. 2009. Cochrane Database of Systematic Reviews. Issue 2. Art. No. CD000227. DOI: 10.1002/14651858.CD000227.pub3

PSM Healthcare Ltd. 2010. New Zealand data sheet. Cal.D.Forte® Accessed online at www.medsafe.govt.nz/profs/Datasheet/c/CalDFortetab.pdf

Aaseth JO, Finnes TE, Askim M, Alexander J. The Importance of Vitamin K and the Combination of Vitamins K and D for Calcium Metabolism and Bone Health: A Review. Nutrients. 2024 Jul 25;16(15):2420.

Abboud M. Vitamin D Supplementation and Sleep: A Systematic Review and Meta-Analysis of Intervention Studies. Nutrients. 2022 Mar 3;14(5):1076.

ACC. Information for health professionals. Accessed online October 2011 at http://www.acc.co.nz/preventing-injuries/at-home/older-people/information-for-healthprofessionals/index.htm#P4_396

ACC. November 2008. Vitamin D Prescribing Criteria. ACC4697. Accessed online at www.acc.co.nz/preventing-injuries/at-home/older-people/information-for-healthprofessionals/index.htm

Acharya P, Dalia T, Ranka S, Sethi P et al, The Effects of Vitamin D Supplementation and 25-Hydroxyvitamin D Levels on the Risk of Myocardial Infarction and Mortality. J Endocr Soc. 2021 Jul 15;5(10):bvab124.

Afonso ML, Capelas ML, Pimenta NM, Santos T et al, A Systematic Review of Vitamin D Supplementation in Oncology: Chance of Science or Effectiveness? Nutrients. 2025 Feb 11;17(4):634.

Al Noman A, Afrosa H, Lihu IK, Sarkar O, Nabin NR, Datta M, Pathak R, Sharma H. Vitamin D and Neurological Health: Unraveling Risk Factors, Disease Progression, and Treatment Potential. CNS Neurol Disord Drug Targets. 2025;24(4):245-256.

Aldana A, Aljaroudi W, Estes C, Rizvi F, Okeke-Moffatt C, Minakova V. Childhood Obesity and Its Correlation With Vitamin D: A Systematic Review. Cureus. 2025 May 29;17(5):e85047.

Armas LAG, Hollis BW and Heaney RP. 2004. Vitamin D2 is much less effective than vitamin D3 in humans. J Clin Endocrinol Metab 89: 5387-5391

Ashoor TM, Abd Elazim AEH, Mustafa ZAE, Anwar MA et al, Outcomes of High-Dose Versus Low-Dose Vitamin D on Prognosis of Sepsis Requiring Mechanical Ventilation: A Randomized Controlled Trial. J Intensive Care Med. 2024 Oct;39(10):1012-1022.

Avenell A, MacLennan GS, Jenkinson DJ, McPherson GC et al, RECORD Trial Group. Long-term follow-up for mortality and cancer in a randomized placebo-controlled trial of vitamin D(3) and/or calcium (RECORD trial). J Clin Endocrinol Metab. 2012 Feb;97(2):614-22.

Balvers MG, Brouwer-Brolsma EM, Endenburg S, de Groot LC, Kok FJ, Gunnewiek JK. Recommended intakes of vitamin D to optimise health, associated circulating 25-hydroxyvitamin D concentrations, and dosing regimens to treat deficiency: workshop report and overview of current literature. J Nutr Sci. 2015 May 25;4:e23.

Barbarawi M, Kheiri B, Zayed Y, Barbarawi O et al,. Vitamin D Supplementation and Cardiovascular Disease Risks in More Than 83 000 Individuals in 21 Randomized Clinical Trials: A Meta-analysis. JAMA Cardiol. 2019 Aug 1;4(8):765-776.

Barot KS, Abbasi ZA, Krishna Mohan GV, Abid SA, Hussain SA, Wei CR, Ali N. Prevalence of Vitamin D Deficiency in Children and Adolescents With Type 1 Diabetes Mellitus: A Systematic Review and Meta-Analysis. Cureus. 2025 May 10;17(5):e83843.

Beauchet O, Cooper-Brown LA, Allali G. Vitamin D Supplementation and Cognition in Adults: A Systematic Review of Randomized Controlled Trials. CNS Drugs. 2021 Dec;35(12):1249-1264.

Bendotti G, Biamonte E, Leporati P, Goglia U, Ruggeri RM, Gallo M. Vitamin D Supplementation: Practical Advice in Different Clinical Settings. Nutrients. 2025 Feb 24;17(5):783.

Benedik E. Sources of vitamin D for humans. Int J Vitam Nutr Res. 2022 Mar;92(2):118-125.

Bikle DD. Vitamin D Regulation of Immune Function. Curr Osteoporos Rep. 2022 Jun;20(3):186-193.

Bilezikian JP, Binkley N, De Luca HF, Fassio A et al, Consensus and Controversial Aspects of Vitamin D and COVID-19. J Clin Endocrinol Metab. 2023 Apr 13;108(5):1034-1042.

Bischoff-Ferrari HA, Dawson-Hughes B, Orav EJ, Staehelin HB et al, A. Monthly High-Dose Vitamin D Treatment for the Prevention of Functional Decline: A Randomized Clinical Trial. JAMA Intern Med. 2016 Feb;176(2):175-83.

Bischoff-Ferrari HA, Dawson-Hughes B, Staehelin HB, Oral JE, Stuck AE, Theiler R, Wong JB, Egli A, Kiel DP and Henschkowski J. 2009a. Fall prevention with supplemental and active forms of vitamin D: a meta-analysis of randomised controlled trials. BMJ. 339: 843-946.

Bischoff-Ferrari HA, Willett WC, Wong JB, Stuck AE, Staehelin HB, Orav JE, Thoma A, Kiel DP and Henschkowski J. 2009b. Prevention of nonvertebral fractures with oral vitamin D and dose dependency. Arch Intern Med. 169(6): 551-561.

Bischoff-Ferrari HA, Willett WC, Wong JB, Stuck AE, Staehelin HB, Orav JE, Thoma A, Kiel DP and Henschkowski J. 2009b. Prevention of nonvertebral fractures with oral vitamin D and dose dependency. Arch Intern Med. 169(6): 551-561.

Bjelakovic G, Gluud LL, Nikolova D, Whitfield K, Krstic G, Wetterslev J, Gluud C. Vitamin D supplementation for prevention of cancer in adults. Cochrane Database Syst Rev. 2014 Jun 23;2014(6):CD007469.

Bjelakovic G, Gluud LL, Nikolova D, Whitfield K, Wetterslev J, Simonetti RG, Bjelakovic M and Gluud C. 2011. Vitamin D supplementation for prevention of mortality in adults. Cochrane Database of Systematic Reviews. Issue 7. Art. No. CD007470. DOI: 10.1002/14651858.CD007470.pub2

Bleizgys A, Kurovskij J. Vitamin D Levels of Out-Patients in Lithuania: Deficiency and Hypervitaminosis. Medicina (Kaunas). 2018 Apr 26;54(2):25.

Bolland MJ, Bacon CJ, Horne AM, Mason BH, Ames RW, Wang TK, Grey AB, Gamble GD and Reid IR. 2010. Vitamin D insufficiency and health outcomes over 5 y in older women. AmJClinNutr. 91: 82-89 (Abstract only sighted).

Bouillon R, Manousaki D, Rosen C, Trajanoska K, Rivadeneira F, Richards JB. The health effects of vitamin D supplementation: evidence from human studies. Nat Rev Endocrinol. 2022 Feb;18(2):96-110.

Bouillon R, Marcocci C, Carmeliet G, Bikle D et al, Skeletal and Extraskeletal Actions of Vitamin D: Current Evidence and Outstanding Questions. Endocr Rev. 2019 Aug 1;40(4):1109-1151.

Bouillon R. Comparative analysis of nutritional guidelines for vitamin D. Nat Rev Endocrinol. 2017 Aug;13(8):466-479.

Bournot AR, Darling AL, Givens ID, Lovegrove JA et al, Effect of vitamin D status and vitamin D supplementation on immune function and prevention of acute respiratory tract infections in dark-skinned individuals: a systematic review and meta-analysis. Public Health Nutr. 2024 Oct 28;27(1):e224

Burt LA, Billington EO, Rose MS, Kremer R, Hanley DA, Boyd SK. Adverse Effects of High-Dose Vitamin D Supplementation on Volumetric Bone Density Are Greater in Females than Males. J Bone Miner Res. 2020 Dec;35(12):2404-2414.

Burt LA, Billington EO, Rose MS, Kremer R, Hanley DA, Boyd SK. Reply to Burt LA, et al.: Adverse Effects of High-Dose Vitamin D Supplementation on Volumetric Bone Density Are Greater in Females Than Males. J Bone Miner Res. 2021 Jul;36(7):1417-1418.

Burt LA, Billington EO, Rose MS, Raymond DA, Hanley DA, Boyd SK. Effect of High-Dose Vitamin D Supplementation on Volumetric Bone Density and Bone Strength: A Randomized Clinical Trial. JAMA. 2019 Aug 27;322(8):736-745.

Cameron ID, Murray GR, Gillespie LD, Robertson MC, H ill KD, Cumming RG and Kerse N. 2010. Interventions for preventing falls in older people in nursing care facilities and hospitals. Cochrane Database of Systematic Reviews. Issue 1. Art. No. CD005465. DOI: 10.1002/14651858.D005465. Ub2.

Camici M, Galetta F, Franzoni F, Carpi A, Zangeneh F. Vitamin D and heart. Intern Emerg Med. 2013 Apr;8 Suppl 1:S5-9. doi: 10.1007/s11739-013-0926-x.

Cappellani D, Brancatella A, Morganti R, Borsari et al. Hypercalcemia due to CYP24A1 mutations: a systematic descriptive review. Eur J Endocrinol. 2021 Dec 10;186(2):137-149.

Cashman KD, Dowling KG, Škrabáková Z, Gonzalez-Gross M et al,. Vitamin D deficiency in Europe: pandemic? Am J Clin Nutr. 2016 Apr;103(4):1033-44.

Cashman KD, Kiely ME, Andersen R, Grønborg IM et al. Individual participant data (IPD)-level meta-analysis of randomised controlled trials to estimate the vitamin D dietary requirements in dark-skinned individuals resident at high latitude. Eur J Nutr. 2022 Mar;61(2):1015-1034.

Charoenngam N. Vitamin D and Rheumatic Diseases: A Review of Clinical Evidence. Int J Mol Sci. 2021 Oct 1;22(19):10659. doi: 10.3390/ijms221910659.

Chel V, Wijnhoven HAH, Smit JH, Ooms M and Lips P. 2007. Efficacy of different doses and time intervals of oral vitamin D supplementation with or without calcium in elderly nursing home residents. Osteoporos In. 19: 663-671.

Chen S, Chen H, Chen X, Zheng D, Lin Y, Cai Y, Yang L, Zheng Q. Bidirectional Mendelian randomization analysis of the causal associations between serum vitamin D levels and multiple kidney diseases. Sci Rep. 2025 Jul 4;15(1):23908. doi: 10.1038/s41598-025-10305-6.

Correia A, Azevedo Mdo S, Gondim F, Bandeira F. Ethnic aspects of vitamin D deficiency. Arq Bras Endocrinol Metabol. 2014 Jul;58(5):540-4.

Crowe FL, Steur M, Allen NE, Appleby PN, Travis RC, Key TJ. Plasma concentrations of 25-hydroxyvitamin D in meat eaters, fish eaters, vegetarians and vegans: results from the EPIC-Oxford study. Public Health Nutr. 2011 Feb;14(2):340-6.

Cui A, Zhang T, Xiao P, Fan Z, Wang H, Zhuang Y. Global and regional prevalence of vitamin D deficiency in population-based studies from 2000 to 2022: A pooled analysis of 7.9 million participants. Front Nutr. 2023 Mar 17;10:1070808.

DIPART (vitamin D Individual Patient Analysis of Randomised Trials) Group. 2010. Patient level pooled analysis of 68,500 patients from seven major vitamin D fracture trials in US and Europe. BMJ. 12:340:b5463. doi: 10.1136/bmj.b5463

Doyle D, Browne U, Brickley A, Murphy D. Vitamin D-induced hypercalcaemia and acute kidney injury in sarcoidosis. BMJ Case Rep. 2023 Jan 23;16(1):e250580

EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA). Dietary reference values for vitamin D. EFSA J. 2016;14:4547.

Ezcurra-Hualde M, Zalba S, Bella Á, Arrizabalaga L et al, Liposomal encapsulation of cholecalciferol mitigates in vivo toxicity and delays tumor growth. Front Immunol. 2025 Jan 27;16:1529007.

Falk SSI, Schröder G, Mittlmeier T. Is There a Need for Vitamin D Supplements During Summer Time in Northern Germany? A Study of Hospitalised Fracture Patients. Nutrients. 2024 Nov 30;16(23):4174.

Falk SSI, Schröder G, Mittlmeier T. Is There a Need for Vitamin D Supplements During Summer Time in Northern Germany? A Study of Hospitalised Fracture Patients. Nutrients. 2024 Nov 30;16(23):4174.

Fang A, Zhao Y, Yang P, Zhang X, Giovannucci EL. Vitamin D and human health: evidence from Mendelian randomization studies. Eur J Epidemiol. 2024 May;39(5):467-490.

Farghali M, Ruga S, Morsanuto V, Uberti F. Can Brain Health Be Supported by Vitamin D-Based Supplements? A Critical Review. Brain Sci. 2020 Sep 22;10(9):660.

Fassio A, Adami G, Rossini M, Giollo A et al, Pharmacokinetics of Oral Cholecalciferol in Healthy Subjects with Vitamin D Deficiency: A Randomized Open-Label Study. Nutrients. 2020 May 27;12(6):1553.

Feige J, Moser T, Bieler L, Schwenker K, Hauer L, Sellner J. Vitamin D Supplementation in Multiple Sclerosis: A Critical Analysis of Potentials and Threats. Nutrients. 2020 Mar 16;12(3):783.

Formisano E, Proietti E, Borgarelli C, Pisciotta L. Psoriasis and Vitamin D: A Systematic Review and Meta-Analysis. Nutrients. 2023 Jul 30;15(15):3387.

Fraser DR. Vitamin D toxicity related to its physiological and unphysiological supply. Trends Endocrinol Metab. 2021 Nov;32(11):929-940.

Fu L, Fei J, Tan ZX, Chen YH et al, Low Vitamin D Status Is Associated with Inflammation in Patients with Chronic Obstructive Pulmonary Disease. J Immunol. 2021 Feb 1;206(3):515-523.

Gallagher JC, Rosen CJ. Vitamin D: 100 years of discoveries, yet controversy continues. Lancet Diabetes Endocrinol. 2023 May;11(5):362-374. doi: 10.1016/S2213-8587(23)00060-8. Epub 2023 Mar 30. Erratum in: Lancet Diabetes Endocrinol. 2023 Jun;11(6):e8.

Gallo S, McDermid JM, Al-Nimr RI, Hakeem R et al, Vitamin D Supplementation during Pregnancy: An Evidence Analysis Center Systematic Review and Meta-Analysis. J Acad Nutr Diet. 2020 May;120(5):898-924.e4.

Gariballa S, Al-Bluwi GSM, Yasin J. The Effect of Vitamin D Supplementation with or without Calcium on Vitamin D Epimer and Metabolites. Metabolites. 2024 Sep 27;14(10):524

Gezen-Ak D, Dursun E. Vitamin D, a Secosteroid Hormone and Its Multifunctional Receptor, Vitamin D Receptor, in Alzheimer's Type Neurodegeneration. J Alzheimers Dis. 2023;95(4):1273-1299.

Giampà E, Celletti E, DI Bonito M, Ferretti V, Gigliotti P, Nuvoli G, Paoletti F, Piazzini M, Ranieri M, Vinicola V. Safety and effects of calcifediol 0.266 milligrams soft capsules monthly and cholecalciferol 25000 international units monthly in osteoporotic women undergoing therapy with alendronate: a cross-sectional study. Minerva Endocrinol (Torino). 2024 Jun;49(2):141-149.

Gillespie LD, Roberston MC, Gillespie WJ, Lamb SE, Gates S, Cumming RG and Rowe BH. 2009. Interventions for preventing falls in older people living in the community. Cochrane Database of Systematic Reviews. Issue 2. Art. No. CD007146. DOI: 10.1002/14651858.CD007146.pub2.

Giustina A, Bilezikian JP, Adler RA, Banfi G et al,. Consensus Statement on Vitamin D Status Assessment and Supplementation: Whys, Whens, and Hows. Endocr Rev. 2024 Sep 12;45(5):625-654.

Gluba-Brzózka A, Franczyk B, Ciałkowska-Rysz A, Olszewski R, Rysz J. Impact of Vitamin D on the Cardiovascular System in Advanced Chronic Kidney Disease (CKD) and Dialysis Patients. Nutrients. 2018 Jun 1;10(6):709.

Gnagnarella P, Raimondi S, Aristarco V, Johansson HA, Bellerba F, Corso F, Gandini S. Vitamin D Receptor Polymorphisms and Cancer. Adv Exp Med Biol. 2020;1268:53-114.

Gombart AF, Borregaard N, Koeffler HP. Human cathelicidin antimicrobial peptide (CAMP) gene is a direct target of the vitamin D receptor and is strongly up-regulated in myeloid cells by 1,25-dihydroxyvitamin D3. FASEB J. 2005 Jul;19(9):1067-77.

Grant WB, Boucher BJ. How Follow-Up Period in Prospective Cohort Studies Affects Relationship Between Baseline Serum 25(OH)D Concentration and Risk of Stroke and Major Cardiovascular Events. Nutrients. 2024 Nov 1;16(21):3759.

Grant WB, Wimalawansa SJ, Pludowski P, Cheng RZ. Vitamin D: Evidence-Based Health Benefits and Recommendations for Population Guidelines. Nutrients. 2025 Jan 14;17(2):277.

Gruber-Bzura BM. Vitamin D-is the sun enough for us? Nutr Metab (Lond). 2025 Jul 1;22(1):70.

Hathcock JN, Shao A, Vieth R and Heaney R. 2007. Risk assessment for vitamin D. Am J Clin Nutr. 85: 6-18.

Heaney RP, Holick MF. Why the IOM recommendations for vitamin D are deficient. J Bone Miner Res. 2011 Mar;26(3):455-7.

Holcik MF, Biancuzzo RM, Chen TC, Klein EK, Young A, Bibuld D, Reitz R, Salameh W, Americ A and Tannenbaum AD. 2008. J Clin Endocrinol Metab. 93(3): 677-681.

Holick MF, Binkley NC, Bischoff-Ferrari HA, Gordon CM et al, Evaluation, treatment, and prevention of vitamin D deficiency: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab. 2011 Jul;96(7):1911-30.

Holick MF, Matsuoka LY, Wortsman J. Age, vitamin D, and solar ultraviolet. Lancet. 1989 Nov 4;2(8671):1104-5.

Holick MF. Vitamin D deficiency. 2007. NEnglJMed. 357: 266-281.

Homann CN, Homann B, Ivanic G, Urbanic-Purkart T. Vitamin D supplementation in later life: a systematic review of efficacy and safety in movement disorders. Front Aging Neurosci. 2024 Jan 26;16:1333217.

Inderjeeth CA, Glennon D, Petta A, Soderstrom J, Boyatzis I and Tapper J. 2007. Vitamin D and muscle strength in patient with previous fractures. NZMJ. 120(1262). Accessed online at www.nzma.org.nz/journal/120-1262/2730/

Institute of Medicine. 2011. A. Catharine Ross, Christine L. Taylor, Ann L. Yaktine, and Heather B. Del Valle, Editors; Committee to Review Dietary Reference Intakes for Vitamin D and Calcium. The National Academies Press. Washington DC.

Ismail NH, Mussa A, Al-Khreisat MJ, Mohamed Yusoff S, Husin A, Johan MF, Islam MA. The Global Prevalence of Vitamin D Deficiency and Insufficiency in Patients with Multiple Myeloma: A Systematic Review and Meta-Analysis. Nutrients. 2023 Jul 20;15(14):3227.

Israel A, Weizman A, Israel S, Ashkenazi S et al, Vitamin D Deficiency, Supplementation, and Risk of Mortality and Chronic Disease: Evidence from Matched Cohorts in Israel and the US. medRxiv [Preprint]. 2025 Jun 4:2025.05.29.25328548.

Jääskeläinen T, Itkonen ST, Lundqvist A, Erkkola M et al, The positive impact of general vitamin D food fortification policy on vitamin D status in a representative adult Finnish population: evidence from an 11-y follow-up based on standardized 25-hydroxyvitamin D data. Am J Clin Nutr. 2017 Jun;105(6):1512-1520.

Jia H, Sheng F, Yan Y, Liu X, Zeng B. Vitamin D supplementation for prevention of acute respiratory infections in older adults: A systematic review and meta-analysis. PLoS One. 2024 May 24;19(5):e0303495.

Jolliffe DA, Camargo CA Jr, Sluyter JD, Aglipay M et al, Vitamin D supplementation to prevent acute respiratory infections: systematic review and meta-analysis of stratified aggregate data. Lancet Diabetes Endocrinol. 2025 Apr;13(4):307-320. doi: 10.1016/S2213-8587(24)00348-6. Epub 2025 Feb 21. Erratum in: Lancet Diabetes Endocrinol. 2025 Jul;13(7):e10.

Kanno K, Akutsu T, Ohdaira H, Suzuki Y, Urashima M. Effect of Vitamin D Supplements on Relapse or Death in a p53-Immunoreactive Subgroup With Digestive Tract Cancer: Post Hoc Analysis of the AMATERASU Randomized Clinical Trial. JAMA Netw Open. 2023 Aug 1;6(8):e2328886

Kaufman HW, Niles JK, Kroll MH, Bi C, Holick MF. SARS-CoV-2 positivity rates associated with circulating 25-hydroxyvitamin D levels. PLoS One. 2020 Sep 17;15(9):e0239252.

Kaviani M, Nikooyeh B, Etesam F, Behnagh SJ et al, Effects of vitamin D supplementation on depression and some selected pro-inflammatory biomarkers: a double-blind randomized clinical trial. BMC Psychiatry. 2022 Nov 11;22(1):694.

Keum N, Giovannucci E. Vitamin D supplements and cancer incidence and mortality: a meta-analysis. Br J Cancer. 2014 Aug 26;111(5):976-80.

Khan S, Tariq MW, Akhtar M, Raza MTS, Manzoor M. The Dark Side of the Sunshine Vitamin: A Case of Acute Renal Failure and Hypercalcaemia From Vitamin D Overconsumption. Cureus. 2024 Sep 26;16(9):e70237.

Khatoon R. Unlocking the Potential of Vitamin D: A Comprehensive Exploration of Its Role in Neurological Health and Diseases. Biology (Basel). 2025 Mar 10;14(3):280.

Khatri K, Kaur M, Dhir T, Kankaria A, Arora H. Role of calcium &/or vitamin D supplementation in preventing osteoporotic fracture in the elderly: A systematic review & meta-analysis. Indian J Med Res. 2023 Jan;158(1):5-16.

Lappe J, Watson P, Travers-Gustafson D, Recker R et al, Effect of Vitamin D and Calcium Supplementation on Cancer Incidence in Older Women: A Randomized Clinical Trial. JAMA. 2017 Mar 28;317(12):1234-1243

Latacz M, Rozmus D, Fiedorowicz E, Snarska J et al, Vitamin D Receptor (VDR) Gene Polymorphism in Patients Diagnosed with Colorectal Cancer. Nutrients. 2021 Jan 11;13(1):200.

Li Y, Zhang J, Tian F, Anvarifard P, Li N. Association between vitamin D receptor polymorphism and breast cancer in women: An umbrella review of meta-analyses of observational investigations. Exp Gerontol. 2024 Sep;194:112502.

Lin C, Liu H. Relationship between vitamin D deficiency and gestational diabetes: a narrative review. Front Endocrinol (Lausanne). 2024 Dec 19;15:1504930. doi: 10.3389/fendo.2024.1504930. Erratum in: Front Endocrinol (Lausanne). 2025 Jan 06;15:1548353.

Liu D, Meng X, Tian Q, Cao W et al, Vitamin D and Multiple Health Outcomes: An Umbrella Review of Observational Studies, Randomized Controlled Trials, and Mendelian Randomization Studies. Adv Nutr. 2022 Aug 1;13(4):1044-1062.

Liu S, Zhao T, Liu Q. Vitamin D effects on Chlamydia trachomatis infection: a case-control and experimental study. Front Cell Infect Microbiol. 2024 Apr 18;14:1366136.

Lorenzon F, Gregorio T, Niebisch F, Stolte RCK et al, Maternal vitamin D administration attenuates metabolic disturbances induced by prenatal exposure to dexamethasone in a sex-dependent manner. J Steroid Biochem Mol Biol. 2021 Sep;212:105941..

Lu K, Tan JS, Li TQ, Yuan J, Wang H, Wang W. An inverse causal association between genetically predicted vitamin D and chronic obstructive pulmonary disease risk. Front Nutr. 2023 Mar 15;10:1111950.

Luttmann-Gibson H, Mora S, Camargo CA, Cook NR et al, Serum 25-hydroxyvitamin D in the VITamin D and OmegA-3 TriaL (VITAL): Clinical and demographic characteristics associated with baseline and change with randomized vitamin D treatment. Contemp Clin Trials. 2019 Dec;87:105854.

Malihi Z, Wu Z, Lawes CMM, Scragg R. Adverse events from large dose vitamin D supplementation taken for one year or longer. J Steroid Biochem Mol Biol. 2019 Apr;188:29-37.

Malihi Z, Wu Z, Mm Lawes C, Scragg R. Noncalcemic adverse effects and withdrawals in randomized controlled trials of long-term vitamin D2 or D3 supplementation: a systematic review and meta-analysis. Nutr Rev. 2017 Dec 1;75(12):1007-1034.

Manoj P, Derwin R, George S. What is the impact of daily oral supplementation of vitamin D3 (cholecalciferol) plus calcium on the incidence of hip fracture in older people? A systematic review and meta-analysis. Int J Older People Nurs. 2023 Jan;18(1):e12492.

Manson JE, Cook NR, Lee IM, Christen W et al, VITAL Research Group. Vitamin D Supplements and Prevention of Cancer and Cardiovascular Disease. N Engl J Med. 2019 Jan 3;380(1):33-44.

Martindale: The Complete Drug Reference. 2011. Medicines Complete. Accessed online at www.medicinescomplete.com/mc/martindale/current/index.htm

Massoodi A, Javadian Koutanaei S, Faraz Z, Geraili Z, Zavarmousavi SM. Comparison of serum vitamin D levels between healthy and ADHD children. Caspian J Intern Med. 2023 Fall;14(4):681-686.

McCullough ML, Zoltick ES, Weinstein SJ, Fedirko V et al, Circulating Vitamin D and Colorectal Cancer Risk: An International Pooling Project of 17 Cohorts. J Natl Cancer Inst. 2019 Feb 1;111(2):158-169.

McCullough ML, Zoltick ES, Weinstein SJ, Fedirko V et al, Circulating Vitamin D and Colorectal Cancer Risk: An International Pooling Project of 17 Cohorts. J Natl Cancer Inst. 2019 Feb 1;111(2):158-169.

Mehta S, Patel V, Agarwal S, Pant N, Suman S, Sohliya AEL. Vitamin D deficiency and immune health in polar populations: a systematic review and hypothesis-driven narrative analysis. Immunol Res. 2025 May 21;73(1):84.

Mellor-Pita S, Tutor-Ureta P, Rosado S, Alkadi K, Granado F, Jimenez-Ortiz C, Castejon R. Calcium and vitamin D supplement intake may increase arterial stiffness in systemic lupus erythematosus patients. Clin Rheumatol. 2019 Apr;38(4):1177-1186.

Michos ED, Kalyani RR, Blackford AL, Sternberg AL et al, The Relationship of Falls With Achieved 25-Hydroxyvitamin D Levels From Vitamin D Supplementation: The STURDY Trial. J Endocr Soc. 2022 Apr 16;6(6):bvac065.

Mirhosseini N, Rainsbury J, Kimball SM. Vitamin D Supplementation, Serum 25(OH)D Concentrations and Cardiovascular Disease Risk Factors: A Systematic Review and Meta-Analysis. Front Cardiovasc Med. 2018 Jul 12;5:87.

Mohamed ZA, Bai M, Dong H, Xue Y, Jia F, Feng J. Efficacy of high-dose vs. low-dose vitamin D_3 supplementation in children with chronic tic disorders: a randomized controlled trial. Nutr J. 2025 Mar 17;24(1):44. doi: 10.1186/s12937-025-01112-w.

Molani-Gol R, Rafraf M, Asghari Jafarabadi M, Aftabi-Yousefabad S, Shanehbandi D. The interaction of vitamin D supplementation with Omentin-1 gene polymorphism on metabolic biomarkers, omentin-1 levels and anthropometric measures in women with prediabetes: A double-blind randomized controlled trial. Diabetes Obes Metab. 2025 Aug;27(8):4522-4536.

Mot CI, Horhat DI, Balica NC, Hirtie B et al, Vitamin D and Clinical Outcomes in Head and Neck Cancer: A Systematic Review. Nutrients. 2025 Mar 21;17(7):1100.

Mot CI, Horhat DI, Balica NC, Hirtie B, Varga NI, Prodan-Barbulescu C, Alexandru A, Ciurariu E, Galis R. Vitamin D and Clinical Outcomes in Head and Neck Cancer: A Systematic Review. Nutrients. 2025 Mar 21;17(7):1100.

Moukayed M, Grant WB. The roles of UVB and vitamin D in reducing risk of cancer incidence and mortality: A review of the epidemiology, clinical trials, and mechanisms. Rev Endocr Metab Disord. 2017 Jun;18(2):167-182.

Muñoz A, Grant WB. Vitamin D and Cancer: An Historical Overview of the Epidemiology and Mechanisms. Nutrients. 2022 Mar 30;14(7):1448.

Nutrient Reference Values (NRV) for Australia and New Zealand. 2006. Accessed online at www.nrv.gov.au/index.htm

O'Callaghan KM, Hennessy Á, Hull GLJ, Healy K et al, Estimation of the maternal vitamin D intake that maintains circulating 25-hydroxyvitamin D in late gestation at a concentration sufficient to keep umbilical cord sera ≥25-30 nmol/L: a dose-response, double-blind, randomized placebo-controlled trial in pregnant women at northern latitude. Am J Clin Nutr. 2018 Jul 1;108(1):77-91.

Oristrell J, Oliva JC, Casado E, Subirana I, Domínguez D, Toloba A, Balado A, Grau M. Vitamin D supplementation and COVID-19 risk: a population-based, cohort study. J Endocrinol Invest. 2022 Jan;45(1):167-179.

Ortiz-Prado E, Vasconez-Gonzalez J, Izquierdo-Condoy JS, Suárez-Sangucho IA et al, Cholecalciferol (vitamin D3): efficacy, safety, and implications in public health. Front Nutr. 2025 Jun 9;12:1579957.

Pal R, Banerjee M, Bhadada SK, Shetty AJ, Singh B, Vyas A. Vitamin D supplementation and clinical outcomes in COVID-19: a systematic review and meta-analysis. J Endocrinol Invest. 2022 Jan;45(1):53-68.

Pal R, Banerjee M, Bhadada SK, Shetty AJ, Singh B, Vyas A. Vitamin D supplementation and clinical outcomes in COVID-19: a systematic review and meta-analysis. J Endocrinol Invest. 2022 Jan;45(1):53-68.

Pérez-López FR, Pilz S, Chedraui P. Vitamin D supplementation during pregnancy: an overview. Curr Opin Obstet Gynecol. 2020 Oct;32(5):316-321.

PHARMAC. June 2010. Vitamin D. The Pharmaceutical Schedule. Accessed online at www.pharmac.govt.nz/patients/Schedule?code=A013710

Pludowski P, Grant WB, Karras SN, Zittermann A, Pilz S. Vitamin D Supplementation: A Review of the Evidence Arguing for a Daily Dose of 2000 International Units (50 µg) of Vitamin D for Adults in the General Population. Nutrients. 2024 Jan 29;16(3):391.

Pludowski P, Grant WB, Karras SN, Zittermann A, Pilz S. Vitamin D Supplementation: A Review of the Evidence Arguing for a Daily Dose of 2000 International Units (50 µg) of Vitamin D for Adults in the General Population. Nutrients. 2024 Jan 29;16(3):391.

Pludowski P, Holick MF, Grant WB, Konstantynowicz J et al, Vitamin D supplementation guidelines. J Steroid Biochem Mol Biol. 2018 Jan;175:125-135.

Pludowski P, Takacs I, Boyanov M, Belaya Z, Diaconu CC, Mokhort T, Zherdova N, Rasa I, Payer J, Pilz S. Clinical Practice in the Prevention, Diagnosis and Treatment of Vitamin D Deficiency: A Central and Eastern European Expert Consensus Statement. Nutrients. 2022 Apr 2;14(7):1483.

Ramasamy I. Vitamin D Metabolism and Guidelines for Vitamin D Supplementation. Clin Biochem Rev. 2020 Dec;41(3):103-126.

Reis AR, Santos RKF, Dos Santos CB, Santos BDC et al, Supplementation of vitamin D isolated or calcium-associated with bone remodeling and fracture risk in postmenopausal women without osteoporosis: A systematic review of randomized clinical trials. Nutrition. 2023 Dec;116:112151.

Rizzoli R. Vitamin D supplementation: upper limit for safety revisited? Aging Clin Exp Res. 2021 Jan;33(1):19-24.

Robertson MC and Campbell AJ. November 2008. Optimisation of ACC's fall prevention programmes for older people. Accessed online at www.acc.co.nz/PRD_EXT_CSMP/groups/external_ip/documents/reference_tools/pi00349.p df

Rockell JEP, Skeaff CM, Williams SM, and Green TJ. 2006. Serum 25-hydroxyvitamin D concentrations of New Zealanders aged 15 years and older. Osteoporosis Int. 17: 1382- 1389.

Robien K, Oppeneer SJ, Kelly JA, Hamilton-Reeves JM. Drug-vitamin D interactions: a systematic review of the literature. Nutr Clin Pract. 2013 Apr;28(2):194-208.

Rosen CJ, Abrams SA, Aloia JF, Brannon PM et al, IOM committee members respond to Endocrine Society vitamin D guideline. J Clin Endocrinol Metab. 2012 Apr;97(4):1146-52.

Roșian A, Zdrîncă M, Dobjanschi L, Vicaș LG, Mureșan ME, Dindelegan CM, Platona RI, Marian E. The Role of Vitamin D in the Management of Major Depressive Disorder: A Systematic Review. Pharmaceuticals (Basel). 2025 May 25;18(6):792.

Ross AC, Manson JE, Abrams SA, Aloia JF et al, The 2011 report on dietary reference intakes for calcium and vitamin D from the Institute of Medicine: what clinicians need to know. J Clin Endocrinol Metab. 2011 Jan;96(1):53-8.

Ross AC, Manson JE, Abrams SA, Aloia JF et al, The 2011 report on dietary reference intakes for calcium and vitamin D from the Institute of Medicine: what clinicians need to know. J Clin Endocrinol Metab. 2011 Jan;96(1):53-8.

Roy NM, Al-Harthi L, Sampat N, Al-Mujaini R et al, Impact of vitamin D on neurocognitive function in dementia, depression, schizophrenia and ADHD. Front Biosci (Landmark Ed). 2021 Jan 1;26(3):566-611.

Saeidlou SN, Vahabzadeh D, Karimi F, Babaei F. Determining the vitamin D supplementation duration to reach an adequate or optimal vitamin D status and its effect on blood lipid profiles: a longitudinal study. J Health Popul Nutr. 2024 Jun 12;43(1):81.

Scragg R and Bartley J. 2007. Vitamin D – how do we define deficiency and what can we do about it in New Zealand. NZJM. 120(1262). Accessed online at http://journal.nzma.org.nz/journal/120-1262/2735

Scragg R, Khaw KT, Toop L, Sluyter J, Lawes CMM, Waayer D, Giovannucci E, Camargo CA Jr. Monthly High-Dose Vitamin D Supplementation and Cancer Risk: A Post Hoc Analysis of the Vitamin D Assessment Randomized Clinical Trial. JAMA Oncol. 2018 Nov 1;4(11):e182178.

Seo TR, Lee I, Chun YG, Park DJ, Lee SH, Kim BK. Improved Stability of Polyglycerol Polyricinoleate-Substituted Nanostructured Lipid Carrier Cholecalciferol Emulsions with Different Carrier Oils. J Food Sci. 2019 Apr;84(4):782-791.

Sîrbe C, Rednic S, Grama A, Pop TL. An Update on the Effects of Vitamin D on the Immune System and Autoimmune Diseases. Int J Mol Sci. 2022 Aug 29;23(17):9784.

Solnier J, Chang C, Zhang Y, Kuo YC, Du M, Roh YS, See J, Brix J, Gahler RJ, Green T, Wood S. A Comparison and Safety Evaluation of Micellar versus Standard Vitamin D3 Oral Supplementation in a Randomized, Double-Blind Human Pilot Study. Nutrients. 2024 May 22;16(11):1573

Sosa Henríquez M, Gómez de Tejada Romero MJ. Cholecalciferol or Calcifediol in the Management of Vitamin D Deficiency. Nutrients. 2020 May 31;12(6):1617.

Tabsh N, Bilezikian JP. Vitamin D Status as a Risk Factor for Tuberculosis Infection. Adv Nutr. 2025 Apr;16(4):100394.

Tebben PJ, Singh RJ, Kumar R. Vitamin D-Mediated Hypercalcemia: Mechanisms, Diagnosis, and Treatment. Endocr Rev. 2016 Oct;37(5):521-547. doi: 10.1210/er.2016-1070. .

Thompson B, Waterhouse M, English DR, McLeod DS et al, Vitamin D supplementation and major cardiovascular events: D-Health randomised controlled trial. BMJ. 2023 Jun 28;381:e075230.

Thomson, Barbara M. (Barbara Mary); Cressey, P. J. (Peter J.), 2014; Determination of vitamin D in foods : current knowledge and data gaps / prepared for Ministry of Agriculture and Forestry under project NUT/09/01 - Science Programme Reporting, as part of overall contract for scientific services, client report no. FW 10011, New Zealand. Ministry for Primary Industries, Wellington.

Uçar N, Holick MF. Illuminating the Connection: Cutaneous Vitamin D3 Synthesis and Its Role in Skin Cancer Prevention. Nutrients. 2025 Jan 22;17(3):386.

Vanstone MB, Oberfield SE, Shader L, Ardeshirpour L, Carpenter TO. Hypercalcemia in children receiving pharmacologic doses of vitamin D. Pediatrics. 2012 Apr;129(4):e1060-3.

Vellekkatt F, Menon V. Efficacy of vitamin D supplementation in major depression: A meta-analysis of randomized controlled trials. J Postgrad Med. 2019 Apr-Jun;65(2):74-80.

Vieira EF, Souza S. Formulation Strategies for Improving the Stability and Bioavailability of Vitamin D-Fortified Beverages: A Review. Foods. 2022 Mar 16;11(6):847

Vieth R. Vitamin D toxicity, policy, and science. J Bone Miner Res. 2007 Dec;22 Suppl 2:V64-8.

Virtanen JK, Hantunen S, Kallio N, Lamberg-Allardt C et al. The effect of vitamin D3 supplementation on the incidence of type 2 diabetes in healthy older adults not at high risk for diabetes (FIND): a randomised controlled trial. Diabetologia. 2025 Apr;68(4):715-726.

Visser M, Deeg DJH, Puts MTE, Seidell JC and Lips P. 2006. Low serum concentrations of 25-hydroxyvitamin D in older persons and the risk of nursing home admission. AmJClinNutr. 84: 616-622.

Vogiatzi MG, Jacobson-Dickman E, DeBoer MD; Drugs, and Therapeutics Committee of The Pediatric Endocrine Society. Vitamin D supplementation and risk of toxicity in pediatrics: a review of current literature. J Clin Endocrinol Metab. 2014 Apr;99(4):1132-41.

Vogiatzi MG, Jacobson-Dickman E, DeBoer MD; Drugs, and Therapeutics Committee of The Pediatric Endocrine Society. Vitamin D supplementation and risk of toxicity in pediatrics: a review of current literature. J Clin Endocrinol Metab. 2014 Apr;99(4):1132-41.

von Hurst P, Mazahery H, Reynolds E, Thomson A, Franklin M, Conlon C. Knowledge, attitudes and behaviours towards vitamin D and sun exposure of parents of infants and young children and health professionals in New Zealand. Nutr Health. 2023 Jul 2:2601060231185190.

Wacker M, Holick MF. Sunlight and Vitamin D: A global perspective for health. Dermatoendocrinol. 2013 Jan 1;5(1):51-108.

Wan M, Patel A, Patel JP, Rait G, Jones SA, Shroff R. Quality and use of unlicensed vitamin D preparations in primary care in England: Retrospective review of national prescription data and laboratory analysis. Br J Clin Pharmacol. 2021 Mar;87(3):1338-1346.

Wang AY, Yeh YC, Cheng KH, Han YY, Chiu CT, Chang CC, Wang IT, Chao A. Efficacy and safety of enteral supplementation with high-dose vitamin D in critically ill patients with vitamin D deficiency. J Formos Med Assoc. 2025 Apr;124(4):355-360.

Wasike R, Mobegi V, Maina E, Makokha F, Armstrong R, Mbithi A. Vitamin D status and risk for breast cancer in Kenya. J Health Popul Nutr. 2025 Jul 3;44(1):234.

Weller RB. Sunlight: Time for a Rethink? J Invest Dermatol. 2024 Aug;144(8):1724-1732. doi: 10.1016/j.jid.2023.12.027.

Working Group of the Australian and New Zealand Bone and Mineral Society (ANZBMS), Endocrine Society of Australia and Osteoporosis Australia. 2005. Vitamin D and adult bone health in Australia and New Zealand: a position statement. MJA. 182: 281-285.

Xu J, Li J, Sun YJ, Quan W, Qin YD, Song J, Chen JJ. Effect of vitamin D supplementation on motor symptoms in Parkinson's disease: a meta-analysis of randomized controlled trials. Front Nutr. 2025 Jun 9;12:1500875.

Yang W, Liu L, Masugi Y, Qian ZR et al, Calcium intake and risk of colorectal cancer according to expression status of calcium-sensing receptor (CASR). Gut. 2018 Aug;67(8):1475-1483.Zhu Z, Wan X, Liu J, Zhang D et al, Vitamin D status and chronic obstructive pulmonary disease risk: a prospective UK Biobank study. BMJ Open Respir Res. 2023 Jun;10(1):e001684.

Yang WC, Chitale R, O'Callaghan KM, Sudfeld CR, Smith ER. The Effects of Vitamin D Supplementation During Pregnancy on Maternal, Neonatal, and Infant Health: A Systematic Review and Meta-analysis. Nutr Rev. 2025 Mar 1;83(3):e892-e903.

Yao P, Bennett D, Mafham M, Lin X, Chen Z, Armitage J, Clarke R. Vitamin D and Calcium for the Prevention of Fracture: A Systematic Review and Meta-analysis. JAMA Netw Open. 2019 Dec 2;2(12):e1917789.

Yeung WG, Palmer SC, Strippoli GFM, Talbot B et al, Vitamin D Therapy in Adults With CKD: A Systematic Review and Meta-analysis. Am J Kidney Dis. 2023 Nov;82(5):543-558.

Yu CH, Tseng HK, Chien DK, Liao EC. Over-supplement of vitamin D may cause delirium, abdominal distension, and muscle weakness in the elderly: A case report and literature review. Medicine (Baltimore). 2024 Dec 27;103(52):e41057.

Zhang, Z. September 2007. Vitamin D supplementation for fracture prevention in older people. ACC Evidence Based Healthcare Advisory Group. Accessed online at: www.acc.co.nz/about-acc/research-sponsorship-and-projects/research-anddevelopment/evidence-based-healthcare-reports/index.htm

Zhao S, Qian F, Wan Z, Chen X, Pan A, Liu G. Vitamin D and major chronic diseases. Trends Endocrinol Metab. 2024 Dec;35(12):1050-1061.

Zhao W, Zhu DM, Shen Y, Zhang Y, Chen T, Cai H, Zhu J, Yu Y. The protective effect of vitamin D supplementation as adjunctive therapy to antidepressants on brain structural and functional connectivity of patients with major depressive disorder: a randomized controlled trial. Psychol Med. 2024 Jul;54(10):2403-2413.

Zhou YF, Luo BA, Qin LL. The association between vitamin D deficiency and community-acquired pneumonia: A meta-analysis of observational studies. Medicine (Baltimore). 2019 Sep;98(38):e17252.

Zittermann A, Trummer C, Theiler-Schwetz V, Pilz S. Long-term supplementation with 3200 to 4000 IU of vitamin D daily and adverse events: a systematic review and meta-analysis of randomized controlled trials. Eur J Nutr. 2023 Jun;62(4):1833-1844.

Żórawska J, Szczepaniak W. Problem podwyższonego stężenia witaminy D3 w grupie pacjentów hospitalizowanych w klinice geriatrii [The problem of increased vitamin D3 level in a group of patients hospitalized in a geriatrics clinic]. Med Pr. 2024 Jun 26:188616.