

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^{1–3}

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ABSTRACT

Background: A systematic vitamin D fortification of fluid milk products and fat spreads was started in 2003 in Finland to improve vitamin D status.

Objective: We investigated the effects of the vitamin D fortification policy on vitamin D status in Finland between 2000 and 2011.

Design: Serum 25-hydroxyvitamin D [S-25(OH)D] concentrations of a nationally representative sample comprising 6134 and 4051 adults aged ≥ 30 y from the Health 2000 and Health 2011 surveys, respectively, were standardized according to the Vitamin D Standardization Program with the use of liquid chromatography–tandem mass spectrometry. Linear and logistic regression models were used to assess the change in S-25(OH)D concentrations.

Results: Between 2000 and 2011, the mean S-25(OH)D increased from 48 nmol/L (95% CI: 47, 48 nmol/L) to 65 nmol/L (95% CI: 65, 66 nmol/L) ($P < 0.001$). The prevalence of vitamin D supplement users increased from 11% to 41% ($P < 0.001$). When analyzing the effect of fortification of fluid milk products, we focused on supplement nonusers. The mean increase in S-25(OH)D in daily fluid milk consumers ($n = 1017$) among supplement nonusers was 20 nmol/L (95% CI: 19, 21 nmol/L), which was 6 nmol/L higher than nonconsumers ($n = 229$) (14 nmol/L; 95% CI: 12, 16 nmol/L) ($P < 0.001$). In total, 91% of nonusers who consumed fluid milk products, fat spreads, and fish based on Finnish nutrition recommendations reached S-25(OH)D concentrations > 50 nmol/L in 2011.

Conclusions: The vitamin D status of the Finnish adult population has improved considerably during the time period studied. The increase is mainly explained by food fortification, especially of fluid milk products, and augmented vitamin D supplement use. Other factors, such as the difference in the ultraviolet radiation index between 2000 and 2011, may partly explain the results. When consuming vitamin D sources based on the nutritional recommendations, vitamin D status is sufficient [S-25(OH)D ≥ 50 nmol/L], and supplementation is generally not needed. *Am J Clin Nutr* 2017;105:1512–20.

Keywords: 25-hydroxyvitamin D, general fortification, standardization, vitamin D, population survey

INTRODUCTION

In 2001, Lamberg-Allardt et al. (1) demonstrated a potential public health problem of inadequate vitamin D status (represented as serum 25-hydroxyvitamin D [S-25(OH)D]¹³ < 40 nmol/L) in healthy adults in Finland (1). This inadequacy arose from a combination of a lack of dermal synthesis of vitamin D₃ during the winter because of limited UVB irradiation (2) and low dietary vitamin D intake (1, 3). Several subsequent studies have likewise indicated inadequate vitamin D status in various population subgroups in Finland (4–6).

Because there are only a few good natural dietary sources of vitamin D, fortifying household fat spreads (not butter) with vitamin D was once mandatory but has been voluntary since the 1950s (7). The Finnish National Nutrition Council enacted a

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³ Supplemental Figures 1–3 and Supplemental Table 1 are available from the “Online Supporting Material” link in the online posting of the article and from the same link in the online table of contents at <http://ajcn.nutrition.org>.

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¹³ Abbreviations used: FFQ, food-frequency questionnaire; H2000, Health 2000; H2011, Health 2011; IOM, Institute of Medicine; S-25(OH)D, serum 25-hydroxyvitamin D; VDSP, Vitamin D Standardization Program.

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nutritional policy in 2003 aimed at increasing vitamin D intake by a systematic voluntary fortification of food (8, 9). The recommendation, based on simulations with the use of population food intake data (8), was to add vitamin D to fat spreads at a concentration of 10 $\mu\text{g}/100\text{ g}$, and as a new vitamin D source, all fluid milk products (with the exception of organic products) and respective lactose-free milk-, soy-, and cereal-based drinks were to be fortified at a concentration of 0.5 $\mu\text{g}/100\text{ g}$ (10). With the use of these food fortification measures it was projected that the intake of most of the adult population would reach the previous Nordic vitamin D intake recommendation of 5 $\mu\text{g}/\text{d}$ (11), which was subsequently increased to 7.5 $\mu\text{g}/\text{d}$ in 2005 (12). An investigation of different population subsets showed that vitamin D intake increased after the implementation of the fortification policy in 2003, but in winter 21% of all participants and 33% of those not using vitamin D supplements still had inadequate S-25(OH)D concentrations ($<40\text{ nmol/L}$) (13). In 2010, the recommendation for the fortification concentrations for fluid milk products and fat spreads was doubled based on new simulations (14, 15) (**Supplemental Table 1**). Although data from a recent cross-sectional study in Finland showed that vitamin D status seems to have improved, prospective individual-level data on the effects of food fortification are still lacking (16). Further, the recommendation for vitamin D intake in Nordic countries was increased to 10 $\mu\text{g}/\text{d}$ for adults in 2013 (17).

In this 11-y prospective study we aimed to assess the impact of food fortification on vitamin D nutritional status [including intake and S-25(OH)D concentration] in a nationally representative adult population. The follow-up period reflected the time before (i.e., 2000) and after (i.e., 2011) notable changes in vitamin D food fortification policy. Because the S-25(OH)D concentrations in the Health 2000 (H2000) and Health 2011 (H2011) surveys were analyzed with different methods that could confound the comparison, the results were standardized according to the Vitamin D Standardization Program (VDSP), which aims to promote a measurement of S-25(OH)D that is accurate and comparable over time, location, and laboratory procedure to improve clinical and public health practice worldwide (18, 19).

METHODS

Study populations

This study was based on a nationally representative sample of Finnish adults aged $\geq 30\text{ y}$ from H2000, which was conducted from 2000 to 2001 (20), and its follow-up, H2011, which was conducted from 2011 to 2012 (21). In H2000, a 2-stage stratified cluster sample was drawn from the nationwide population register in Finland. The sample consisted of a total of 9922 members, of whom 8028 were aged $\geq 30\text{ y}$. The survey included questionnaires, interviews, and a comprehensive health examination. The participation rate of the health examination was 85%. All members of the H2000 sample who were alive, living in Finland in 2011, and did not refuse requests to be invited to further studies were invited to participate in H2011 ($n = 7964$). The analyses herein included only those participants for whom S-25(OH)D concentration data were available ($n = 6134$ in H2000, $n = 4051$ in H2011, and $n = 3328$ in both years). The consort diagram for the study is provided in **Supplemental Figure 1**.

H2000 was approved by the Ethical Committee for Research in Epidemiology and Public Health, whereas H2011 was approved by the Coordinating Ethics Committee at the Hospital District of Helsinki and Uusimaa in Finland. The studies were conducted according to the Declaration of Helsinki. Written informed consent was obtained from all participants.

Background characteristics of the survey participants

The survey methodologies were largely the same for H2000 and H2011 (20, 21). Information on age, sex, and region was obtained from the Population Register Centre. Interviews and self-administered questionnaires provided information on sociodemographic background (education and marital status) and lifestyle factors (physical activity and smoking status). A comprehensive health examination included anthropometric and clinical measurements as well as blood sampling. Weight and height were measured in light clothing without shoes, and BMI (in kg/m^2) was also calculated. Obesity was defined as $\text{BMI} \geq 30$ (22).

Measurement of S-25(OH)D

Fasting ($\geq 4\text{ h}$) blood samples drawn as a part of the health examination in both surveys were processed to serum and stored at -70°C until required for analysis. In H2000, the samples were taken from September to March; in H2011, the samples were taken from August to December. In H2000, the proportion of blood samples taken during the winter was higher ($n = 3976$; 65%) than that in H2011 ($n = 1493$; 37%).

In H2000, S-25(OH)D concentrations were analyzed with the use of radioimmunoassay (DiaSorin), whereas in H2011, S-25(OH)D concentrations were analyzed with the use of chemiluminescent immunoassay (Architect ci8200; Abbott Laboratories, Abbott Park, IL). The interassay CVs for the S-25(OH)D concentrations were 7.8% and 3.6% in H2000 and H2011, respectively. As a consequence of the widely accepted method-related differences in S-25(OH)D estimates (18), S-25(OH)D concentrations from both surveys were standardized with the use of VDSP protocol for standardizing S-25(OH)D values from past surveys, as described in detail elsewhere (18, 23), allowing for a more valid comparison of vitamin D status over the 11-y period. The S-25(OH)D concentrations from H2011 were previously standardized (24), and the existing S-25(OH)D concentrations from H2000 (25) were standardized as part of this study according to VDSP protocol. The CDC-certified liquid chromatography–tandem mass spectrometry method was used to reanalyze the specific subsets of both overall survey samples per VDSP protocol (18, 23). In both human serum and plasma, 25(OH)D metabolites have been shown to be stable when stored frozen (26) and when subjected to multiple freeze-thaw cycles (27). In addition, Hollis (28) reported that long-term ($>10\text{ y}$) storage of pooled human 25(OH)D internal controls at -20°C led to no detectable degradation of 25(OH)D, and concentrations of 25(OH)D in frozen serum have been shown to be stable for $\leq 24\text{ y}$ (29).

S-25(OH)D thresholds

The following S-25(OH)D thresholds were prioritized for use in our analysis per Institute of Medicine (IOM) 2011 definitions:

≤30 nmol/L (vitamin D-deficient), 30–49.9 nmol/L (insufficient), and ≥50 nmol/L (sufficient) (30). The Nordic Nutrition Recommendations (17), on which the most recent Finnish recommendations are based (31), also use 50 nmol/L as being consistent with the requirements of 50% of individuals aged >1 y (i.e., the Estimated Average Requirement), and that a sustained S-25(OH)D >125 nmol/L may be some cause for concern has also been discussed (30). Finally, as the Task Force for the Clinical Guidelines Subcommittee of the Endocrine Society has suggested, to maximize the effect of vitamin D on calcium, bone, and muscle metabolism, S-25(OH)D concentrations should exceed 75 nmol/L (32); this is also discussed.

Assessment of dietary vitamin D, categorization by major source, and use of vitamin D supplements

Dietary data were collected by a validated self-administered food-frequency questionnaire (FFQ) designed to estimate mean food intakes over the last 12 mo (33, 34). The FFQ included 128 (H2000) or 131 (H2011) commonly used food items and dishes with specified serving sizes (e.g., glass, slice) or weight or volume measures. The participants recorded their mean consumption of food items and prepared dishes in 9 frequency categories ranging from never or seldom to ≥6 times/d. The mean intakes of vitamin D per day were calculated with the use of the continuously updated National Finnish Food Composition Database (Fineli) (35). The FFQ also included questions on dietary supplements (e.g., single-ingredient vitamin D supplements and multivitamins). The participants were asked whether they had used supplements during the last 12 mo. The regular supplement users were classified as users and those who were not using supplements at all or used them irregularly as nonusers. In the individual-level longitudinal analysis, those participants who were not using supplements regularly in either year were classified as supplement nonusers. In this study, dietary data were available for 91% of the participants in H2000 ($n = 5584$) and 90% of the participants in H2011 ($n = 3635$).

The following definitions were used to categorize participants based on the consumption of the main dietary sources of vitamin D: the daily consumption of fluid milk products, based on frequency categories, as one glass of fluid milk or sour milk products (e.g., low-fat milk or yogurt) ≥1 time/d; the daily consumption of fat spreads as 1 teaspoon of margarines or low-fat spreads (butter and butter-vegetable oil mixture excluded) ≥1 time/d; and 1 portion of fish as a plateful of fish soup or a portion of salmon. The sum of main dietary sources of vitamin D was also calculated based on the daily consumption of fluid milk and fat spreads and fish consumption ≥2 times/wk based on Finnish nutrition recommendations to reach adequate vitamin D intake (31). All components were scored 0–1 (0 = no; 1 = yes) and summed to the total score, which ranged from 0 (lowest) to 3 (highest). Finally, the dietary intake of vitamin D was also categorized in 2 classes based on being above or below a cutoff of 10 μg/d according to Nordic and Finnish nutrition recommendations (17, 31).

Statistical methods

All analyses were carried out with the use of SAS version 9.3 (SAS Institute) and SUDAAN version 11.0.1 (Research Triangle

Institute) and took into account the sampling design. The baseline and updated weights for H2011 were used for the corresponding survey data sets (36). Weighted model-adjusted mean and prevalence estimates were based on predictive margins (37). The joint H2000 and H2011 data were used as a standard population representing the Finnish adult population so that changes of the distribution of confounding factors between H2000 and H2011 did not confound the interpretation of the results.

The weighted prevalences of vitamin D supplement use were analyzed with the use of logistic regression models adjusted for sex and categorical age (30–44, 45–54, 55–64, 65–74, ≥75 y). When analyzing vitamin D intake, the population was stratified by sex. The weighted means of vitamin D intake and prevalences of intake ≥10 μg/d were analyzed with the use of linear and logistic regression models adjusted for categorical age. The contribution of fluid milk products, fat spreads, and fish to the vitamin D intake was calculated as crude values for men and women separately.

Linear and logistic regression models were used to estimate the mean S-25(OH)D concentration and prevalence of insufficiency (<50 nmol/L) and other categories of S-25(OH)D concentration (30), respectively. When analyzing the weighted means and prevalences of S-25(OH)D in categories of sociodemographic and lifestyle factors (**Figure 1**, **Table 1**), the interaction term between the study year and the factor studied was included in the model to calculate the estimates based on the joint data for each year. All analyses were adjusted for sex, categorical age, and month of blood sampling (categorical variable: September through March in the H2000 and August through December in the H2011). Multivariate models included additional sociodemographic and lifestyle factors [living area, (Southern Finland: university hospital regions of Helsinki, Turku and Tampere; Northern Finland: university hospital regions of Kuopio and Oulu), marital status, educational status, BMI, physical inactivity, smoking status].

For the subset of participants with follow-up data on S-25(OH)D, linear regression was used to estimate the weighted mean change (i.e., the difference in S-25(OH)D between H2011 and H2000) in S-25(OH)D concentration at the individual level in

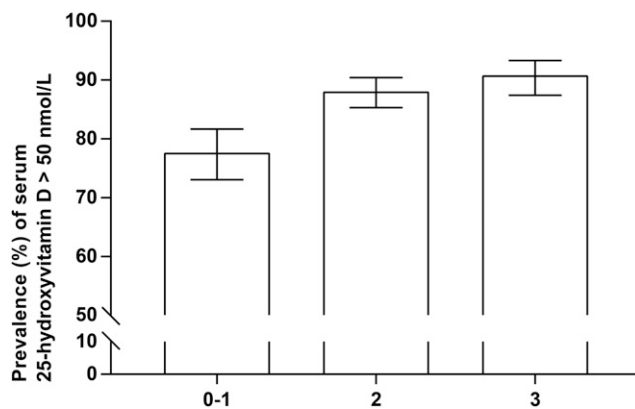


FIGURE 1 The weighted prevalence (95% CI) of Vitamin D Standardization Program-standardized serum 25-hydroxyvitamin D concentration >50 nmol/L in 2011 according to the sum score of the consumed vitamin D sources applied from Finnish nutrition recommendations (fluid milk products daily, fat spreads daily, fish ≥2 times/wk) (31) among supplement nonusers in 2011 (total $n = 2110$; score 0–1, $n = 497$; score 2, $n = 984$; and score 3, $n = 639$). Groups 0 and 1 were combined because of the small number of subjects in group 0. P for heterogeneity <0.001 (Wald F test).

TABLE 1

The VDSP-standardized mean S-25(OH)D concentrations and prevalences of S-25(OH)D <50 nmol/L according to sociodemographic and lifestyle factors for participants from H2000 and H2011¹

| | <i>n</i> | | Mean S-25(OH)D, nmol/L (95% CI) | | Prevalence with S-25(OH)D <50 nmol/L, % (95% CI) | |
|-----------------------------|----------|-------|------------------------------------|----------------------|---|----------------------|
| | H2000 | H2011 | H2000 | H2011 | H2000 | H2011 |
| Sex | | | | | | |
| Men | 2796 | 1811 | 47.6 (47.1, 48.2) | 65.2 (64.6, 65.9) | 54.8 (52.9, 56.8) | 9.4 (7.9, 11.2) |
| Women | 3338 | 2240 | 47.5 (47.0, 48.1) | 65.6 (65.0, 66.3) | 56.5 (54.7, 58.3) | 8.9 (7.5, 10.4) |
| <i>P</i> value | | | 0.81 | 0.35 | 0.17 | 0.59 |
| Age, y | | | | | | |
| 30–44 | 2082 | 895 | 45.5 (44.8, 46.1) | 65.9 (64.9, 66.9) | 62.3 (60.1, 64.4) | 10.0 (7.9, 12.6) |
| 45–54 | 1583 | 963 | 47.7 (47.0, 48.4) | 65.2 (64.3, 66.1) | 56.0 (53.5, 58.5) | 10.3 (8.3, 12.8) |
| 55–64 | 1071 | 1053 | 51.2 (50.3, 52.1) | 65.4 (64.6, 66.2) | 46.2 (43.3, 49.1) | 8.5 (6.7, 10.7) |
| 65–74 | 778 | 774 | 49.7 (48.6, 50.9) | 66.3 (65.5, 67.2) | 49.4 (46.0, 52.8) | 5.1 (3.5, 7.2) |
| ≥75 | 620 | 366 | 43.0 (41.6, 44.4) | 65.1 (63.8, 66.4) | 65.5 (61.4, 69.4) | 9.7 (6.6, 14.2) |
| <i>P</i> value | | | <0.01 | 0.29 | <0.01 | 0.01 |
| Region | | | | | | |
| Southern Finland | 4178 | 2787 | 47.9 (47.4, 48.3) | 65.7 (65.2, 66.3) | 54.9 (53.3, 56.5) | 8.9 (7.7, 10.3) |
| Northern Finland | 1956 | 1264 | 47.0 (46.3, 47.6) | 64.9 (64.1, 65.6) | 57.6 (55.2, 59.8) | 9.5 (7.6, 11.9) |
| <i>P</i> value | | | 0.03 | 0.07 | 0.05 | 0.63 |
| Blood sampling season | | | | | | |
| Other | 2158 | 2558 | 50.6 (50.0, 51.3) | 69.0 (68.5, 69.5) | 49.2 (47.1, 51.4) | 4.8 (4.0, 5.7) |
| Winter | 3976 | 1493 | 44.2 (43.7, 44.6) | 64.9 (64.1, 65.6) | 64.7 (63.1, 66.3) | 11.8 (10.1, 13.8) |
| <i>P</i> value | | | <0.01 | <0.01 | <0.01 | <0.01 |
| Educational status | | | | | | |
| Low | 2413 | 965 | 46.4 (45.7, 47.0) | 64.1 (63.2, 65.0) | 59.3 (57.1, 61.4) | 9.5 (7.4, 12.3) |
| Middle | 1966 | 1387 | 47.6 (46.9, 48.2) | 65.6 (64.8, 66.3) | 56.1 (53.8, 58.3) | 9.0 (7.3, 10.9) |
| High | 1732 | 1652 | 49.3 (48.6, 50.0) | 66.2 (65.5, 66.9) | 50.4 (48.0, 52.8) | 8.6 (7.1, 10.4) |
| <i>P</i> value | | | <0.01 | 0.04 | 0.01 | 0.81 |
| BMI (in kg/m ²) | | | | | | |
| <30 | 4751 | 3085 | 48.4 (47.9, 48.8) | 66.5 (66.0, 67.1) | 53.3 (51.8, 54.8) | 8.4 (7.3, 9.7) |
| ≥30 | 1372 | 960 | 45.0 (44.2, 45.7) | 61.9 (61.1, 62.6) | 63.9 (61.3, 66.5) | 11.6 (9.3, 14.3) |
| <i>P</i> value | | | <0.01 | <0.01 | <0.01 | 0.02 |
| Physical activity | | | | | | |
| Active | 4350 | 2878 | 49.2 (48.7, 49.6) | 66.5 (65.9, 67.0) | 52.1 (50.5, 53.7) | 7.3 (6.2, 8.6) |
| Inactive | 1640 | 1063 | 43.6 (42.9, 44.3) | 63.2 (62.3, 64.0) | 65.6 (63.1, 68.1) | 13.1 (10.9, 15.7) |
| <i>P</i> value | | | <0.01 | <0.01 | <0.01 | <0.01 |
| Current smoker | | | | | | |
| No | 4500 | 3253 | 48.8 (48.4, 49.3) | 66.2 (65.7, 66.7) | 52.7 (51.1, 54.2) | 7.3 (6.2, 8.5) |
| Yes | 1608 | 724 | 44.1 (43.4, 44.9) | 62.7 (61.6, 63.7) | 64.7 (62.2, 67.1) | 15.3 (12.5, 18.6) |
| <i>P</i> value | | | <0.01 | <0.01 | <0.01 | <0.01 |

¹ Weighted means and prevalences were adjusted for age, sex, and month of blood sampling. *P* values were determined with the use of the *t* test or Wald *F* test (based on β -coefficients). H2000, Health 2000; H2011, Health 2011; S-25(OH)D, serum 25-hydroxyvitamin D; VDSP, Vitamin D Standardization Program.

each IOM category of vitamin D status (adjusted for sex, categorical age at baseline, and the change in season of blood sampling). The change in blood sampling season was defined as follows: 1) same season (blood sampling in H2011 within the same month or ≤ 1 mo earlier or later than in H2000; $n = 1762$), 2) different season (blood sampling in H2011 ≥ 2 mo earlier or later than in H2000; $n = 1566$).

To study the effects of food fortification of specific foodstuffs, the subpopulation of vitamin D supplement nonusers was used. First, it was categorized according to the use of fluid milk products. Those who consumed fluid milk products daily both in H2000 and in H2011 were categorized as consumers, and those who did not consume fluid milk products in either survey were categorized as nonconsumers; those who had changed their consumption of fluid milk products (i.e., had started or stopped between the surveys) were excluded from the analyses. Second, similar categorizations were created according to the use of fat spreads. When estimating the weighted means and weighted mean changes of S-25(OH)D concentrations, linear regression models were adjusted for sex, categorical age and categorical age at baseline, categorical month of blood sampling and change in season of blood sampling, fish consumption in H2000 and H2011, and fat spread consumption in H2000 and H2011 or fluid milk product consumption in H2000 and H2011.

Differences between groups were assessed with the use of the *t* test (binary variables) or Wald *F* test. $P < 0.05$ was considered statistically significant.

RESULTS

Total population vitamin D status findings in H2000 and H2011

In H2011, the mean age of the participants was 56 y, and 55% of the participants were women (Table 1). Approximately 25% of the participants were obese, and 33% were physically inactive. The participants in H2011 were more educated and smoked less than those in H2000. In H2000, 65% of the blood samples were taken during the winter, whereas the equivalent proportion was 37% in H2011 (Supplemental Figure 2).

The prevalence of vitamin D supplement use was higher in H2011 (41%; 95% CI: 39%, 42%) than in H2000 (11%; 95% CI: 11%, 12%) ($P < 0.001$ for differences between years). In H2011, women (51%) and highly educated (46%) participants were more likely to use supplements than men (31%) and participants with the lowest educational status (36%). Supplement use was more common in the older age groups; $\sim 50\%$ of the participants aged ≥ 65 y used supplements, whereas the proportion was $\sim 40\%$ in participants aged 30–54 y.

In H2011, mean vitamin D intake from diet alone was almost twice as high (men, 14 $\mu\text{g}/\text{d}$; 95% CI: 14, 15 $\mu\text{g}/\text{d}$) (women, 12 $\mu\text{g}/\text{d}$; 95% CI: 11, 12 $\mu\text{g}/\text{d}$) than in H2000 (men and women, 7 $\mu\text{g}/\text{d}$; 95% CI: 7, 7 $\mu\text{g}/\text{d}$) ($P < 0.001$ for differences between years), and 74% of men and 58% of women reached the vitamin D recommendation (≥ 10 $\mu\text{g}/\text{d}$) from diet alone (17, 31). In H2011, fluid milk products, fat spreads, and fish contributed 34%, 10%, and 38%, respectively, to the vitamin D dietary intake for both men and women, whereas in H2000, the corresponding proportions were 4%, 9%, and 57%, respectively.

In H2011, the VDSP-standardized mean S-25(OH)D concentration was 65 nmol/L, which was 18 nmol/L higher than in

H2000 ($P < 0.001$ for differences between years) (Table 2). This difference was similar over the months studied (Supplemental Figure 3). Furthermore, 9% of the population had insufficient S-25(OH)D concentrations (< 50 nmol/L) in H2011, whereas the prevalence was 56% in H2000. The same pattern was seen when cutoffs of < 40 and < 30 nmol/L were applied. None of the participants in H2000 and only 8 participants in H2011 (of whom only 1 was a supplement nonuser) had S-25(OH)D concentrations > 125 nmol/L. Although sociodemographic differences in S-25(OH)D concentrations were slightly narrowed between H2000 and H2011, the participants with an unhealthy lifestyle (obese, physically inactive, and current smoker) had still lower S-25(OH)D concentrations than those with a healthy lifestyle (Table 1). However, in H2011, most participants with an unhealthy lifestyle still reached sufficient S-25(OH)D concentrations (≥ 50 nmol/L). Adjusting the analysis additionally for other sociodemographic and lifestyle factors did not change the interpretation of the results, except the differences between educational groups narrowed (data not shown).

Supplement nonusers

The proportion of women was lower among supplement nonusers in H2011 (48%) than in H2000 (53%). Vitamin D intake

TABLE 2

The VDSP-standardized mean S-25(OH)D concentrations and prevalences according to different cutoffs for participants from H2000 and H2011¹

| | Total population | | Supplement nonusers | |
|---|----------------------|----------------------|----------------------|----------------------|
| | H2000 | H2011 | H2000 | H2011 |
| Total | | | | |
| <i>n</i> | 6134 | 4051 | 4956 | 2110 |
| Mean, nmol/L | 47.6 (47.2, 48.0) | 65.4 (65.0, 65.9) | 46.9 (46.5, 47.4) | 61.7 (61.1, 62.3) |
| <30 nmol/L | | | | |
| <i>n</i> | 930 | 17 | 775 | 13 |
| Prevalence, ² % | 13.0 (12.2, 13.8) | 0.6 (0.3, 0.9) | 13.7 (12.8, 14.7) | 0.9 (0.5, 1.6) |
| <40 nmol/L | | | | |
| <i>n</i> | 2230 | 90 | 1881 | 66 |
| Prevalence, % | 32.0 (30.8, 33.2) | 3.2 (2.6, 4.0) | 34.2 (32.8, 35.6) | 5.0 (3.9, 6.5) |
| <50 nmol/L | | | | |
| <i>n</i> | 3729 | 264 | 3119 | 190 |
| Prevalence, % | 55.7 (54.3, 57.1) | 9.1 (8.1, 10.3) | 58.5 (57.1, 60.0) | 13.7 (11.9, 15.7) |
| ≥ 75 nmol/L | | | | |
| <i>n</i> | 212 | 983 | 154 | 376 |
| Prevalence, % | 4.1 (3.6, 4.8) | 19.9 (18.5, 21.3) | 3.8 (3.3, 4.5) | 12.6 (11.2, 14.1) |
| ≥ 125 nmol/L³ | | | | |
| <i>n</i> | 0 | 8 | 0 | 1 |

¹All values in parentheses are 95% CIs. Weighted means and prevalences of S-25(OH)D were adjusted for age, sex, and month of blood sampling. *P* values were determined with the use of the Wald *F* test ($P < 0.001$ for differences between H2000 and H2011 for all means and prevalences). H2000, Health 2000; H2011, Health 2011; S-25(OH)D, serum 25-hydroxyvitamin D; VDSP, Vitamin D Standardization Program.

²Exceptionally adjusted with the use of continuous variables for month of blood sampling (based on predictive margins).

³Prevalences could not be analyzed because of the limited number of participants.

from food was almost the same as seen in the total population: 14 $\mu\text{g}/\text{d}$ (95% CI: 14, 14 $\mu\text{g}/\text{d}$) in men and 11 $\mu\text{g}/\text{d}$ (95% CI: 11, 12 $\mu\text{g}/\text{d}$) in women. Furthermore, 71% of men and 55% of women reached a vitamin D intake ≥ 10 $\mu\text{g}/\text{d}$.

The VDSP-standardized mean S-25(OH)D concentration was 62 nmol/L in H2011, which was 15 nmol/L higher than in H2000 (47 nmol/L) (Table 2). A total of 14% of supplement nonusers had insufficient S-25(OH)D concentrations (< 50 nmol/L) in H2011, whereas the prevalence was 59% in H2000. There were also considerable declines over the 11-y follow-up in the prevalences of participants who had S-25(OH)D concentrations < 30 and < 40 nmol/L. In all, 91% of those who consumed the main dietary sources of vitamin D (i.e., fish consumption ≥ 2 times/wk and daily use of fluid milk products and fat spreads) reached a sufficient S-25(OH)D concentration in H2011 (Figure 1).

Individual-level prospective changes in vitamin D status over the 11 y

In the total population, the VDSP-standardized S-25(OH)D concentrations improved the most (~ 34 nmol/L) in participants with vitamin D deficiency (< 30 nmol/L) and the least (~ 11 nmol/L) in participants with adequate (≥ 50 nmol/L) S-25(OH)D concentrations at baseline (Figure 2). The same pattern was observed in the subpopulation of supplement nonusers.

The effect of food fortification with vitamin D on the VDSP-standardized S-25(OH)D concentrations was analyzed in the subpopulation of supplement nonusers. Among those who consumed fluid milk products daily both at baseline and at follow-up ($n = 1017$), the mean change was 20 nmol/L (95% CI: 19, 21 nmol/L), which was 6 nmol/L higher than milk nonconsumers ($n = 229$) ($P < 0.001$). In H2011, milk consumers had 5 nmol/L higher VDSP-standardized mean S-25(OH)D concentrations than did nonconsumers (Figure 3). Those who consumed fat spreads daily ($n = 558$) had higher VDSP-standardized mean S-25(OH)D concentrations in H2000 (49 nmol/L; 95% CI: 48, 51 nmol/L) than did nonconsumers ($n = 436$) (44 nmol/L; 95% CI: 43, 45 nmol/L) ($P < 0.001$). The mean change in S-25(OH)D concentrations among daily fat spread consumers was 5 nmol/L lower than among nonconsumers, and in H2011 there was no difference in the mean VDSP-standardized S-25(OH)D concentration between the groups (65 nmol/L; 95% CI: 64, 66 nmol/L vs. 65 nmol/L; 95% CI: 64, 66 nmol/L) ($P = 0.79$).

DISCUSSION

Major findings

This investigation of the temporal changes in vitamin D status in the Finnish adult population with the use of standardized S-25(OH)D concentrations showed considerable improvements in vitamin D status in both men and women and provides, to our knowledge, the first prospective evidence at the population level of the benefits of the vitamin D food fortification policy. In H2011, 97% and 91% of the study population reached standardized S-25(OH)D concentrations of > 40 and > 50 nmol/L (30), respectively, whereas the equivalent proportions in H2000 were 68% and 44%, respectively. The application of the VDSP standardization protocol (18) was important in this study in that it minimized the well-reported method-related differences in

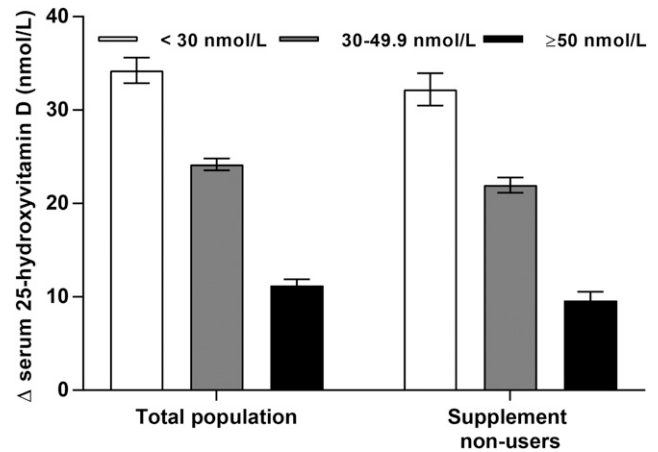


FIGURE 2 Change (Δ) in the longitudinal weighted mean (95% CI) of the Vitamin D Standardization Program–standardized serum 25-hydroxyvitamin D concentration between 2000 and 2011 according to the baseline serum 25-hydroxyvitamin D concentration (adjusted for categorical age, sex, and change in blood sampling season) stratified by supplement use. The number of subjects according to the baseline concentration was as follows: total population, $n = 3328$; supplement nonusers, $n = 1578$; < 30 nmol/L, $n = 381$; 30–49.9 nmol/L, $n = 1507$; ≥ 50 nmol/L, $n = 1440$; and missing dietary data, $n = 422$. P for heterogeneity between the groups < 0.001 in total population and supplement nonusers (Wald F test).

S-25(OH)D estimates (38) and allowed for a more meaningful comparison of temporal changes in vitamin D status and the possible impact of food fortification with vitamin D status. The validity of the VDSP protocol for standardizing S-25(OH)D values from past surveys was demonstrated in the Irish National Adult Nutrition Survey (39). The application of the VDSP protocol projected a prevalence of 11.4%. The entire Irish National Adult Nutrition Survey biobank was reanalyzed with the use of a certified liquid chromatography–tandem mass spectrometry method and confirmed the true prevalence estimate as 11.2%, which was almost twice as high as the original immunoassay-based estimate and almost identical to the VDSP projection (39).

The increased uptake of vitamin D supplement use in Finland over the decade (from 11% to 41%) would have contributed to the improved vitamin D status. This is explained, for example, by the changes in supplementation recommendations (12). Of interest, Schleicher et al. (40) in their temporal trend analysis of S-25(OH)D in US NHANES participants aged ≥ 12 y showed that although there was no time trend from 1988 to 2006, from 2007 to 2010 mean S-25(OH)D increased by 5–6 nmol/L. The authors suggested that this increase in status coincided with a time during which there was a noted increase in the use of supplements containing higher amounts of vitamin D. It is also worth noting that there was no time trend among supplement nonusers (40). By selecting out the supplement nonusers in this combined data set, we have shown that the nutritional policy recommendations of voluntary vitamin D fortification of certain foods has had an independent positive impact on the population's S-25(OH)D status. Furthermore, this work showed that among those with only dietary vitamin D intake, the proportion of standardized S-25(OH)D < 40 nmol/L [a concentration underpinning the IOM's Estimated Average Requirement of 10 $\mu\text{g}/\text{d}$ (30) and a benchmark of the degree of inadequacy in the population] decreased from $\sim 33\%$ in H2000 to 5% in H2011.

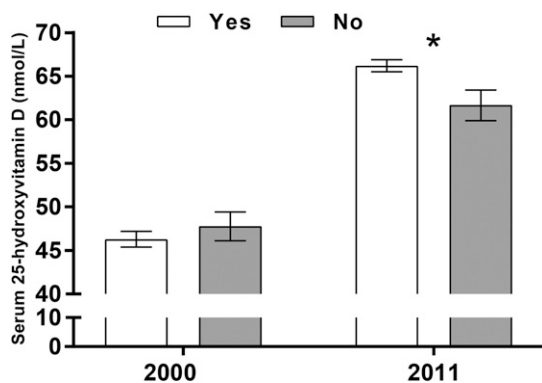


FIGURE 3 The weighted mean (95% CI) of the Vitamin D Standardization Program—standardized serum 25-hydroxyvitamin D concentration between 2000 and 2011 among supplement nonusers according to the daily consumption of fluid milk products (subjects with unchanged fluid milk consumption habits between 2000 and 2011: fluid milk consumers, $n = 1017$; nonconsumers, $n = 229$) (adjusted for categorical age, sex, month of blood sampling, fish consumption in 2000 and 2011, and fat spread consumption in 2000 and 2011). P values for heterogeneity were determined with the use of the Wald F test ($*P < 0.001$).

To our knowledge, this is the first prospective study based on nationally representative data that has evaluated the effects of food fortification with vitamin D on S-25(OH)D concentration in the general population. The impact of fortification was recently evaluated based on 3 independent cross-sectional population samples in Finland in 2002, 2007, and 2012 (16). Our results support the findings therein that both vitamin D intake and S-25(OH)D concentrations improved after fortification policy actions. However, the results we obtained with the use of prospective data give more sophisticated evidence on the effect of fortification. Our S-25(OH)D results were standardized, and we analyzed the effect of specific foodstuffs on the change in S-25(OH)D at the individual level. Furthermore, these population-level findings extend the positive effect of food fortification with vitamin D on the S-25(OH)D concentrations reported in earlier, generally small randomized controlled trials (41–43).

Further investigation of the impact of vitamin D–fortified foods on improving population vitamin D status

A considerable increase in the contribution of fluid milk to vitamin D intake between H2000 and H2011 was demonstrated because vitamin D–fortified fluid milk products were introduced as a novel vitamin D source in Finland during the study period (10). Thus, as we hypothesized, we found that when focusing on supplement nonusers the mean increase in S-25(OH)D was 6 nmol/L higher among those who consumed fluid milk products daily than among milk nonconsumers, suggesting the success of a fortification policy. In daily fat spread consumers, however, the mean change in S-25(OH)D was lower than among nonconsumers. This is explained by the fact that, in contrast to fluid milk products, fat spreads were already a substantial source of vitamin D in H2000 because they were recommended to be fortified with 5–10 μg vitamin D/100 g before systematic fortification started in 2003 (44). As a result, fat spread consumers had substantially higher S-25(OH)D concentrations in H2000 than did nonconsumers. Moreover, by the time of the follow-up (in H2011), some fat spread manufacturers had not increased their concentration of vitamin D fortification to 20 μg /100 g,

despite the new fortification recommendations from the preceding year. Thus, there are some uncertainties concerning the vitamin D contents of the fat spreads in both years, and most likely the effect of fat spread fortification on S-25(OH)D cannot be properly evaluated with the use of this time period. However, the contribution of fat spreads to dietary vitamin D intake remained similar in H2000 and H2011, showing the significance of fat spreads as a vitamin D source. It is important to note that these data also show that when fluid milks and fat spreads were combined with fish consumption into an overall dietary vitamin D score, $\geq 90\%$ of those with the highest score and thus most compliant with Finnish nutrition recommendations (31) had S-25(OH)D concentrations > 50 nmol/L, whereas the prevalence was considerably lower among low or nonconsumers of fortified foods and fish.

Methodologic issues

Interestingly, we found that a part of the increase in S-25(OH)D (~ 10 nmol/L) that has occurred over the period cannot be explained either by fortification or by the increased use of vitamin D supplements. One explanation is that there was a difference in UVB availability between the years that we could not take into account in the analysis—the mean UV radiation index in Southern Finland from June to August 2011 was 18% higher than during the same period in 2000 (45, 46). We did not have data on sunbed use or sunny vacations, but generally the amount of vacations spent abroad has increased during the follow-up period (47). At the same time, however, there probably have been some changes in the sunbathing habits and sunscreen use because of the growing awareness of skin cancer risk. In addition, the other vitamin D–fortified foodstuffs may have some role in vitamin D intake, but on the population level it must have been marginal in 2011, as only single products from food groups other than fluid milks and fat spreads were available (48). Furthermore, there are some methodologic problems that may partly explain the observed increase in S-25(OH)D concentrations. Although the data were adjusted for the month in which the blood samples were taken, the blood samples of only 53% of the participants had been taken in the same season in H2000 and H2011. This may partly explain the observed increase in the S-25(OH)D concentrations because in H2011 higher proportions of the blood samples were drawn closer to summer than in 2000. Furthermore, the irregular supplement users were classified into the nonuser group, which may have slightly increased vitamin D intake and positively contributed to the S-25(OH)D concentrations in this group. In addition to the previously mentioned factors, there might have been some other residual confounding that we have not been able to define. In addition, one limitation of our study is that the participation rates were lower in H2011 than in H2000, especially among men, those in younger age groups, and those with a lower educational status (36). To handle the missing data, we used both baseline and updated H2011 weights, which take into account the increased nonparticipation (36).

This study has many strengths. First, the results are based on a nationally representative sample of the Finnish adult population. Because of the prospective study design, we could uniquely compare the vitamin D status of the Finnish population before and after vitamin D food fortification. The study population was

studied at 2 time points with similar reliable methods (20, 21), and the dietary data were based on the same validated FFQ (33, 34). The S-25(OH)D data, which arose from the 2 different assays used, were standardized with the use of the VDSP protocols, allowing for more valid comparisons of changes over time (24). If the S-25(OH)D data sets had not been standardized, the mean increase in S-25(OH)D concentration over the 11-y period would have been 10 nmol/L higher, leading to a biased interpretation of the results (24).

In conclusion, the vitamin D status of the Finnish adult population has improved substantially during the time period studied. The increase is mainly explained by food fortification, especially of fluid milk products and augmented vitamin D supplement use. However, other factors, such as differences in the UVB irradiation index between 2000 and 2011, also partly explain the results. It is also noteworthy that the data suggest that when the nutritional recommendations pertaining to vitamin D intake are followed, vitamin D status is sufficient [S-25(OH)D \geq 50 nmol/L], and vitamin D supplementation is generally not needed.

The authors' responsibilities were as follows—AL and SM: conceived the studies; TJ, STI, AL, ME, HK, JK, EK, SM, and CL-A: contributed to the study design; KGD, GLJH, and KDC: standardized the S-25(OH)D data; TJ: carried out the statistical analysis with input from AL, TH, and SM; TK and KL: interpreted the UVB data; STI: wrote the initial draft with input from TJ; CL-A: had primary responsibility for the final content; and all authors: read and approved the final manuscript. None of the authors reported a conflict of interest related to the study.

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