Vitamin D and health in adults in Australia and New Zealand: a position statement

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Since the previous position statement released in 2005, vitamin D status has increasingly become a significant public health issue in Australia and New Zealand. It is timely to re-examine past recommendations to guide clinicians and health professionals in light of the increasing number of medical conditions (unrelated to bone) associated with low vitamin D status, and a recent review on calcium and vitamin D conducted by the United States Institute of Medicine (Box 1).

The major circulating form and the metabolite routinely used to assess overall vitamin D status is 25-hydroxyvitamin D (25-OHD). The main source of vitamin D is exposure of skin to ultraviolet B (UVB) radiation in sunlight. In Australia, there is a relatively high prevalence (31%) of inadequate vitamin D status (serum 25-OHD level < 50 nmol/L), which increases to more than 50% in women during winter–spring and in people residing in southern states. Most adults are unlikely to obtain more than 5%–10% of their vitamin D requirement from dietary sources. Vitamin D_3 is found naturally in small quantities in a few foods such as wild-caught fatty fish, liver and eggs, as well as in fortified foods such as margarine and some low-fat milk products. Some mushrooms that have been exposed to UV radiation contain vitamin D_2.

For people with moderately fair skin, adequate vitamin D levels are likely to be maintained in summer by a walk outside with arms (or equivalent area) exposed for 6–7 minutes mid morning or mid afternoon, on most days. In winter, the task is more difficult, and in many parts of the country, there is only sufficient UVB radiation to produce vitamin D around noon. People with dark skin are likely to need 3–6 times longer sun exposure. Normal window glass prevents synthesis of vitamin D in the skin, as do sunscreens, but these are often inadequately applied and may have little impact on vitamin D status. Lack of skin exposure to sunlight is a more common issue, but given the high incidence of skin cancer in Australasia, sunscreens and other UV radiation avoidance measures should be used if exposure is likely to be prolonged and/or there is a risk of skin damage. People at high risk of skin cancer need more rigorous sun protection and should discuss with their medical practitioner whether supplements might be more appropriate. Short UV radiation exposures (of a few minutes) may be more efficient at producing vitamin D and cause less skin damage.

1 What has changed since 2005?*

- There is more evidence that a significant proportion of Australian adults (31%) have inadequate vitamin D status (serum 25-hydroxyvitamin D [25-OHD] level < 50 nmol/L).
- Improving vitamin D status reduces all-cause mortality (Level I), and vitamin D plus calcium supplementation reduces the risk of falls and fractures in older people (Level I).
- Vitamin D insufficiency is associated with many more diseases (Level III-1 and Level III-2), such as insulin resistance (Level II) and some cancers (Level III-1).
- There is recent evidence of U-shaped exposure–risk relationships between serum 25-OHD levels and certain disease outcomes (Level III).
- Adverse effects of megadoses of vitamin D in older women have been reported (Level II).
- Classification of vitamin D deficiency and recommended dietary intakes in the United States have been updated.
- Assuming minimal sun exposure, the recommended daily dose of vitamin D from dietary sources and supplementation sufficient to maintain adequate vitamin D levels has increased to 600 IU (15 μg) for most people.
- Vitamin D supplement preparations available in Australia are now primarily vitamin D_3, not vitamin D_2.

* Diamond TH, Eisman JA, Mason RS, et al. Vitamin D and adult bone health in Australia and New Zealand: a position statement. *Med J Aust* 2005; 182: 281-285.
Levels of evidence based on: National Health and Medical Research Council. NHMRC levels of evidence and grades for recommendations for developers of guidelines. Canberra: NHMRC, 2009. ◆

Effect of vitamin D on mineral metabolism, bone health, muscle function and disease

Vitamin D maintains calcium and phosphate homeostasis, and optimises bone health and muscle function. In addition, almost every nucleated cell expresses the vitamin D receptor, with pathways involving local synthesis and actions. The hormonal form of vitamin D, 1,25-dihydroxyvitamin D ($1,25\text{-}(OH)_2D$), increases active intestinal calcium (and phosphate) absorption. Severe vitamin D deficiency causes impaired bone mineralisation, resulting in rickets in children and osteomalacia in adults. There is Level II evidence that optimal mineral metabolism, bone density and muscle function is achieved at serum 25-OHD concentrations of 50–60 nmol/L, with no consistent evidence that higher levels are beneficial. Vitamin D deficiency is an independent predictor of falls in older people, and circulating 25-OHD levels < 60–75 nmol/L are associated with lower-extremity muscle weakness and impaired balance, and accelerated losses in muscle mass, strength and physical function. Most Level I evidence indicates that vitamin D (at daily doses of > 800 IU [20 μg]) needs to be combined with adequate calcium (> 1000 mg per day) to reduce the risk of falls and fractures, although there may be benefits with single therapies.

A wide range of diseases have been associated with low levels of circulating serum 25-OHD, including autoimmune diseases, cardiovascular and metabolic diseases,

some cancers, microbial and respiratory diseases, and some neurological and mental health conditions including schizophrenia, as well as all-cause and cardiovascular mortality. Most of these studies were observational and did not adjust for important confounders. While there are studies in animal models that support the epidemiological evidence, and plausible mechanisms to explain the effects of vitamin D, there have been very few randomised controlled trials (RCTs), most of which have marked limitations.

Other epidemiological studies have recently provided Level III evidence of U-shaped exposure–risk relationships between serum 25-OHD levels and disease outcomes (ie, increased risk at both low [< 30 nmol/L] and high [> 75 or > 125 nmol/L] concentrations) for mortality, schizophrenia, prostate cancer, and frailty in women.

Toxicity

The main concerns with excessive vitamin D levels are hypercalciuria and hypercalcaemia. Vitamin D toxicity can be caused by excess oral intake through supplementation, but not by prolonged exposure of the skin to sunlight. Adverse effects can probably no longer be defined solely by hypercalcaemia, as a large RCT in older Australian women found that a single annual dose of 500 000 IU vitamin D_3 for 3–5 years resulted in a 15% increase in falls and 26% increase in fractures. Administration of vitamin D is contraindicated in most cases of hypercalciuria or hypercalcaemia. Vitamin D treatment is not contraindicated in patients with primary hyperparathyroidism and vitamin D deficiency.

Serum 25-OHD status and target values

Based on our review of the available evidence, vitamin D status can be defined according to the following levels of serum 25-OHD:

- Vitamin D adequacy: ⩾ 50 nmol/L at the end of winter (level may need to be 10–20 nmol/L higher at the end of summer, to allow for seasonal decrease).
- Mild vitamin D deficiency: 30–49 nmol/L
- Moderate vitamin deficiency: 12.5–29 nmol/L
- Severe vitamin D deficiency: < 12.5 nmol/L

On the basis of the evidence discussed above, and allowing for a decrease over winter, a target level for vitamin D adequacy for mineral homeostasis, bone health and muscle function would seem to be > 50 or 60 nmol/L, although optimal values, even for bone and muscle health, are not clear.

Clinicians, researchers and policymakers should be aware of the imprecision of current 25-OHD testing, and exercise caution when interpreting results in clinical practice.

Supplemental vitamin D doses required to achieve targets

There is considerable individual variation in the plateau level of 25-OHD achieved with different doses of supplementation. Although the increment is negatively correlated to the baseline 25-OHD concentration, it is not significantly affected by race, sex or age. Obesity, however, is associated with lower levels of 25-OHD and a reduced dose response to oral vitamin D or UV radiation. It is not clear if vitamin D_3 is more effective than vitamin D_2 in raising 25-OHD levels, but virtually all oral vitamin D supplements available in Australasia are vitamin D_3. To treat moderate to severe deficiency, it would be reasonable to use 3000–5000 IU (75–125 μg) of vitamin D per day for at least 6–12 weeks, with most patients requiring ongoing treatment at a maintenance dose of around 1000–2000 IU (25–50 μg) per day or equivalent (Box 2). As low calcium intake and associated hyperparathyroidism increase the degradation of vitamin D compounds, a daily intake of 1000–1300 mg of calcium, preferably from calcium-rich foods, should be encouraged.

Although it is likely that serum 25-OHD levels that are somewhat higher than those required for musculoskeletal health play a small role in prevention of some disease states, there is evidence emerging of potential adverse effects of higher serum 25-OHD levels under some circumstances. More data from RCTs are needed to test these hypotheses before higher targets can be recommended with confidence.

2 Recommendations for assessment and management of vitamin D deficiency states

High-risk groups

- Screening blood test for 25-hydroxyvitamin D (25-OHD) level performed by a reputable laboratory participating in the Vitamin D External Quality Assessment Scheme (DEQAS) proficiency program, followed by appropriate vitamin supplementation
- Supplementation without initial screening may be appropriate in some high-risk groups (eg, dark-skinned migrants, people in residential care establishments)

Minimum sun exposure to prevent deficiency

- For moderately fair-skinned people, a walk with arms exposed for 6–7 minutes mid morning or mid afternoon in summer, and with as much bare skin exposed as feasible for 7–40 minutes (depending on latitude) at noon in winter, on most days, is likely to be helpful in maintaining adequate vitamin D levels in the body

Vitamin D intake required from dietary sources and supplementation to prevent deficiency

- At least 600 IU (15 μg) per day for those aged ⩽ 70 years, and 800 IU (20 μg) per day for those aged > 70 years
- Those in high-risk groups or with substantial sun avoidance may require higher doses
- Vitamin D supplementation of 1000 IU (25 μg) per day, combined with adequate calcium intake, is required to reduce fracture risk in older people

Vitamin D supplementation required to treat moderate to severe deficiency

- 3000–5000 IU (75–125 μg) per day for at least 6–12 weeks, with a check on 25-OHD concentrations for most people after 3 months, followed by ongoing treatment with a lower dose of around 1000–2000 IU per day (eg, 3–5 × 1000 IU vitamin D_3 capsules per day or 0.6–1 mL of 5000 IU/mL liquid vitamin D_3 for 6–12 weeks, followed by 1 capsule of 1000 IU or 0.2 mL of 5000 IU/mL liquid per day) and adequate calcium intake
- An alternative is 50 000 IU vitamin D_3 (eg, Calciferol Strong, API Consumer Brands, New Zealand only), 1 tablet, once per month for 3–6 months*
- Most patients will need ongoing treatment with a lower dose (eg, 1000 IU per day or equivalent)

* Monthly dosing is similarly effective and apparently safe but takes 3–5 months for plateau 25-OHD levels to be reached. ◆

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