Vitamin D in adolescence: evidence-based dietary requirements and implications for public health policy

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Vitamin D is a unique nutrient. First, it acts as a pro-hormone and secondly, the requirement for vitamin D can be met by both endogenous synthesis from sunlight and by dietary sources. This complicates the determination of dietary requirements for vitamin D, which along with the definition of optimal vitamin D status, have been highly controversial and much debated over recent years. Adolescents are a population group at high risk of low vitamin D status, which is concerning given the important role of vitamin D, and calcium, in promoting normal bone mineralisation and attainment of peak bone mass during this rapid growth phase. Dietary vitamin D recommendations are important from a public health perspective in helping to avoid deficiency and optimise vitamin D status for health. However limited experimental data from winter-based dose–response randomised trials in adolescents has hindered the development of evidence-based dietary requirements for vitamin D in this population group. This review will highlight how specifically designed randomised trials and the approach adopted for estimating such requirements can lead to improved recommendations. Such data indicate that vitamin D intakes of between 10 and about 30 µg/d may be required to avoid deficiency and ensure adequacy in adolescents, considerably greater than the current recommendations of 10–15 µg/d. Finally this review will consider the implications of this on public health policy, in terms of future refinements of vitamin D requirement recommendations and prioritisation of public health strategies to help prevent vitamin D deficiency.

Vitamin D: 25-hydroxyvitamin D: Adolescence: Dietary requirements

Overview and basic biology of vitamin D: sources, metabolism and function

Diet

There are two main forms of vitamin D, namely vitamin D2 (ergocalciferol) and vitamin D3 (cholecalciferol), both of which are found in the diet in predominantly plant-based and animal-based foods, respectively. While there are few foods which are a natural-rich source of vitamin D, good sources include oily fish and egg yolks (vitamin D3) and wild mushrooms (vitamin D2)(1). Foods can also be fortified, on a voluntary or mandatory basis, with vitamin D2 or D3, although fortification policies vary quite considerably between countries, with minimal voluntary fortification found in the UK and across much of Europe (with the exception of Finland; for review see Kiely and Black(2)). Consequently, dietary vitamin D intakes among adolescents are typically low (<3 µg/d). In the UK National Diet and Nutrition Survey (NDNS) rolling programme (2008/09–2011/12), mean vitamin D intakes from food sources alone were 1.9 and 2.4 µg/d in females and males aged 11–18 years, respectively(3). Main food group contributors were meat and meat products (35 %), fat spreads (20 %) and cereal/cereal products (17 %), with eggs and oily fish, both good sources of vitamin D, contributing only 9 % each, emphasising the low consumption of oily fish among adolescents(5). While supplement use can be an

Abbreviations: 1,25(OH)2D, 1,25-dihydroxyvitamin D; 25(OH)D, 25-hydroxyvitamin D; EAR, estimated average requirement; EFSA, European Food Safety Authority; IOM, Institute of Medicine; NDNS, National Diet and Nutrition Survey; ODIN, Food-based solutions for optimal vitamin D nutrition through the life cycle; RCT, randomised controlled trial; SACN, Scientific Advisory Committee on Nutrition; UVB, ultraviolet B.

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effective means of increasing dietary vitamin D intakes, uptake tends to be greater among infants, young children and elderly adults and low among adolescents. Indeed, in the UK NDNS, only 8% of adolescents aged 11–18 years reported taking any type of supplement (compared with 16, 22 and 41% of 4–10, 19–64 and 65+ year olds, respectively) and mean vitamin D intakes increased only marginally to 2.1 and 2.6 µg/d in females and males, respectively, when supplements were included(11).

Endogenous synthesis

Vitamin D is unique in that the majority of this nutrient (80–90%) is synthesised within the human body following skin exposure to sunlight, hence vitamin D’s recognition as the ‘sunshine nutrient’. Ultraviolet B (UVB) radiation (wavelength 290–315 nm) mediates the conversion of 7-dehydrocholesterol, a cholesterol precursor contained within the skin, to vitamin D3. This synthesised vitamin D3, along with dietary vitamin D2/D3, then undergoes a two-step hydroxylation process: first in the liver to form the biologically inactive 25-hydroxyvitamin D (25(OH)D; the main circulating and storage form of vitamin D and that measured to assess vitamin D status), and secondly in the kidneys to the active 1,25-dihydroxyvitamin D (1,25(OH)2D) when required by the body(1).

The amount of vitamin D3 endogenously produced is a function of the amount of UVB radiation reaching the skin, therefore being affected by a number of environmental and individual factors, including season and latitude, skin pigmentation, concealing clothing, use of sunscreen, time spent outdoors and other individual factors such as obesity and ageing(2). Season and latitude dramatically affect vitamin D3 synthesis, and at high latitudes (>40°N) during the winter time (October–March), there are marked decreases in endogenous vitamin D3 production, giving rise to striking seasonal variations in vitamin D status throughout the year(3). This is demonstrated in the NDNS data of sex-combined adolescents aged 11–18 years, whose mean plasma 25(OH)D concentrations ranged from 52.3 nmol/l when blood samples were collected during the months of July–September, down to 31.5 nmol/l when sampled during the winter months of January–March(3).

Physiological function

The primary and well-recognised function of the biologically active metabolite 1,25(OH)2D is in the maintenance of calcium and phosphorus homeostasis via endocrine mechanisms targeting the intestine, kidneys and bone(1,2). This is essential for skeletal health throughout the life cycle, from bone accretion and growth in infancy, childhood and adolescence, through to maintenance of healthy bones and prevention of bone loss in later adulthood. Vitamin D, along with calcium, is important during the adolescent years when the most rapid bone accrual occurs(4). Approximately 80–90% of peak bone mass is achieved by late adolescence and maximising this may help reduce age-related bone loss in later life(5,6).

In recent years however, more attention has been paid to the paracrine/autocrine functions of vitamin D in the facilitation of gene expression. It was previously believed that the kidneys were the only site of 1,25(OH)2D synthesis, although it is now recognised that many extra renal tissues (e.g. colon, prostate, breast and immune cells) have the ability to locally convert 25(OH)D to 1,25 (OH)2D due to the presence of the vitamin D receptor and 1α-hydroxylase enzymes(7,11). Epidemiological studies have therefore indicated a broader role of vitamin D in common cancers, CVD and respiratory diseases(12–14). Although vitamin D is emerging as a promising nutrient in many extra skeletal health outcomes, it must be borne in mind that the evidence is largely observational and thus further data from robust randomised controlled trials (RCT) is required to help clarify the causal role of vitamin D and the underlying mechanisms.

Vitamin D deficiency: definitions, prevalence and consequences

Defining vitamin D deficiency and adequacy

Currently there is no international consensus on the optimal circulating 25(OH)D concentrations for health, with debate surrounding the cut-off thresholds to be applied to define vitamin D deficiency and adequacy. Table 1 summarises the current cut-off thresholds proposed by various international authoritative bodies and agencies.

There is generally good agreement that populations should not have circulating 25(OH)D concentrations below 25–30 nmol/l based on an increased risk of rickets and impaired bone growth in adolescents. At present, the Institute of Medicine (IOM), European Food Safety Authority (EFSA), European Society for Paediatric Gastroenterology, Hepatology and Nutrition and the American Academy of Pediatrics, all suggest that a serum 25(OH)D concentration >50 nmol/l is adequate based on ensuring optimal bone health(15–18), while others have proposed much greater 25(OH)D sufficiency thresholds. The Society for Adolescent Health and Medicine and the Endocrine Society, for example, consider sufficiency at 25(OH)D concentrations >75 nmol/l and that concentrations <50 nmol/l are indicative of deficiency(19,20). It is worth noting however that the Endocrine Society guidelines target patient care of those at risk of vitamin D deficiency (e.g. obese patients, patients with malabsorption syndromes or those on medication that affects vitamin D metabolism), in contrast to the IOM, EFSA and the UK Scientific Advisory Committee on Nutrition (SACN), who propose recommendations for the general healthy population(15,16,21). Regardless it may be premature to recommend circulating 25(OH)D concentrations >75 nmol/l due to the lack of evidence from RCT to date supporting higher serum 25(OH)D concentrations and health outcomes beyond musculoskeletal health.

Prevalence of vitamin D deficiency among adolescent populations

Adolescents are a population group with a recognised risk of low vitamin D status, and several nationally
Consequences of vitamin D deficiency and inadequacy during adolescence

This susceptibility to low vitamin D status in adolescent populations is concerning given the important role of vitamin D in promoting normal bone mineralisation and attainment of peak bone mass during periods of rapid growth and development. It is well recognised that prolonged and severe vitamin D deficiency leads to an increased risk of rickets and altered bone development in children and adolescents, although the effects of mild vitamin D inadequacy (25(OH)D between 30 and 50 nmol/l), which has been widely reported in adolescent populations worldwide, remains less clear. Observational studies in adolescent females have suggested adverse effects of circulating 25(OH)D concentrations <40–50 nmol/l on bone mass at various skeletal sites, although the evidence is inconsistent with others reporting no association between vitamin D status and bone mass in adolescents. A 3-year prospective study in Finnish females aged 9–15 years found a 4% difference in lumbar spine bone mineral density accrual between those with serum 25(OH)D concentrations >37.5 nmol/l and those with concentrations <20 nmol/l at baseline. Importantly, there is limited data available in male adolescents, a research gap recognised in the National Osteoporosis Foundation’s 2016 position statement on peak bone mass development.

Intervention studies, predominantly in white females, have failed to consistently find a beneficial effect of vitamin D supplementation on bone health indices in adolescents and a 2010 Cochrane systematic review concluded that supplementation may only benefit those with inadequate circulating 25(OH)D concentrations below 35 nmol/l. There is currently no consensus on the 25(OH)D concentration that is optimal for the acquisition of bone mass in adolescents or the outcome measures that should be targeted.

As previously alluded to, there is a growing body of evidence that vitamin D may be associated with other non-musculoskeletal, chronic diseases, such as CVD, cancer, diabetes and autoimmune diseases. However, much of the evidence base for this has been derived from epidemiologic studies of adults and much less is known of the effect of low vitamin D status during adolescence on these health outcomes in the short and long terms.

Cross-sectional studies in children and adolescents aged 2–19 years have found circulating 25(OH)D concentrations to be inversely associated with total and LDL-cholesterol concentrations, glucose, and systolic blood pressure and positively correlated with HDL-cholesterol, although not consistently. Furthermore, vitamin D status below 50 nmol/l has been associated with an increased prevalence of metabolic syndrome in adolescents aged 12–19 years in the USA, however, no association was found in Portuguese adolescents aged 13 years. A 2013 systematic review concluded that there was no consistent association between 25(OH)D and lipid and glucose concentrations in adolescents and that systolic blood pressure was inversely associated with 25(OH)D in

representative and individual studies have highlighted the global nature of vitamin D deficiency and inadequacy among adolescent populations. Estimates of vitamin D deficiency (defined across studies as 25(OH)D <22.5–27.5 nmol/l) have ranged from 4–17% in the USA and Canada, 15–40% in Europe, 13–33% in Asia (Korea, India and China) and up to 81% in Saudi Arabia. If a cut-off of 50 nmol/l is applied, these estimates increase to 19–91% of the population as having inadequate vitamin D concentrations. Data from the UK NDNS rolling programme (2008–2011/12) demonstrated that 22% of adolescents aged 11–18 years had year-round plasma 25(OH)D concentrations <25 nmol/l and this increased to 40% during the winter months (January–March).

Caution must be taken when comparing data from different studies due to variations in participant characteristics (e.g. age, ethnicity, cultural dress), latitude and season of sampling and in the analytical techniques and assays used to measure 25(OH)D (for review of the impact of different analytical techniques on 25(OH)D results, see Fraser and Milan). A recent study, based on standardised serum 25(OH)D data from European cohorts and national surveys, found adolescents aged 15–18 years to have the highest risk of vitamin D deficiency (25(OH)D <30 nmol/l) in the range of 12–40%, compared with 4–7% in younger children (1–14 years), 9–24% in adults (19–60 years) and 1–8% in older adults (>61 years). The underlying causes of this apparent increased risk and higher prevalence of vitamin D deficiency in adolescents are unclear, although negative associations between pubertal status and circulating 25(OH)D concentrations have been reported, which may be due to behavioural (e.g. reduced outdoor time, sedentary lifestyles) and/or biological mechanisms. In order to meet the increased calcium demands for skeletal growth during adolescence, the metabolism of 25(OH)D to the active 1,25(OH)2D is increased, and a concomitant decrease in circulating 25(OH)D has been reported, although not consistently.

Table 1. Circulating 25-hydroxyvitamin D deficiency and adequacy cut-off thresholds currently proposed by various international agencies

<table>
<thead>
<tr>
<th>Agency</th>
<th>Deficiency cut-off threshold (nmol/l)</th>
<th>Adequacy cut-off threshold (nmol/l)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scientific Advisory Committee on Nutrition</td>
<td>&lt;25</td>
<td></td>
</tr>
<tr>
<td>Institute of Medicine</td>
<td>&lt;30</td>
<td>&gt;50</td>
</tr>
<tr>
<td>European Food Safety</td>
<td>&lt;30</td>
<td>&gt;50</td>
</tr>
<tr>
<td>Authority</td>
<td>&lt;25</td>
<td>&gt;50</td>
</tr>
<tr>
<td>ESPGHAN</td>
<td>&lt;25</td>
<td>&gt;50</td>
</tr>
<tr>
<td>American Academy of Pediatrics</td>
<td>&lt;25</td>
<td>&gt;50</td>
</tr>
<tr>
<td>The Society for Adolescent Health and Medicine</td>
<td>&lt;50</td>
<td>75–125</td>
</tr>
<tr>
<td>Endocrine Society</td>
<td>&lt;50</td>
<td>&gt;75</td>
</tr>
</tbody>
</table>

ESPGHAN, European Society for Paediatric Gastroenterology, Hepatology and Nutrition.
cross-sectional studies, but no association was found in prospective cohort studies\(^{(62)}\).

**Current vitamin D recommendations**

From a public health perspective, dietary vitamin D recommendations are of great importance in helping to prevent vitamin D deficiency, particularly during the winter months when UVB exposure is inadequate for cutaneous synthesis. Many countries and authoritative bodies worldwide have proposed vitamin D intake recommendations and some have recently been re-evaluated and revised (Table 2). Due to difficulties in establishing the contribution of UVB exposure to vitamin D status, such recommendations are often set assuming minimal sun exposure and are the average daily intakes needed to meet the requirements of the majority of the population (i.e. the vitamin D intake needed to maintain serum 25(OH)D concentrations above the specified threshold in 97.5% of the population). Furthermore, these recommendations are based upon intakes that will ensure adequate vitamin D status to protect against poor musculoskeletal health and do not, at this stage, consider the prevention or reduction in risk of non-musculoskeletal health outcomes. Additionally, recommendations can vary between different life stage groups, with vitamin D supplementation specifically recommended for infants, pregnant and lactating women and the elderly, and are often determined based on the evidence from white Caucasian populations. As demonstrated in Table 2, at present there is a lack of consensus on the intakes required to maintain circulating 25(OH)D concentrations above differing levels of defined adequacy.

**Development and re-evaluation of the UK recommendations**

In 1991, the UK Department of Health published dietary reference values for most nutrients and energy\(^{(68)}\). At this time, it was assumed that free-living individuals aged between 4 and 64 years of age would synthesise sufficient vitamin D from summer sun exposure to ensure adequate vitamin D throughout the winter months to avoid deficiency (25(OH)D <25 nmol/l). Thereby no reference nutrient intake was set for these age groups, although intake recommendations were determined for population subgroups perceived to be at risk of vitamin D deficiency, namely infants, those aged ≥65 years and pregnant and lactating women (Table 2). Subsequent reviews in 1998 and 2007 by the Department of Health and SACN, respectively, concluded that these recommendations should remain unchanged while further evidence was generated from RCT\(^{(65,69)}\). In 2010, SACN agreed to reassess the evidence relating to vitamin D and health on the basis of new data that had become available since the previous review. The revised dietary intake recommendations for vitamin D were released by SACN in 2016 and a daily intake of 10 µg was set for those aged ≥4 years to ensure a serum 25(OH)D concentration >25 nmol/l, which was deemed protective against adverse musculoskeletal health outcomes\(^{(21)}\). This year-round recommendation also includes those of ethnic minority groups and with limited sun exposure (e.g. institutionalised individuals).

**Other notable recommendations**

The 2011 IOM dietary reference intakes was the first landmark publication of vitamin D (and calcium) requirements, based on a risk assessment framework and provided a comprehensive review of vitamin D requirements for health\(^{(15)}\). The risk assessment framework, which has previously been reviewed in detail\(^{(70,71)}\), has since been adopted in more recent re-evaluations of vitamin D requirements by EFSA, SACN and the Nordic Nutrition Recommendations\(^{(16,21,64)}\). Briefly, the risk assessment framework involves undertaking independent systematic evidence-based reviews, which are then used by the committee to identify, describe and rate potential indicators (e.g. rickets, osteomalacia, calcium absorption and fracture risk) in order to derive population targets for 25(OH)D status. The associated dietary vitamin D intake requirements were then established by the IOM via a simulated dose–response meta-regression exercise using group mean/median 25(OH)D response data from selected RCT (winter-based at latitudes >49°N)\(^{(15)}\). Based upon this method, the IOM committee proposed a RDA of 15 µg/d for those aged 1–70 years (20 µg/d for those >70 years), which corresponds to a serum 25(OH)D concentration of 50 nmol/l that meets the needs of 97.5% of the population. Additionally, an estimated average requirement (EAR) of 10 µg/d for those aged ≥1 year was set to maintain serum 25(OH)D of 40 nmol/l in 50% of the population\(^{(15)}\).

Interestingly, using the same simulated dose–response meta-regression method, the Nordic Nutrition Recommendations set a recommended intake (RDA equivalent) of 10 µg/d to maintain serum 25(OH)D >50 nmol/l, using data from winter-based RCT conducted at latitudes covering the Nordic region (49–60°N)\(^{(64)}\).

Of note are also the recent EFSA vitamin D dietary reference values (15 µg/d to maintain serum 25(OH)D >50 nmol/l), which defined an adequate intake instead of an average requirement, based on the committee’s assertion that there was insufficient evidence to allow for an average requirement to be established for all population groups\(^{(16)}\).

In contrast to the meta-regression approach adopted by the IOM, EFSA and the Nordic Nutrition Recommendations as described earlier, SACN generated its vitamin D intake estimates by modelling individual participant-level data and it has been suggested that this method may lead to improved dietary requirement guidelines\(^{(72,73)}\). This may also be an underlying reason...
for the variability in the current recommendations and is discussed in more detail later.

**Meta-regression v. individual participant-level modelling in determining vitamin D intake requirements**

The use of meta-regression and individual participant-level modelling and the impacts on dietary vitamin D intake estimates has been described previously in detail (74,75) and so will be reviewed briefly here. The meta-regression approach used by the IOM, and more recently EFSA, in establishing vitamin D requirements used group mean/median data from intervention arms of selected RCT, together with estimates of vitamin D intakes (from diet and supplements) in a simulated dose–response relationship (15,16). While this avoids over-reliance on data from any particular RCT, the disadvantage is that data are combined from different RCT that use a variety of analytical methods to measure 25(OH)D concentrations (8). The use of group mean/median data and the resulting regression line and 95% CI in the meta-regression model generates average responses, and as such the intake estimates of 10 and 15 µg/d might only be expected to offer protection for 50% of the population (EAR-type estimate) instead of the intended 97.5% (RDA-type estimate). Furthermore, the meta-regression approach does not take into consideration the inter-individual variability in 25(OH)D response to increasing vitamin D intakes. This can be overcome with the use of individual participant-level data and 95% prediction intervals (Fig. 1), as applied by SACN (21). Individual data from three winter-based RCT in female adolescents aged 11–12 years (76) and adults aged 20–40 and ≥64 years (77,78) was modelled by SACN in order to derive vitamin D intake estimates for the UK population. With this method, it is possible to estimate with more confidence the distribution of intakes required to achieve specific serum 25(OH)D concentrations.

**Evidence-based dietary vitamin D requirements in adolescence: use of individual participant-level data to fill knowledge gaps**

While vitamin D intake recommendations have been set for the adolescent age group (Table 2), the regulatory authorities tasked with establishing these recommendations have highlighted the significant knowledge gaps in relation to winter-based dose–response RCT specifically designed to estimate dietary vitamin D intakes required to maintain 25(OH)D above certain cut-off thresholds in younger populations. Consequently, intake recommendations for adolescents are often extrapolated from adult data in the absence of adolescent-specific data. Of the three RCT in children and adolescents included in the IOM dose–response model, a 1 month long study was conducted in twenty participants (6–14 years) (79) and another was carried out in 1988 in sixty participants (8–10 years) using doses of 0 and 10 µg/d (80). Other under-researched population sub-groups identified with a lack of dose–response experimental data also included younger children, pregnant women and ethnic minority

### Table 2. Dietary reference values for vitamin D (µg/d) by life stage as proposed by various international agencies to maintain adequate circulating 25-hydroxyvitamin D (25(OH)D) concentrations

<table>
<thead>
<tr>
<th>Agency</th>
<th>Year</th>
<th>Country/countries</th>
<th>Recommended dietary vitamin D intake (µg/d)</th>
<th>0–12 months</th>
<th>1 to &lt;4 years</th>
<th>4–18 years</th>
<th>19–69 years</th>
<th>&gt;70 years</th>
<th>Pregnancy/lactation</th>
<th>25(OH)D Threshold (nmol/l)</th>
</tr>
</thead>
<tbody>
<tr>
<td>UK Department of Health(63)</td>
<td>1998</td>
<td>UK</td>
<td>8.5–7</td>
<td>7</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>SACN(21)</td>
<td>2016</td>
<td>UK</td>
<td>8.5–10</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>25</td>
<td>25</td>
</tr>
<tr>
<td>Europe EFSA(16)</td>
<td>2016</td>
<td>Europe</td>
<td>10</td>
<td>15</td>
<td>15</td>
<td>15</td>
<td>15</td>
<td>15</td>
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</tr>
<tr>
<td>Nordic Nutrition Recommendations(64)</td>
<td>2012</td>
<td>Denmark, Finland, Iceland, Norway, Sweden</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>20</td>
<td>10</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>Health Council of the Netherlands(65)</td>
<td>2012</td>
<td>The Netherlands</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>20</td>
<td>10</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>German Nutrition Society(66)</td>
<td>2012</td>
<td>Germany, Austria, Switzerland</td>
<td>10</td>
<td>20</td>
<td>20</td>
<td>20</td>
<td>20</td>
<td>20</td>
<td>20</td>
<td>20</td>
</tr>
<tr>
<td>Other IOM(15)</td>
<td>2011</td>
<td>North America and Canada</td>
<td>10</td>
<td>15</td>
<td>15</td>
<td>15</td>
<td>20</td>
<td>15</td>
<td>15</td>
<td>15</td>
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<tr>
<td>The Endocrine Society(120)</td>
<td>2011</td>
<td>Worldwide</td>
<td>25</td>
<td>25</td>
<td>25</td>
<td>25</td>
<td>37.5–50</td>
<td>37.5–50</td>
<td>37.5–50</td>
<td>75</td>
</tr>
<tr>
<td>WHO/FAO Joint Expert Consultation(87)</td>
<td>2004</td>
<td>Worldwide</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>10</td>
<td>10</td>
<td>10</td>
</tr>
</tbody>
</table>

SACN, Scientific Advisory Committee on Nutrition; EFSA, European Food Safety Authority; IOM, Institute of Medicine.

* For those aged 4–64 years, it was assumed that sun exposure during the summer months would ensure an adequate vitamin D status year-round, so no intake was set.

† Requirements set under conditions of minimal cutaneous synthesis and in the presence of cutaneous vitamin D3 synthesis the requirement for dietary vitamin D is lower or may even be zero.

§ Target concentration of 50 nmol/l for those aged >70 years.

¶ Estimated value of adequate vitamin D intake without cutaneous synthesis.

∥ Recommendations for populations at risk of vitamin D deficiency.
populations. Winter-based dose–response RCT, designed and implemented within the Food-based solutions for optimal vitamin D nutrition through the life cycle (ODIN) project aimed to fill these knowledge gaps by modelling individual participant-level data in order to estimate dietary requirements for vitamin D in these population sub-groups(81).

In the ODIN adolescent study, 110 healthy white males and females aged 14–18 years were randomly allocated to receive 0, 10 or 20 µg vitamin D3 daily for 20 weeks throughout the winter (October–March)(82). Via mathematical modelling of individual participant-level 25(OH)D and total vitamin D intake data, the vitamin D intakes required to maintain serum 25(OH)D concentrations above 25, 30, 40 and 50 nmol/l in 50, 90, 95 and 97.5 % of the adolescents were estimated. Of particular note, the vitamin D intakes needed to avoid deficiency and maintain serum 25(OH)D concentrations >25 and >30 nmol/l in 97.5 % of the population were 10.1 and 13.1 µg/d, respectively(82). The 10.1 µg/d estimate supports the SACN recommendation for the UK population aged ≥4 years. In order to maintain serum 25(OH)D >40 nmol/l in 50 % of the population, corresponding to the EAR-type intake, 6-6 µg/d was estimated for adolescents. While lower than the 10 µg/d recommendation of the IOM, this is close agreement with the 6-3 µg/d estimate in Danish and Finnish females aged 11–12 years in a similarly designed RCT(79). However, greater discrepancies arise when considering the RDA-type intake (to maintain serum 25(OH)D >50 nmol/l in 97.5 % of the population). The intake estimate of about 30 µg/d in adolescents derived from the ODIN study is considerably higher than the IOM recommendation of 15 µg/d. The large inter-individual variability in 25(OH)D response to vitamin D intakes and the inability of the meta-regression using aggregate data to consider this, explains, in part, the wide variation in these estimates at the 97.5th percentile(73).

It is important to note that the adolescent trial aforementioned and many of those included by the IOM, SACN and EFSA were conducted in healthy white populations. A winter-based RCT in 8–14 year old black African American and white children and adolescents estimated that vitamin D intakes of 28 and 52 µg/d would maintain serum 25(OH)D >30 and >50 nmol/l, respectively, in 97.5 % of the population(83). Unfortunately intake estimates were not determined for the ethnic groups separately, limiting the opportunity to compare intake estimates. In a recent food-based dose–response RCT in Swedish children aged 5–7 years, it was estimated, using 95 % prediction intervals, that vitamin D intakes of 6 and 20 µg/d would maintain 25(OH)D >30 and >50 nmol/l, respectively, in fair-skinned children, while the corresponding intakes in dark-skinned children were 14 and 28 µg/d, respectively(84). These data provide early indications that greater

**Fig. 1.** Relationship between serum 25-hydroxyvitamin D (25(OH)D) concentration and total vitamin D intake using data from randomised controlled trials. The central thick solid line is the regression line and the two curved lines represent the 95 % CI around the mean. The outer two dashed lines represent the 95 % prediction intervals. IU, international units (to convert IU to µg/d divide by 40). Reprinted from Journal of Steroid Biochemistry and Molecular Biology, 148, Cashman KD, Vitamin D: dietary requirements and food fortification as a means of helping achieve adequate vitamin D status, 19–26, Copyright (2015), with permission from Elsevier.
intakes may be required by ethnic minority populations; however, this should be confirmed in further winter-based vitamin D dose–response RCT\(^{85}\).

Achieving vitamin D intakes: supplements vs. food fortification

Current recommendations, along with the new data presented here, propose that vitamin D intakes of between 10 and about 30 µg/d are required by adolescents in order to avoid vitamin D deficiency and ensure adequacy. Population-based dietary intake surveys in the UK and beyond have highlighted significant gaps between typical vitamin D intakes in adolescents and these recommendations, especially in countries with limited food fortification, which includes the UK. Current intakes in UK adolescents aged 11–18 years participating in the NDNS were about 2 µg/d\(^{93}\). Strategies therefore need to be implemented in order to help the UK population achieve higher dietary vitamin D intakes and this becomes increasingly important during times of insufficient UVB exposure for cutaneous synthesis. While vitamin D supplements can be useful in increasing vitamin D intakes and consequently vitamin D status, relying on supplements may not be a viable public health strategy to increase intakes at the population level. Supplement use is not widespread and will only be effective in those that take them, which varies by age, sex and by individuals’ health motivation and purchasing power. As previously mentioned, supplement uptake is typically low among adolescents compared with younger and older age groups, and so adolescents are far less likely to acquire the same level of benefit as other population groups do from supplements. Therefore, sustainable public health strategies to ensure vitamin D intakes need to be designed and implemented to continually meet the needs of the majority, irrespective of age, sex and other individual factors.

Food fortification presents an opportunity to increase vitamin D intakes at the population level. Using data from the 2003–2006 National Health and Nutrition Examination Survey in the USA, fortification has been shown to considerably improve dietary vitamin D intakes above that obtained from the basal diet\(^{86}\). Intakes of 1–7 µg/d were reported in children aged 2–18 years and adolescents from naturally occurring food sources, with 100 % having intakes below the IOM EAR of 10 µg/d. Intakes increased to 6–1 µg/d when fortified foods were included, with 86–8 % having intakes below the EAR. Commonly fortified foods in the USA include milk, breakfast cereals, yoghurts, cheeses, juices and spreads. When supplement use was also considered, intakes further increased to 8–3 µg/d, with 73–2 % of intakes remaining below 10 µg/d. However, dietary diversity needs to be given important consideration when developing and initiating fortification policies. While fortification of milk and other staple commodities (e.g. margarine/fat spreads, other dairy products and breakfast cereals) will be important for increasing vitamin D in the food supply, this will not be an effective strategy in non- or infrequent consumers. For example, routine fortification of milk with vitamin D in Finland had little impact on the vitamin D intakes of female adolescents (12–18 years)\(^{87}\).

Intakes increased from 4–0 µg/d prior to the introduction of the fortification policy to 5–4 µg/d following fortification introduction, with no change in serum 25(OH)D concentrations (48–3 and 48–1 nmol/l, respectively)\(^{87}\). Additionally the prevalence of serum 25(OH)D concentrations <50 nmol/l in these adolescent females was 60.6 and 65.5 % prior to and following fortification, respectively. Conversely fortification of milk and fat spreads in Finland was found to have a positive impact on the dietary vitamin D intakes of adults and young children\(^{88–91}\). This may be due to low and/or infrequent consumption of milk and other dairy products among adolescent females. These data from Finland demonstrate the importance of giving consideration to food consumption patterns in fortification policies and several widely consumed foods should be fortified to ensure widespread reach. Dietary diversity among different ethnic groups can also influence vitamin D intakes, with African American adolescent females reported to consume more vitamin D from meat and bean food sources compared with white females who consumed more from milk, which is routinely fortified in the USA\(^{92}\). Biofortification of foods presents a novel opportunity to increase vitamin D in the food supply through a range of foods, alongside more traditional fortification practices. The vitamin D content of animal produce (e.g. pork, beef, chicken, eggs and fish) can be increased via the fortification of livestock feeds, where permissible. RCT conducted within the aforementioned ODIN project have initiated investigation into the efficacy and safety of vitamin D fortification and bio-fortification of a variety of foods from different population groups and we await these findings\(^{81}\).

Conclusions

Vitamin D recommendations are of great importance from a public health perspective in terms of preventing vitamin D deficiency and optimising vitamin D status for health. It is crucial therefore that recommendations are evidence-based in order to establish more accurate and precise requirements for population sub-groups. Limited experimental data continue to be an issue for certain population sub-groups, particularly those of ethnic minority populations, and further research and targeted dose–response RCT should be undertaken to continue to fill these gaps in the evidence base. This will have important implications for public health policy as presented here: whilst the current recommendations of 10–15 µg/d may help avoid winter-time vitamin D deficiency in adolescents (circulating 25(OH)D concentrations <25–30 nmol/l), they remain inadequate to achieve and maintain 25(OH)D concentrations above 50 nmol/l. This upper threshold of circulating 25(OH)D concentration may be optimal for health, particularly with respect to bone accretion in adolescents, although this needs to be confirmed in RCT, along with other
non-musculoskeletal health outcomes. Consideration should also be given to the model adopted for the estimation of dietary requirements for vitamin D and future refinements of these should consider the use of individual participant-level data from dose–response RCT as more data become available. Understanding optimal vitamin D concentrations, clinical outcomes and vitamin D intake requirements will help prioritise and inform public health strategies to prevent vitamin D deficiency.

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**Conflicts of Interest**

None.

**Authorship**

T. J. S. wrote the manuscript; L. T., S. A. L.-N. and K. H. H. assisted with manuscript editing; T. J. S. had primary responsibility for the final content; all authors read and approved the final manuscript.

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