A Review of Vitamin D Fortification: Implications for Nutrition Programming in Southeast Asia

Article in Food and nutrition bulletin · June 2013
DOI: 10.1177/15648265130342S110 · Source: PubMed

5 authors, including:

- Arnaud Laillou
  UNICEF
  63 PUBLICATIONS  345 CITATIONS
  SEE PROFILE

- Regina Moench-Pfanner
  ibn360 - investing for better n…
  66 PUBLICATIONS  821 CITATIONS
  SEE PROFILE

Some of the authors of this publication are also working on these related projects:

- Vietnam Home Fortification of Complementary Foods View project
- Reconciling the Irreconcilable View project

All content following this page was uploaded by Regina Moench-Pfanner on 14 May 2014.

The user has requested enhancement of the downloaded file.
A review of vitamin D fortification: Implications for nutrition programming in Southeast Asia

Zhenyu Yang, Arnaud Laillou, Geoffry Smith, Dominic Schofield, and Regina Moench-Pfanner

Abstract

Background. Vitamin D is vital for bone health and has important roles in nonskeletal health and organ function. Most vitamin D is generated in the body by exposure to sunlight, with limited amounts added by the diet. Despite the presence of regular sunshine in Southeast Asia, vitamin D deficiency or insufficiency is being found there more commonly, primarily due to reduction of sunlight exposure as a result of lifestyle changes. Some of these lifestyle changes are unlikely to be reversed, and foods naturally containing vitamin D are not widely consumed, so fortification of foods with vitamin D may raise vitamin D status.

Methods. The literature database was searched for studies of vitamin D fortification, and we estimated potential vitamin D intakes from fortified vegetable oil.

Results. Almost all of the studies showed that circulating vitamin D (25-hydroxyvitamin D [(25OHD)]) increased in a dose-dependent manner with increased intake of vitamin D–fortified foods. However, in a number of studies the additional intake was insufficient to increase vitamin D levels to 50 nmol/L. Vegetable oil fortified with vitamin D at a level of 10 µg/100 g could provide 3.9% to 21% of the Institute of Medicine Estimated Average Requirement (EAR) of vitamin D for adults in Southeast Asia.

Conclusions. Fortification of widely consumed foods, such as edible oil, with vitamin D could contribute to improved vitamin D status in Southeast Asian countries. Intake modeling studies should be conducted to calculate the resulting additional intakes, and fortification of additional foods should be considered. More nationally representative studies of vitamin D status in the region are urgently needed.

Key words: Fortification, nutrition impact, Southeast Asia, supplementation, vitamin D

Background

Vitamin D is a fat-soluble “vitamin” and is now recognized as a prohormone. This is because the body can synthesize vitamin D from its precursor (7-dehydrocholesterol) when exposed to ultraviolet light at a wavelength between 290 and 315 nm. Vitamin D in this form is not biologically active and must be converted by two enzymatic hydroxylation reactions to function physiologically. The first of these conversions takes place in the liver and transforms vitamin D to the main circulating form, 25-hydroxyvitamin D (25OHD). This is further converted in the kidney to the active hormonal form 1,25-dihydroxyvitamin D (calcitriol). This hormonal form of the synthesized vitamin D acts at different target organs [1]. The physiological functions of active vitamin D (calcitriol) are related to calcium homeostasis and osteoporosis, with possible roles in diabetes, cancer, ischemic heart disease, and autoimmune and infectious diseases [1]. The major source of body vitamin D is from cutaneous synthesis when the skin is exposed to ultraviolet B.* Season, latitude, time of day, skin pigment, sunscreen use, and aging can affect cutaneous vitamin D synthesis [1]. The natural food sources of vitamin D include oily fish, egg yolk, and fish liver oil, which are not commonly consumed in many diets [2].

* Ultraviolet B is one of the three types of invisible light rays (together with ultraviolet A and ultraviolet C) given off by the sun.
< 50 nmol/L or vitamin D insufficient (defined as 25OHD < 75 nmol/L) [1]. Vitamin D deficiency is quite common in regions and countries including North America, northern Europe, Saudi Arabia, the United Arab Emirates, Australia, Turkey, India, and Lebanon [1]. Vitamin D deficiency is believed to be less common in Southeast Asia than in India [3]; however, it has not been well characterized. The prevalence of vitamin D deficiency varies across countries in Southeast Asia (table 1). The reported prevalence was lower in Thailand and Vietnam (5.7% to 7%) in two studies [4, 5] and was higher in Indonesia and Malaysia (41% to 87%) [6–8], but only the Thai study was nationally representative. However, another recent study in Vietnam found that the prevalence of vitamin D deficiency was 40% for women and 37% for children [9].

Some observational studies have shown that vitamin D deficiency is associated with greater risk of cardiovascular diseases (e.g., stroke, sudden cardiac death) and their risk factors (e.g., hypertension, diabetes) [10]. However, few randomized, controlled trials are available, and the evidence from observational studies is not conclusive [10]. A recent systematic review found that the relationship between 25OHD and cancer mortality was mixed [11]. However, cancer patients with higher 25OHD tended to have lower risk of mortality, especially patients with colorectal cancer [11].

There was no significant association between vitamin D supplementation and breast cancer incidence in a randomized, controlled trial [12]. A recent longitudinal polymorphisms study also did not show a conclusive causal relationship between 25OHD and myocardial infarction, type 2 diabetes, cancer, or all-cause mortality [13]. Some of the inconsistency in the evidence may be due to issues of study design and interpretation [14]. Major trials are under way and may address some of these issues (VITAL in the United States, the European DO-HEALTH study on vitamin D and omega 3 distribution of vitamin D fortification to improve daily vitamin D intake in Southeast Asian countries.

### Methods

Sources searched and search strategy for evidence on vitamin D fortification

A meta-analysis of the efficacy of vitamin D fortification in improving 25OHD concentrations was conducted in 2006 [2]. Therefore, we began our search for relevant publications starting with 2006, searching for specific key words on PubMed. All titles and abstracts were assessed for their relevance to vitamin D fortification. The key phrase (“Vitamin D”[MAJR] AND “Food, Fortified”[MAJR]) was used for the search. References were extracted from the search results and included if they met one of the following criteria: randomized clinical trial, quasi-experimental design, or program evaluation. These criteria were used in order to assess both efficacy and effectiveness. A total of 91 papers were found, 13 of which were included in this review. Six were reports of randomized, controlled trials and seven were reports of quasi-experimental designs or program evaluations with preintervention control.

<table>
<thead>
<tr>
<th>Country</th>
<th>Sampling site</th>
<th>Age (yr)</th>
<th>Sex</th>
<th>Prevalence (%)a</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vietnam</td>
<td>Northern</td>
<td>Childbearing age</td>
<td>F</td>
<td>7</td>
<td>[4]</td>
</tr>
<tr>
<td>Thailand</td>
<td>National</td>
<td>15–98</td>
<td>M and F</td>
<td>5.7</td>
<td>[5]</td>
</tr>
<tr>
<td>Indonesia</td>
<td>Jakarta</td>
<td>18–40</td>
<td>F</td>
<td>63</td>
<td>[6]</td>
</tr>
<tr>
<td>Malaysia</td>
<td>Kuala Lumpur</td>
<td>18–40</td>
<td>F</td>
<td>60</td>
<td>[6]</td>
</tr>
<tr>
<td>Malaysia</td>
<td>Kuala Lumpur</td>
<td>48.2 ± 5.2</td>
<td>M (42%) and F (58%)</td>
<td>41 (M) 87 (F)</td>
<td>[7]</td>
</tr>
<tr>
<td>Malaysia</td>
<td>Kuala Lumpur</td>
<td>7–12</td>
<td>M and F</td>
<td>72.4</td>
<td>[8]</td>
</tr>
</tbody>
</table>

a. Vitamin D deficiency is defined as 25-hydroxyvitamin D (25OHD) < 50 nmol/L [48, 49]
Estimation of vitamin D intakes from fortified foods

The objective of this study was to estimate, based on dietary intakes available from several Southeast Asian countries, whether food fortification has the potential to increase daily vitamin D intakes among women of reproductive age and other targeted groups. The Institute of Medicine (IOM) Estimated Average Requirements (EAR) of 10 µg/day (400 IU) nutrient intake for vitamin D [20] was used to assess the contribution of dietary intakes to the coverage of daily micronutrient requirements.

Results

Existing evidence

Moderate exposure to sunshine and fortification of food with vitamin D can improve the vitamin D status of the population [3]. Fortification with vitamin D has been assessed for the past decade (table 2). For example, since 2003 the Finnish Government has recommended vitamin D fortification of milk (0.5 µg/100 mL) and of margarine and spreads (10 µg/100 g). In one study, adolescent girls aged 12 to 18 years (n = 142) were followed from 2000 to 2004, one year after the initiation of fortification [21]. The mean 25OHD concentration did not differ between 2000 and 2004 (48.3 and 48.1 nmol/L, respectively). The prevalence of low vitamin D status (defined as 25OHD < 50 nmol/L) was also similar in these two years (60.6% and 65.5%, respectively). Another study assessed the effectiveness of the program among young Finnish men by following them from 2001 to 2004. The median 25OHD concentration was significantly higher in 2004 than in 2001 (27 vs. 24 nmol/L, p < .0015) [22]. The third study examined the impact of the vitamin D fortification program on 4-year-old children [23]. 25OHD concentration was significantly higher among children in 2004 than in 2000 (64.9 vs 54.7 nmol/L, p = .002). Dietary vitamin D intake was also significantly higher after fortification than before fortification.

In a recent meta-analysis (considering studies up to 2006), eight of nine randomized, controlled trials consistently showed that vitamin D fortification improved 25OHD concentration in both younger and older subjects [2]. The change in 25OHD concentration varied from 14.5 to 34.5 nmol/L after consumption of 3.4 to 25 µg/day of vitamin D from fortified products. Only one study, in which the subjects were given vitamin D–fortified cheese, did not find significant improvement in 25OHD concentration, even though vitamin D intake increased significantly [24].

Since 2006, many studies have evaluated the impact of foods fortified with vitamin D and/or calcium on elderly men or postmenopausal women and have shown improvement [25–30]. Other groups were also studied. In a study in New Zealand, women aged 18 to 45 years were randomly assigned to a group receiving vitamin D–fortified milk (5 µg/day, n = 37) or a control milk group (n = 36) [31]. After 12 weeks of intervention, the mean serum 25OHD concentration was significantly greater in the fortification group than in the control group (65 vs. 53 nmol/L, p < .001). The prevalence of vitamin D insufficiency (defined as 25OHD < 75 nmol/L) was significantly lower in the fortification group than in the control group (53% vs. 79%, p = .011). A study in the United States assessed the bioavailability of vitamin D3 and D3 in fortified orange juice [32]. Adult subjects (18 to 79 years old, n = 105) were randomly assigned to receive vitamin D2–fortified orange juice, vitamin D3–fortified orange juice, vitamin D2 supplement, vitamin D3 supplement, or placebo, at a level of vitamin D supplementation or fortification of 25 µg/day. There were no significant differences in 25OHD concentration between the groups receiving vitamin D–fortified orange juice and vitamin D supplement, but 25OHD concentrations were significantly higher in both the fortification and the supplementation groups than in the placebo group (28.1 vs. 18.1 ng/mL). In Mongolia, schoolchildren (9–11 years old, n = 46) were given vitamin D–fortified (7.5 µg/day) milk for 1 month [33]. The prevalence of low vitamin D status (defined as 25OHD < 50 nmol/L) decreased from 76% to 7% and the prevalence of vitamin D deficiency (defined as 25OHD < 37 nmol/L) decreased from 32% to 0% after 1 month of treatment.

The common food carriers for vitamin D fortification included milk, cheese, and other dairy products (both regular-fat and low-fat); margarine; oil spread; orange juice; and bread. The fortification level in these studies varied from 2.5 to 125 µg/day, and the most common doses were between 5 and 25 µg/day (33% to 166% of EAR [34]). The fortification level for each food depended on the intake and characteristics of that food (e.g., 0.5 µg/100 mL for milk and 10 µg/100 g for margarine in Finland). Two studies showed that the bioavailability of vitamin D used as a fortificant was similar to the bioavailability of supplemental vitamin D [30, 32]. The principal findings are summarized in table 3. Contribution of vitamin D fortification

Dairy products (e.g., milk and cheese), margarine, vegetable oil, and orange juice are the common food carriers for fortification with vitamin D, mainly in Western countries. Vitamin D fortification of those products has been shown to improve 25OHD levels significantly across studies and could be an efficacious way to prevent and control vitamin D deficiency in Southeast Asia. Unfortunately, the consumption of
<table>
<thead>
<tr>
<th>Country, date, ref.</th>
<th>Subjects</th>
<th>Vitamin D level</th>
<th>Calcium level</th>
<th>Food carrier</th>
<th>Duration</th>
<th>25OHD assay</th>
<th>Food carrier</th>
<th>Calcium level</th>
<th>Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>France, 2009 [25]</td>
<td>Elderly women in nursing homes</td>
<td>Vitamin D3 (2.5 µg/day)</td>
<td>300 mg/day</td>
<td>Cheese</td>
<td>1 mo</td>
<td>RIA</td>
<td>RIA</td>
<td>125 nmol/L (p &lt; .001); BMD at lumbar spine: +0.83% vs. +0.96% vs. +0.73%</td>
<td>Compared with baseline, 25OHD3 increased significantly; PTH decreased significantly from 125 nmol/L (p &lt; .001); BMD at lumbar spine was significantly higher at 1 mo than at baseline (0.83% vs. 0.96% vs. 0.73%). Time effects were observed between baseline and endline, but no true control group was available in this study. Results should be interpreted with caution.</td>
</tr>
<tr>
<td>Romania, 2009 [26]</td>
<td>Nursing home residents</td>
<td>Vitamin D3 (125 µg/day)</td>
<td>320 mg/day</td>
<td>Bread</td>
<td>1 yr</td>
<td>RIA</td>
<td>RIA</td>
<td>After 12 mo of intervention, mean 25OHD significantly increased from 28.5 nmol/L to 125 nmol/L (p &lt; .001); BMD at lumbar spine was significantly higher at 1 yr than at baseline (0.83% vs. 0.96% vs. 0.73%). Time effects were observed between baseline and endline, but no true control group was available in this study. Results should be interpreted with caution.</td>
<td></td>
</tr>
<tr>
<td>Greece, 2009 [27]</td>
<td>Postmenopausal women (mean age 61.5 yr)</td>
<td>Vitamin D3 (7.5 µg/day)</td>
<td>1,200 mg/day (supplementation)</td>
<td>Dairy product</td>
<td>5 mo</td>
<td>Chemiluminescence immunoassay</td>
<td>RIA</td>
<td>1,300 mg/day</td>
<td>After 5 mo of treatment, the increase in PTH was marginally lower in the fortified group and the control group than in the supplemented group. Time effects were observed between baseline and endline, but no true control group was available in this study. Results should be interpreted with caution.</td>
</tr>
<tr>
<td>Greece, 2009 [28]</td>
<td>Elderly men (≥ 50 yr)</td>
<td>Vitamin D3 (20 µg/day)</td>
<td>1,000 mg/day</td>
<td>Milk</td>
<td>2 yr</td>
<td>RIA</td>
<td>RIA</td>
<td>After 2 yr of treatment, 25OHD and PTH concentration changes were significantly greater in the treatment group (−4.8 nmol/L and −2.0 pg/mL) than in the control group (−2.1 nmol/L and −0.7 pg/mL). BMD at the hip and ultradistal radius was significantly improved in the group receiving fortified dairy product and had significantly greater improvements in pelvis, total spine, and total-body BMD than did the other 2 groups (p &lt; .05).</td>
<td></td>
</tr>
<tr>
<td>Canada, 2008 [30]</td>
<td>Elderly men and postmenopausal women (2006–12)</td>
<td>Vitamin D3 (100 µg/day)</td>
<td>NA</td>
<td>NA</td>
<td>1 yr</td>
<td>RIA</td>
<td>RIA</td>
<td>After 8 wk of intervention, the 25OHD concentration changes were significantly greater than in all other vitamin D treatment groups (60.3 nmol/L). PTH decreased significantly from baseline to 8 wk. No true control group was available in this study. Results should be interpreted with caution.</td>
<td></td>
</tr>
</tbody>
</table>

**Notes:**
- **25OHD:** 25-hydroxyvitamin D
- **PTH:** parathyroid hormone
- **RIA:** radioimmunoassay
- **BMD:** bone mineral density
- **NA:** not available
- **25OHD3:** 25-hydroxyvitamin D3
- **PTH:** parathyroid hormone
- **RIAl:** radioimmunoassay

**TABLE 2. Description of studies evaluating the impact of food fortified with vitamin D and calcium on elderly men and postmenopausal women (2006–12).**
The fortification level of these studies varied from 2.5 to 125 µg /day; the most common doses were between 5 and 25 µg/day (1 to 5 times AI). The fortification level for each food depended on the intake and characteristics of that food (e.g., 0.5 µg/100 mL for milk and 10 µg/100 g for margarine in Finland).

20 studies showed beneficial effects of vitamin D fortification on 25OHD concentration or vitamin D deficiency. The magnitude of mean 25OHD concentration improvement varied from 2 to 97.1 nmol/L; the most common improvements were between 9.9 and 34.5 nmol/L. The magnitude was significantly related to the fortification level used (n = 8, r = 0.98, p < .01), which is also supported by the meta-analysis of Black et al. [19]. For example, fortification with the lowest (2.5 µg/day) and the highest (125 µg/day) amounts of vitamin D resulted in the smallest (2 nmol/L) and the largest (97.1 nmol/L) improvements in 25OHD, respectively.

Vitamin D fortification suppressed PTH in 8 of 14 studies. When products fortified with both vitamin D and calcium were consumed, BMD increased in various locations, including hip, femoral neck, ultradistal radius, spine, and pelvis. However, it is difficult to attribute the benefits to vitamin D or calcium alone, due to the design of these studies.

No adverse effects were reported when food fortified with 100 µg/day vitamin D was consumed for 2 months. Serum calcium concentration, a biomarker for vitamin D toxicity, did not increase during 1 year of intervention with 125 µg/day vitamin D, although urinary calcium concentration increased at 3, 6, and 9 months, but not at 12 months. When 25 µg/day vitamin D or less was consumed, some subjects reported gastrointestinal discomfort.

AI, Adequate Intake; BMD, bone mineral density; 25OHD, 25-hydroxyvitamin D; PTH, parathyroid hormone.

Discussion

Over the past decade, Southeast Asian countries have focused nutrition strategies on iron and vitamin A deficiencies. It seems relevant also to include vitamin

milk and milk products is still marginal in Southeast Asia, and vegetable oil seems to be more suitable as a potential food vehicle for fortification.

Since vitamin D is a fat-soluble vitamin, it is commonly added to lipid-containing foods, although stabilized forms can be added to a wide variety of foods. For example, vegetable oils are suitable as vehicles for fortification with vitamins A, D, and E, which are easily uniformly distributed in oil [35]. The production and refining of oils is often a centralized process and therefore is suitable for large-scale intervention. In addition, margarine is fortified with vitamin D in Canada [36], Finland [21], and some other European countries.

As shown in table 4, in several Southeast Asian countries vitamin D–fortified vegetable oil can contribute to a significant daily vitamin D intake among different age groups. For example, in Vietnam 91.5% of women [37] and 38% of children under 5 years of age [38] consume vegetable oil daily (median consumption, 11.1 and 6 g/day, respectively). Therefore, as shown in table 4, vegetable oil fortified at a level of 7.5 to 10 µg/100 g in Vietnam could provide 7% to 9% of the IOM EAR of vitamin D for a woman (400 IU) and 4% to 5% of the IOM EAR for a child under 5 years of age. Overall, in Southeast Asia, if governments decided to support national standards of vitamin D fortification, vitamin D–fortified vegetable oil could provide from 3% to approximately 21% of the IOM EAR for vitamin D for an adult, depending on local practices (table 4). In addition, and as discussed more in depth by Laillou et al. in this supplement [39], the exportation of fortified edible oil from Malaysia and Indonesia has a significant potential to increase vitamin A intake in many neighboring countries. The same can apply to vitamin D–fortified exported vegetable oil. For example, in Afghanistan, vitamin D–fortified vegetable oil can provide up to 23.8% of the IOM EAR for vitamin D for an adult, as vegetable oil consumption is high and most of the oil is imported from Malaysia.

Table 3. Summary of findings of different surveys (including all category groups)

| Places where the studies were implemented | All of these studies except one in Romania and another in Mongolia were conducted in developed countries. Most of these countries were located in high-latitude regions (30°N or higher). Seasonal variation was obvious for vitamin D deficiency, and most studies were conducted during winter. |
| Food vehicles used | The common food carriers for vitamin D fortification included milk, cheese, and other dairy products (both regular-fat and low-fat); margarine; oil spread; orange juice; and bread. |
| Fortification levels | The fortification level of these studies varied from 2.5 to 125 µg /day; the most common doses were between 5 and 25 µg/day (1 to 5 times AI). The fortification level for each food depended on the intake and characteristics of that food (e.g., 0.5 µg/100 mL for milk and 10 µg/100 g for margarine in Finland). |
| Impacts of the studies on 25OHD concentration | 20 studies showed beneficial effects of vitamin D fortification on 25OHD concentration or vitamin D deficiency. The magnitude of mean 25OHD concentration improvement varied from 2 to 97.1 nmol/L; the most common improvements were between 9.9 and 34.5 nmol/L. The magnitude was significantly related to the fortification level used (n = 8, r = 0.98, p < .01), which is also supported by the meta-analysis of Black et al. [19]. For example, fortification with the lowest (2.5 µg/day) and the highest (125 µg/day) amounts of vitamin D resulted in the smallest (2 nmol/L) and the largest (97.1 nmol/L) improvements in 25OHD, respectively. |
| Impact of the studies on other markers | Vitamin D fortification suppressed PTH in 8 of 14 studies. When products fortified with both vitamin D and calcium were consumed, BMD increased in various locations, including hip, femoral neck, ultradistal radius, spine, and pelvis. However, it is difficult to attribute the benefits to vitamin D or calcium alone, due to the design of these studies. |
| Toxicity | No adverse effects were reported when food fortified with 100 µg/day vitamin D was consumed for 2 months. Serum calcium concentration, a biomarker for vitamin D toxicity, did not increase during 1 year of intervention with 125 µg/day vitamin D, although urinary calcium concentration increased at 3, 6, and 9 months, but not at 12 months. When 25 µg/day vitamin D or less was consumed, some subjects reported gastrointestinal discomfort. |

AI, Adequate Intake; BMD, bone mineral density; 25OHD, 25-hydroxyvitamin D; PTH, parathyroid hormone.
D among the targets to prevent micronutrient deficiencies in the region, particularly as the Asian population increases their life expectancy and the risk of osteoporosis increases. In the past, the prevalence of vitamin D deficiency in Southeast Asia was usually not expected to be high, as most vitamin D (80% to 90%) is synthesized in the skin under the action of sunlight [40]. Dermal synthesis through exposure to ultraviolet B is the major natural source of vitamin D in all regions. Increasingly, however, even in countries where the amount of regular sunshine is adequate to achieve recommended vitamin D status, lifestyle changes (fewer outdoor workers, more transportation in covered vehicles) are limiting sun exposure. In addition, in some populations Asian tradition favors avoiding sunlight and people take measures to protect themselves from exposure (long gloves, masks, avoiding exposure between noon and 2 p.m., etc.). In some

### TABLE 4. Contribution of vegetable oil fortified with vitamin D at levels from 7.5 to 10 µg/100 g to the Institute of Medicine (IOM) Estimated Average Requirement (EAR) [20]

<table>
<thead>
<tr>
<th>Target group</th>
<th>Average oil consumption (g/day)</th>
<th>Vitamin D supplied through vegetable oil fortification (µg/day)</th>
<th>% of IOM EAR</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Level 7.5 µg/100 g</td>
<td>Level 10 µg/100 g</td>
</tr>
<tr>
<td>Indonesia</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Women</td>
<td>20.5</td>
<td>1.23</td>
<td>1.64</td>
</tr>
<tr>
<td>Children &lt; 5 yr</td>
<td>17.3</td>
<td>1.04</td>
<td>1.38</td>
</tr>
<tr>
<td>Rich adults</td>
<td>26.0</td>
<td>1.56</td>
<td>2.08</td>
</tr>
<tr>
<td>Poor adults</td>
<td>23.0</td>
<td>1.38</td>
<td>1.84</td>
</tr>
<tr>
<td>Vietnam</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Women of reproductive age</td>
<td>11.1</td>
<td>0.67</td>
<td>0.89</td>
</tr>
<tr>
<td>Children 6–59.9 mo</td>
<td>6.0</td>
<td>0.36</td>
<td>0.48</td>
</tr>
<tr>
<td>China</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adults</td>
<td>25.0</td>
<td>1.50</td>
<td>2.00</td>
</tr>
<tr>
<td>Pregnant women</td>
<td>25.1</td>
<td>1.51</td>
<td>2.01</td>
</tr>
<tr>
<td>Lao People's Democratic Republic</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adults</td>
<td>4.9</td>
<td>0.29</td>
<td>0.39</td>
</tr>
<tr>
<td>Cambodia</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adults</td>
<td>6.6</td>
<td>0.40</td>
<td>0.53</td>
</tr>
<tr>
<td>Philippines</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adults</td>
<td>13.2</td>
<td>0.79</td>
<td>1.06</td>
</tr>
<tr>
<td>Malaysia</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adults</td>
<td>16.1</td>
<td>0.97</td>
<td>1.29</td>
</tr>
<tr>
<td>Imported vegetable oil from Malaysia and Indonesia</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bangladesh</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Breastfeeding women</td>
<td>7.3</td>
<td>0.44</td>
<td>0.58</td>
</tr>
<tr>
<td>Adult women</td>
<td>17.7</td>
<td>1.06</td>
<td>1.42</td>
</tr>
<tr>
<td>Children 4–6 yr</td>
<td>10.5</td>
<td>0.63</td>
<td>0.84</td>
</tr>
<tr>
<td>Children 1–3 yr</td>
<td>8.3</td>
<td>0.50</td>
<td>0.66</td>
</tr>
<tr>
<td>Egypt</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adults</td>
<td>29.3</td>
<td>1.76</td>
<td>2.34</td>
</tr>
<tr>
<td>Ethiopia</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adults</td>
<td>7.1</td>
<td>0.43</td>
<td>0.57</td>
</tr>
<tr>
<td>Afghanistan</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adults</td>
<td>29.8</td>
<td>1.79</td>
<td>2.38</td>
</tr>
</tbody>
</table>

References: Indonesia [53, 54]; Vietnam [37, 38]; Bangladesh [55]; China [56], Malaysia, Cambodia, Ethiopia, and Philippines (data from 2009) [57]; Afghanistan [58]. A 20% loss of vitamin D during processing, storage, and cooking has been assumed [34].
countries, 10% to 20% of vitamin D is acquired from the diet. However, very few unfortified foods contain vitamin D (fatty and oily fish, egg yolk, and fish liver oil are the exceptions), and these are not commonly consumed in most Southeast Asian diets [18]. It is essential to prevent vitamin D deficiency, at least to maintain bone health (while research continues on possible nonskeletal functions of vitamin D) [1]. It is crucial to prevent such deficiency or insufficiency, as low serum 25OHD is significantly associated with low bone mineral density and increased risk of nonvertebral fractures [20] and hip fractures [34]. Evidence on calcium and vitamin D supplementation supports preventive treatment for osteoporosis in adults over 50 years of age [41, 42] and the possibility that calcium and vitamin D supplementation may reduce mortality rates in postmenopausal women. Adequate vitamin D and calcium nutrition throughout life appears to reduce the risk of osteoporosis [43].

The impacts of vitamin D fortification tend to be beneficial, because the majority of studies show positive effects of vitamin D fortification of milk, cheese, bread, margarine, and orange juice on 25OHD concentration. A dose–response relationship can exist between vitamin D dosage and improvement in 25OHD concentration. Recently Black et al. showed a dose–response relationship between vitamin D intake and 25OHD concentration [19]. According to Black et al. [19] and Heaney et al. [19, 44], 1 µg of ingested vitamin D can increase 25OHD concentration by 1 to 1.2 nmol/L. When 10 µg/day or more of vitamin D (1 Adequate Intake [AI]) is used for fortification, the increment in 25OHD concentration can be 10 to 12 nmol/L or more. For example, the fortification level for edible oil could start at 7.5 to 10 µg/100 g, which was suggested as the fortification level for margarine by the international margarine association of the countries of Europe [45]. These levels could contribute to the daily intake of vitamin D, but other interventions will also be needed (supplementation, behavior education on exposure to sunlight, etc.). However, the level of consumption of the oil to be fortified should be taken into account when determining the fortification level. Higher fortification levels should also be considered. A recent review in the United States has proposed a fortification level for vitamin D in edible oil of 42 µg of vitamin D per 100 g of oil [46]. This fortification level would provide 50% or more of the EAR and in some cases 50% of the Dietary Reference Intake (DRI).

Additional foods should also be considered for fortification with vitamin D. Although vitamin D status is significantly affected by seasonality in high latitudes, seasonality may not need to be considered in planning vitamin D fortification programs and determining the dosage of vitamin D in Southeast Asia due to relatively constant sunshine levels.

At present, knowledge of vitamin D deficiency is low among most relevant populations in the region. Better understanding of the regional levels of vitamin D deficiency would help to establish a demand for fortified products. In the meantime, education could be encouraged. During an awareness and knowledge study of osteoporosis in Vietnam, more than 90% of women expressed interest in a prevention and treatment program [47]. Consequently, specific interventions to improve food diversity and quality should be implemented.

Conclusions

The current review and literature search on vitamin D fortification has shown that there are limited data on the impact of vitamin D fortification on 25OHD concentrations. Recent nutrition and health surveys have shown that vitamin D deficiency exists in some Southeast Asian countries. There is a strong need for nationally representative studies in more countries in Southeast Asia. Only Thailand has published a nationally representative study of vitamin D status [5]. The Singapore Health Promotion Board has conducted a national survey, which has not yet been published, and a study in Vietnam has been completed and submitted for publication. With growing understanding of the importance of vitamin D for adequate growth and nutritious diet, it is important that countries start to collect data systematically on vitamin D status in the population. The current study has shown the potential of vitamin D–fortified vegetable oil to increase intakes of vitamin D. Southeast Asian countries where vitamin A fortification of vegetable oil is ongoing should consider adding vitamin D to the fortified oil. Adding vitamin D is easy and feasible; people in Southeast Asia, including children within the 1,000-day window of opportunity, consume substantial amounts of oil; and the oil industry is concentrated in Southeast Asia and their exports have significant potential to reach other vitamin D–deficient regions. In addition to fortification, other interventions should be considered for at-risk populations, such as supplementation and behavior change communication to encourage people to increase exposure to sunlight.

Acknowledgments

This work was funded by the Bill & Melinda Gates Foundation and the Department for International Development. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript. All authors read and approved the final manuscript.
### References