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A Novel Approach to Optimize Vitamin D Intake in Belgium through Fortification Based on Representative Food Consumption Data

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ABSTRACT

Background: Food fortification is a promising means to improve vitamin D intake of a population. Careful selection of food vehicles is needed to ensure that nearly all individuals within the population benefit from the fortification program.

Objectives: The aim of the study was to develop and apply a model that simultaneously selects the optimal combination of food vehicles and defines the optimal fortification level that adequately increases vitamin D intake in the population without compromising safety.

Methods: Food consumption data from the Belgian Food Consumption Survey 2014 ($n = 3200$; age 3–64 y) were used. The optimization model included 63 combinations of 6 potential vehicles for food fortification, namely "bread," "breakfast cereals," "fats and oils," "fruit juices," "milk and milk beverages," and "yogurt and cream cheese." The optimization procedure was designed to minimize inadequate or excessive vitamin D intake in each of the food combinations. This allowed the relative ranking of the different combinations according to their fortification utility. The estimated average requirement and upper intake level were used as thresholds. An age-specific and population-based approach enabled the sensitivity of the population subgroups to adverse health effects to be taken into account. Feasibility, technical aspects, and healthiness of the food vehicles were used to select the optimal combination.

Results: Multiple combinations of food vehicles significantly reduced the prevalence of inadequate vitamin D intake within the Belgian population (from 92–96% to <2%). Taking other aforementioned criteria into account, the fortification of "milk and milk beverages" and "bread" with 6.9 μg vitamin D/100 kcal was proposed as an optimal fortification scenario.

Conclusions: The optimization model allows identification of an effective fortification scenario to improve vitamin D intake within the Belgian population based on acceptable risks of inadequate and excessive intake. The model can be extended to other micronutrients and other populations. *J Nutr* 2019;149:1852–1862.

Keywords: vitamin D intake, fortification, optimization model, inadequate intake, excessive intake

Introduction

Vitamin D deficiency is ubiquitous in Europe at a prevalence that is considered pandemic (1). From a public health perspective the treatment and prevention of vitamin D deficiency is considered an important goal in nutrition policy (1, 2). At northern latitudes, where environmental factors impede year-round dermal synthesis, people rely on bodily storage and dietary sources to maintain a sufficient vitamin D status all year round (3).

In Belgium, the median vitamin D intake from all sources (i.e., food, fortified foods, and supplements) is typically low and varies from 3.8 to 4.6 μg/d (**Supplemental Table 1**). Currently in Belgium some brands of milk, milk substitutes, dairy desserts, cereals, biscuits, chocolate powder, and fruit juices are voluntarily fortified with vitamin D whereas margarines and spreadable fats are mandatorily fortified with vitamin D (6.5–7.5 μg/d) (4). Supplements of 10 μg/d are recommended for children from birth until the age of 6 y. From 7 y onwards a supplement of 10–15 μg/d is recommended in case of limited sun-exposure (5). However, only 25% of the Belgian population consumes a vitamin-D–containing supplement (4).

Considering the low vitamin D intake from dietary sources and the northerly latitude of Belgium, there is a concern for vitamin D deficiency in Belgium, especially for people with limited sun exposure (4).

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National food fortification programs offer a promising means for improving vitamin D intake at a population level and preventing vitamin D deficiency (3). Design of an effective fortification program requires determination of the extent to which vitamin D intake needs to be increased and which foods need to be fortified to attain adequate vitamin D intake for almost the entire population without risk of excessive intake (6).

Dietary reference values (DRVs) provide a framework for the modeling of an effective fortification program (7). Despite the use of similar risk assessment protocols, the DRVs for vitamin D established by several expert authorities differ greatly by type as well as by value (8, 9).

The Belgian Superior Health Council uses an Adequate Intake (AI) as reference value for vitamin D (5). However, an AI does not allow estimation of the prevalence of inadequate intake of a nutrient because the relation to the requirement of the nutrient is unknown. The prevalence of inadequate and excessive vitamin D intake can be estimated using the proportion of the population with vitamin D intake below the estimated average requirement (EAR) and above the upper intake level (UL), respectively (10, 11).

Following the WHO guidelines, the goal of food fortification is to provide most (97.5%) individuals within a population (sub)group at risk for deficiency with an adequate micronutrient intake without increased risk of excessive intake (12). Randomized controlled trials (RCTs) of food fortification have demonstrated the possibilities of different food vehicles for effectively improving vitamin D intake and status (12–16). However, these trials highlight the need to account for the diversity in food consumption patterns and call for the selection of food vehicles based on representative food consumption data (14, 17). Fortifying specific food items such as dairy products that are consumed by only a proportion of the population will not increase vitamin D intake in non- or low-consumers (14). Instead, fortification of a broader range of foods, in particular staple foods, has proven to be more effective (3, 18, 19).

Current fortification models as presented by Hirvonen et al. (20) have focused on estimating the optimal fortification level by which vitamin D intake could be improved without risk of excessive vitamin D intake. The optimal fortification level is estimated by plotting the proportion of the population with vitamin D intake between the recommended intake and the UL for different fortification levels. The choice of the food vehicle is based on evidence of its potential to increase vitamin D status (20). Likewise, the Intake Modelling, Assessment and Planning Program (IMAPP) software allows calculation of the prevalence of inadequate and excessive intake of a nutrient for a given food vehicle and fortification level (21). The model presented here allows both the selection of an optimal fortification level and the selection of an optimal combination of food vehicles by which the majority of the population could be reached. The model is based on reliable and representative national food consumption data reflecting the differing consumption patterns within the population. Additionally, the optimization process is more efficiently implemented by using dedicated optimization algorithms.

The model was applied to the vitamin D intake of the Belgian population (ages 3–64 y) (4). The optimization procedure was performed by comparing age-specific and population-based approaches. These different approaches allow weighing the risk for adverse health effects depending on the sensitivities of different population subgroups to adverse health effects of the nutrient when consumed in inadequate or excessive amounts (22). Additionally, scenarios are presented using different DRVs. The proposed methodology could be useful to design national fortification programs for other micronutrients based on representative national food consumption data.

Sciensano initiated the Belgian study on the intake of vitamins A, D, E, and K (VITADEK). The study was carried out in collaboration with the Department of Food Safety and Food Quality, Ghent University. The Belgian Federal Public Service Health, Food Chain Safety, and Environment financed the study.

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Supplemental Table 1 and Supplemental Figures 1–4 are available from the "Supplementary data" link in the online posting of the article and from the same link in the online table of contents at https://academic.oup.com/jn/.

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Abbreviations used: AI, Adequate Intake; BC, "breakfast cereals"; BR, "bread"; DRV, dietary reference value; EAR, estimated average requirement; EFSA, European Food Safety Authority; FJ, "fruit juices"; FO, "fats and oils"; FPQ, food propensity questionnaire; MB, "milk and milk beverages"; NAM, National Academy of Medicine; P50, 50th percentile; RCT, randomized controlled trial; SPADE, statistical program to assess dietary exposure; UL, upper intake level; YF, "yogurt and cream cheese"; 25(OH)D, 25-hydroxyvitamin D.

Methods

Food consumption and composition data

Dietary intake data of the general Belgian population (n = 3200; ages 3–64 y) were retrieved from the Belgian national food consumption survey (4, 23). The methodology has been described in Bel et al. (23). In brief, a representative sample of the Belgian population was randomly selected from the National Population Register according to a multistage stratified sampling procedure. Food consumption data in adolescents and adults (ages 10–64 y) were collected using 2 face-to-face 24-h recalls on nonconsecutive days (with an interval of 2–4 wk) and a self-administered food propensity questionnaire (FPQ). Data in children (ages 3–9 y) were collected through the proxy respondent (i.e., a parent or legal guardian) by means of 2 nonconsecutive 1-d food diaries, a completion interview by a dietician, and a self-administered FPQ. The FPQ comprised questions concerning the consumption of food supplements in the last year. The interviews were equally divided between all weekdays and seasons to account for day-to-day and seasonal variations (23).

The consumed food items were linked with food composition data of Nubel (a Belgian food composition table) (24) and NEVO-online (a Dutch food composition table) (25), allowing the computation of vitamin D intake. In case of missing vitamin D values, 4 other food composition tables were used in the following order: *1*) McCance and Widdowson's UK food composition table (26); *2*) Ciqual, the French composition table (27); *3*) the Danish food composition table (28); and *4*) the US food composition table (29).

Optimization model

An optimization model was developed to determine the optimal fortification scenario, that is, the optimal combination of food vehicles and related vitamin D fortification level that would result in minimal prevalence of inadequate and excessive vitamin D intakes for the Belgian population. The optimization procedure was applied to all possible combinations of 6 specific food groups that RCTs have previously shown to be effective in improving vitamin D status, namely breakfast cereals (BC), bread (BR), fruit juices (FJ), fats and oils (FO), milk and milk beverages (MB), and yogurt and cream cheese (YF) (13, 14, 16, 30). These 6 food groups resulted in 63 unique combinations of food vehicles including one (6), two (15), three (20), four (15), five (6), or all six (1) food groups.

For each of the 63 combinations, the "baseline" vitamin D intake (μg/d) was calculated, that is, the vitamin D intake from all food groups excluding the food groups in the combination under assessment. In addition, the total energy consumption (kcal/d) for the food groups in the combination was calculated. We then applied optimization models to find the fortification level (μg/kcal) for the food groups in the combination that would lead to the lowest prevalence of inadequate and excessive vitamin D intake for the Belgian population. Next, the food group combinations were ranked according to their fortification utility and their potential for reducing inadequate and excessive vitamin D intake.

Habitual intake modeling.

For each of the 63 combinations, we calculated, per individual, the corresponding vitamin D intake levels (μg/d) from the baseline comprising the consumed foods, fortified foods, and supplements except the foods from the combination under assessment. For instance, the baseline corresponding with the combination "BCBR" (i.e., breakfast cereals and bread), included all foods, fortified foods, and supplements excluding breakfast cereals and bread. Other foods that are currently fortified with vitamin D such as fortified milk and soy drinks, were thus included in the baseline and their vitamin D fortification level was kept constant. We also calculated the total energy consumed (kcal/d) per individual of the foods in the combination.

Next, the habitual vitamin D intake from the baseline, as well as the habitual energy consumption of the food group(s) under assessment, were modeled in SPADE (statistical program to assess dietary exposure) (31). We used the multipart model of SPADE, which estimates the habitual intake distribution from different sources by means of a first-shrink-then-add method. This method accounts for the specific challenges such as within-person variability, the heterogeneity in variances related to differing intakes from the different sources (daily compared with episodic), and the discrete distribution from supplements (31, 32). The energy consumption patterns per age group for each of the single food groups were plotted (**Supplemental Figure 1**).

For both models, the results were exported for further use as a set of "pseudo-persons" (i.e., random realizations of the model), each with a given age and a specific intake level that reflects the between-person variability in habitual intakes. Formally, SPADE allows generating for each respondent $i = 1, \ldots, m$, with age a_i and survey weight w_i, a set of $n_i = 100\, w_i$ pseudo-persons as random realizations from a normal (h_a, σ_b^2) distribution, with h_a the estimated age-specific habitual intake and σ_b^2 the estimated between-person variance. Because SPADE performs a Box–Cox transformation of the observations to address nonnormality, these random realizations are in a final step back-transformed to the original scale.

For each pseudo-person $i(j)$, $i = 1, \ldots, m$, $j = 1, \ldots, n_i$, we calculated the total daily vitamin D intake $t_{i(j)}$ (μg/d) by combining the daily baseline vitamin D intake $b_{i(j)}$ (μg/d) with the daily energy consumption of fortified foods $c_{i(j)}$ (kcal/d) and a given fortification level f (μg/kcal):

$$t_{i(j)} = b_{i(j)} + c_{i(j)}\, f \qquad (1)$$

By calculating total vitamin D intake for each pseudo-person, the between-person variability in baseline vitamin D intake and in energy consumption levels was retained and propagated. No correlation was assumed to exist between the daily baseline vitamin D intake and the daily energy consumption from foods in the concerned combination.

Evaluation of inadequate and excessive intakes.

To evaluate inadequate vitamin D intake, age-group–specific EAR reference values were used. The EAR allows a quantitative estimation of the prevalence of inadequate vitamin D intake at the population level by means of the EAR cutoff method. Two different cutoff values were used: the EAR of the National Academy of Medicine (NAM) (10 μg/d) and the EAR of NNR (Nordic Nutrition Recommendations) (7.5 μg/d) (33, 34). For each pseudo-person $i(j)$, the EAR allowed determination of whether or not the individual total vitamin D intake was inadequate: $d_{i(j)} = I(t_{i(j)} < EAR_{a_i})$. The overall prevalence of inadequate intakes $\bar{d}$ could then be obtained as the average of the $d_{i(j)}$ indicators:

$$\bar{d} = \frac{1}{\sum_{i=1}^{m} n_i} \sum_{i=1}^{m} \sum_{j=1}^{n_i} d_{i(j)} \qquad (2)$$

Likewise, the prevalence of inadequate intakes $\bar{d}(A)$ in a specific age-group A could be obtained for all $i(j)$ for which $a_i \in A$. The sum of the age-group–specific prevalences for K age groups A_k, $k = 1, \ldots, K$, was then given by:

$$\delta = \sum_k \bar{d}(A_k) \qquad (3)$$

To evaluate excessive vitamin D intake, the European Food Safety Authority (EFSA) ULs of 50 μg/d for children aged 1–10 y and 100 μg/d for individuals aged ≥11 y were used (13). For each pseudo-person $i(j)$, the UL allowed determination of whether or not the individual total vitamin D intake was excessive: $e_{i(j)} = I(t_{i(j)} > UL_{a_i})$. The overall prevalence of excessive intakes $\bar{e}$ could then be obtained as the average of the $e_{i(j)}$ indicators:

$$\bar{e} = \frac{1}{\sum_{i=1}^{m} n_i} \sum_{i=1}^{m} \sum_{j=1}^{n_i} e_{i(j)} \qquad (4)$$

Likewise, the prevalence of excessive intakes $\bar{e}(A)$ in a specific age group A could be obtained for all $i(j)$ for which $a_i \in A$. The sum of age-group–specific prevalences for K age groups A_k, $k = 1, \ldots, K$, was then given by:

$$\epsilon = \sum_k \bar{e}(A_k) \qquad (5)$$

Optimization criteria.

The optimal fortification level f_{opt} was determined as the fortification level f for which the prevalence of inadequate (percentage < EAR) and excessive (percentage > UL) vitamin D intake was minimized. We defined criteria at age-group and at population level. At the age-group level, we aimed to minimize the sum of the age-group–specific prevalence of inadequate and excessive intakes, that is, $\delta + \epsilon$. At the population level, we aimed to minimize the sum of the overall prevalence of inadequate and excessive intakes, that is, $\bar{d} + \bar{e}$.

In a scenario analysis, we also explored the use of the AI level as an optimization criterion. The evaluation with an AI is a qualitative evaluation: if the median vitamin D intake of the population is greater than the AI, the prevalence of inadequate intake of vitamin D can be stated as low; otherwise, no statement can be formulated. As determined by the EFSA, the AI for vitamin D is the same for children and adults, that is, 15 μg/d (35). In our optimization process, we sought to minimize the absolute distance between the AI and the P50 (50th percentile) of the total vitamin D habitual intakes. This procedure was also implemented at age-group and at population levels.

All optimization procedures were performed in R 3.5.0 (The R Foundation) using the "optimize" function for 1-dimensional optimization (36). The code is available online (37).

Results

Current situation without fortification program

Using the EAR of the NAM and the UL of the EFSA as reference values and taking account of all sources, the prevalence of inadequate vitamin D intake within the different age groups of the Belgian population varied from 92% to 96%. The risk of exceeding the UL was ≤2% (Supplemental Figure 1).

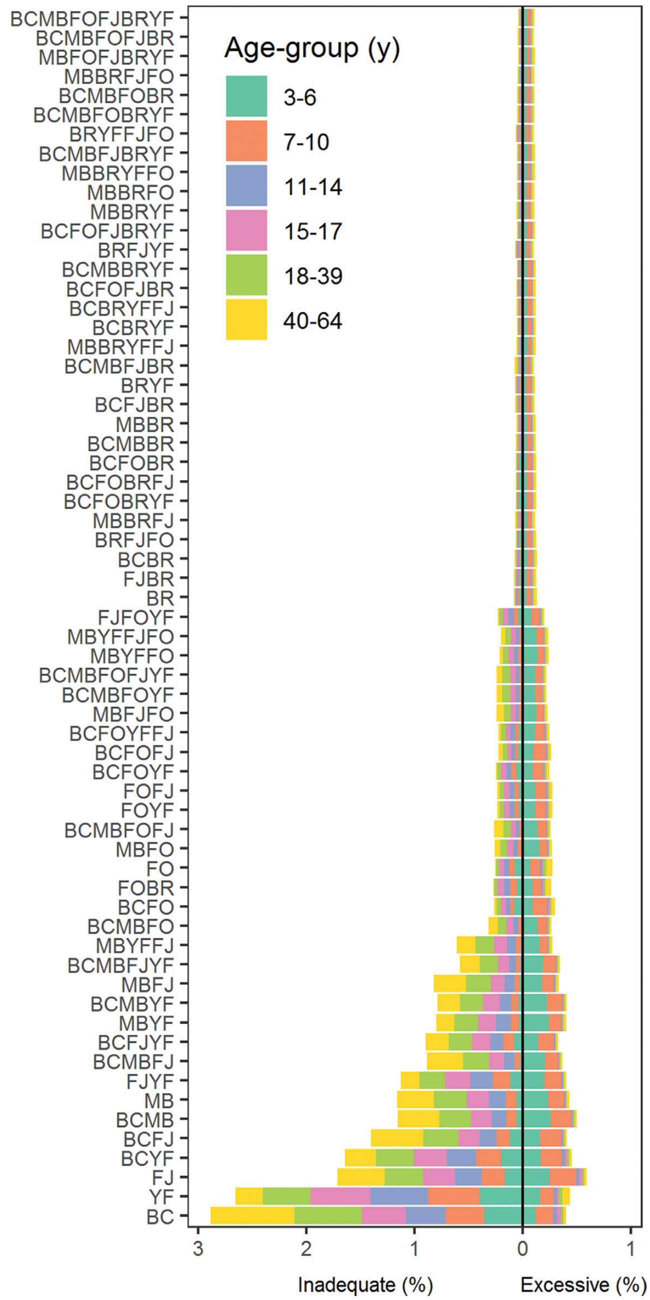

FIGURE 1 Age-specific prevalence of inadequate (left) and excessive (right) vitamin D intake per age group of the Belgian population (ages 3–64 y) at the optimal fortification level for different combinations of fortified foods, namely breakfast cereals (BC), bread (BR), fruit juices (FJ), milk and milk beverages (MB), fats and oils (FO), and yogurt and cream cheese (YF).

Age-specific approach using an EAR of 10 μg/d

In Figure 1 the age-specific prevalence of inadequate and excessive vitamin D intake at the optimal fortification level was plotted per age group for each of the 63 combinations of food vehicles. Single food groups such as BC, FJ, and YF were at the bottom of the pyramid.

At the optimal fortification level of these combinations, a high prevalence of inadequate vitamin D intake remained in all age groups (bars on the left) as well as some excessive vitamin D intake (bars on the right), especially in the youngest age groups (3–6 y and 7–10 y). BR was ranked at the center of the pyramid. From this combination upward the prevalence of inadequate and excessive intakes of vitamin D substantially decreased in all age groups. The combination at the top of the pyramid, that is, "BCMBFOFJBRYF," included all relevant food groups, that is, BC, MB, FO, FJ, BR, and YF. However, as shown in the pyramid, multiple combinations are possible to minimize the prevalence of inadequate and excessive vitamin D intake in all age groups.

The optimization model is further illustrated by means of 3 combinations: a combination with BC only, a combination with BR only, and the combination at the top of the pyramid, including all food groups.

With respect to the combination with BC only, Figure 2 depicts for each age group how the prevalence of inadequate and excessive vitamin D intake changes with increasing vitamin D fortification level. At increasing fortification levels, the prevalence of excessive vitamin D intakes increased at a higher rate in the youngest age groups (3–6 y and 7–10 y) compared with adults (18–39 y and 40–64 y). The prevalence of inadequate vitamin D intake decreased less in the adult population ($\geq$18 y) compared with children (3–6 y and 7–10 y) and adolescents (11–14 y and 15–17 y).

In case of an age-specific approach, the optimal fortification level was found where the sum of inadequate and excessive vitamin D intake, $\delta + \epsilon$, over all age groups was minimal (i. e., 328). The optimal fortification level for BC was found at a fortification level of 0.54 μg/kcal. At this fortification level, however, inadequate vitamin D intakes ranging between 35% (7–10 y) and 78% (39–64 y) remained, as well as excessive intakes ranging up to 16% (6–10 y) (Table 1 and Figure 2).

The remaining prevalence of inadequate and excessive vitamin D intake at the optimal fortification level was related to the heterogeneous consumption pattern of BC both within and between the age groups (Figure 3). The consumption distributions of BC were right-skewed, with a high proportion of nonconsumers and a large variation in consumption quantities between age groups. The median consumed quantities varied between 0 kcal/d a 30 kcal/d whereas the 90% uncertainty interval was 0–37 kcal/d in adults aged 40–64 y compared with 0.5–152 kcal/d in children aged 11–14 y. Nonconsumers would not benefit from the vitamin D fortification of BC and consequently this is not a good approach to enhance vitamin D intake in the Belgian population.

TABLE 1 Median (P50) and 95th percentile (P95) of the distribution of vitamin D intake, and the prevalence of deficient and excessive vitamin D intake per age group of the Belgian population (ages 3–64 y) at the optimal vitamin D fortification level (0.54 μg/kcal) of breakfast cereals[1]

Age group (y)	P50 (μg/kcal)	P95 (μg/kcal)	% < EAR[2]	% > UL[3]
3–6	15	75	36	12
7–10	17	84	35	16
11–14	16	88	37	3
15–17	14	92	41	4
18–39	7	71	62	2
40–64	5	42	78	2

[1]The optimal fortification level, using an age-specific approach, is the vitamin D fortification level for which the sum of inadequate and excessive vitamin D intake over all age groups (i.e., $\delta + \epsilon$) is minimal. EAR, estimated average requirement; UL, upper intake limit.
[2]EAR = 10 μg/d (33).
[3]UL = 50 μg/d for children aged 3–10 y and = 100 μg/d for individuals aged 11–64 y (11).

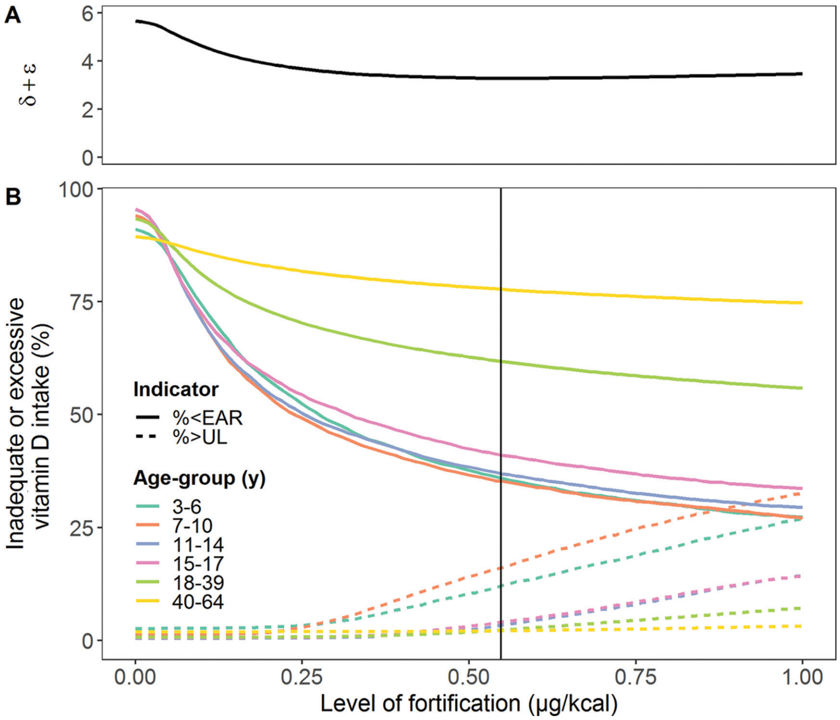

FIGURE 2 (A) Sum of the age-specific prevalence of inadequate (δ) and excessive (ϵ) vitamin D intake. (B) Prevalence of inadequate (solid lines) and excessive (dashed lines) vitamin D intake in different age groups of the Belgian population (ages 3–64 y) with increasing vitamin D fortification level (μg/kcal) for the combination of food vehicles including "breakfast cereals" (BC) only. The vertical line indicates the optimal fortification level of 0.54 μg/kcal, corresponding to the point where the sum of the age-group–specific prevalence ($\delta + \epsilon$) is minimal (i.e., 328). EAR, estimated average requirement; UL, upper intake level.

Similar findings apply to YF and FJ (see Figure 1 and Supplemental Figure 1) and other combinations in the lower half of the pyramid (Figure 1). For these combinations a high prevalence of inadequate and excessive vitamin D intake remained at the optimal fortification level.

BR, as a single commodity or in different combinations, was very effective in reducing the prevalence of inadequate and excessive vitamin D intakes over all age groups. With increasing fortification level of vitamin D in BR, the prevalence of inadequate vitamin D intake decreased with a similar pace in all age groups whereas the prevalence of excessive vitamin D intake increased at a higher rate in the younger age groups (3–6 y and 7–10 y) compared with adults (18–39 y and 40–64 y) (Figure 4). The optimal fortification level for BR

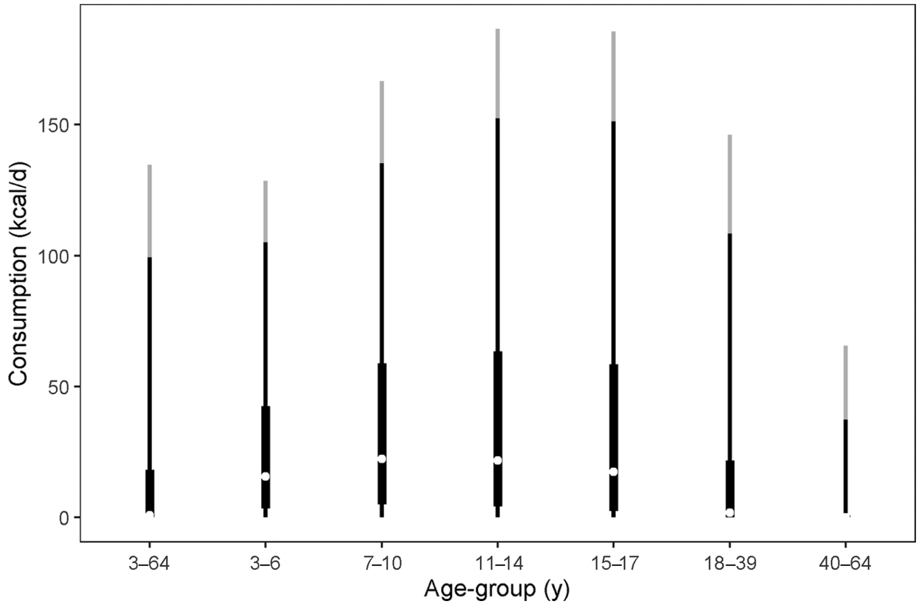

FIGURE 3 Usual consumption distribution of breakfast cereals (kcal/d) per age group of the Belgian population (ages 3–64 y). White dots indicate the median consumption of "breakfast cereals" (BC), black boxes the interquartile range [50% uncertainty interval (UI)], black lines the 5th and 95th percentiles (90% UI), and gray lines the 2.5th and 97.5th percentiles (95% UI).

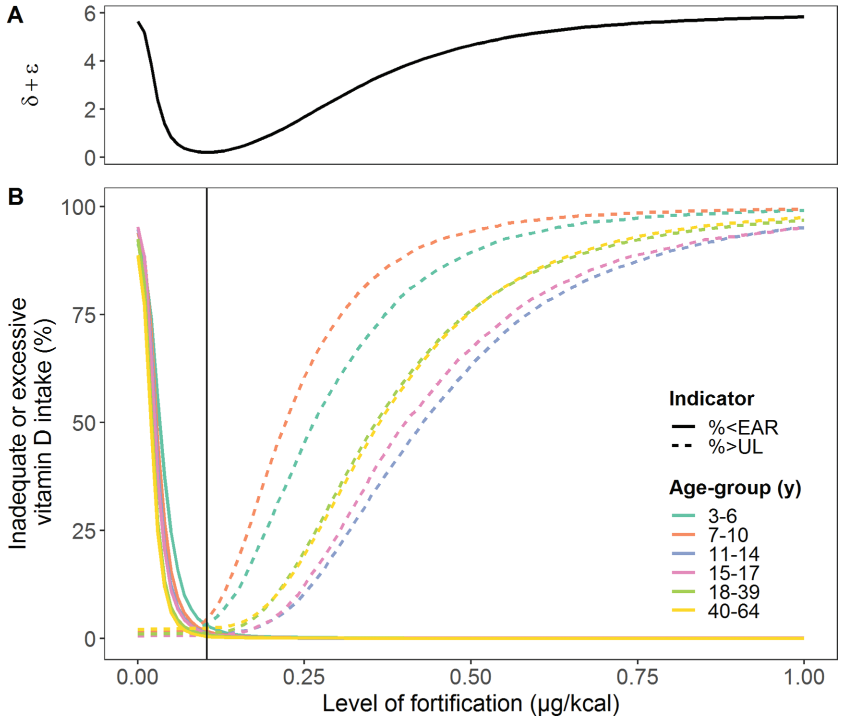

FIGURE 4 (A) Sum of the age-specific prevalence of inadequate (δ) and excessive (ϵ) vitamin D intake. (B) Prevalence of inadequate (solid lines) and excessive (dashed lines) vitamin D intake in different age groups of the Belgian population (ages 3–64 y) with increasing vitamin D fortification level (μg/kcal) for the combination of food vehicles including "bread" (BR) only. The vertical line indicates the optimal fortification level of 0.1 μg/kcal, corresponding to the point where the sum of the age-group–specific prevalence ($\delta + \epsilon$) is minimal (i.e., 0.21). EAR, estimated average requirement; UL, upper intake level.

was found at 0.1 μg vitamin D/kcal, at which inadequate intakes were almost completely counterbalanced but excessive intakes up to 3% were still found in the youngest age groups. Consumption patterns of BR were very similar within each age group (Supplemental Figure 1). BR was consumed at least in small amounts by each population subgroup, with a median consumption that varied between 163 and 262 kcal/d.

The best-ranked combination of food vehicles (at the top of the pyramid in Figure 1) was obtained by fortifying all the food groups in the combination "BCMBFOFJBRYF," that is, BC, MB, FO, FJ, BR, and YF. When increasing the vitamin D fortification level, the prevalence of inadequate vitamin D intake decreased at a similar rate in all age groups. At a fortification level of 0.047 μg/kcal the sum of the prevalence of inadequate and excessive vitamin D intake over all age groups was smallest (**Table 2**). Above this fortification level, the prevalence of excessive vitamin D intake increased at a higher rate in the youngest age groups (3–6 y and 7–10 y) compared with the other age groups (≥15 y), related to the lower UL for the younger age groups (**Figure 5**) (11). At the optimal fortification level the prevalence of inadequate vitamin D intake was significantly reduced in each age group to <1%.

The consumption patterns for this combination were almost identical in all age groups with respect to minimal and maximal consumption quantities as well as variation of consumed quantities (**Figure 6**).

There was limited difference in the sum of the age-specific prevalence of inadequate and excessive intakes in the top 30 combinations (Figure 1). Inadequate vitamin D intakes were greatly reduced for these combinations; however, excessive vitamin D intakes remained in the younger age groups (3–6 y and 7–10 y). This was related to the lower UL in the youngest age group (UL = 50 μg/d) compared with the other age groups (UL = 100 μg/d) resulting in a greater risk of exceeding the UL when increasing the vitamin D fortification level (11). The sum of the prevalence of inadequate and excessive intakes over all age groups ranged from 13% in the BR-only combination to 9% in the best-ranked combination.

Population-based approach using an EAR of 10 μg/d

When using the population-based approach, the most optimal combination, "BRYFFJFO," included the fortification of BR, YF, FJ, and FO at a fortification level of 0.069 μg/kcal. At the optimal fortification level of this combination of food vehicles, the population-weighted average of the age-specific prevalence of inadequate and excessive intake was minimized (Table 2 and **Supplemental Figure 2**). At the optimal fortification level the prevalence of inadequate vitamin D intake was significantly reduced in each age group to <2%.

Age-specific and population-based approaches using an EAR of 7.5 μg/d

Table 3 gives the optimal fortification scenario (i.e., the optimal combination of food vehicles and related vitamin D fortification level) for the age-specific and population-based approach when an EAR of 7.5 μg/d was used as cutoff value. A higher prevalence of excessive vitamin D intake remained in children and adolescents when using the population-based approach.

Age-specific and population-based approach based on the AI level

Supplemental Figures 3 and **4** show the ranking of the different combinations of food vehicles at the optimal fortification level

TABLE 2 Median (P50) and 95th percentile (P95) of the distribution of vitamin D intake, and the prevalence of inadequate and excessive vitamin D intake per age group of the Belgian population (ages 3–64 y) for the optimal vitamin D fortification scenario in case of an age-specific and a population-based approach using an EAR of 10 μg/d (33)[1]

	Age-specific approach[2]				Population based approach[3]			
Age-group (y)	P50 (μg/kcal)	P95 (μg/kcal)	<EAR (%)	>UL[4] (%)	P50 (μg/kcal)	P95 (μg/kcal)	<EAR (%)	>UL[4] (%)
3–6	27	48	0.7	4.1	25	47	2.0	3.8
7–10	26	44	0.6	2.6	27	49	0.8	4.3
11–14	26	43	0.7	0.7	29	50	0.6	0.9
15–17	26	43	0.6	0.7	29	50	0.6	0.5
18–39	26	44	0.7	0.8	31	54	0.4	0.9
40–64	27	49	0.7	2.2	33	59	0.2	1.7

[1] EAR, estimated average requirement; UL, upper intake level.
[2] The optimal combination of food vehicles in case of an age-specific approach is "BCMBFOFJBRYF," including the fortification of "breakfast cereals" (BC), "milk and milk beverages" (MB), "fats and oils" (FO), "fruit juices" (FJ), "bread" (BR), and "yogurt and cream cheese" (YF). The optimal fortification level for this scenario is 0.047 μg/kcal.
[3] The optimal combination in case of a population-based approach is "BRYFFJFO" including the fortification of "bread" (BR), "yogurt and cream cheese" (YF), "fruit juices" (FJ), and "fats and oils" (FO). The optimal fortification level for this scenario is 0.069 μg/kcal.
[4] UL = 50 μg/d for children aged 3–10 y, = 100 μg/d for individuals aged 11–64 y (11).

when minimizing the range between the AI and P50. Table 4 gives the vitamin D intake distributions per age group for the optimal combination of food vehicles. The 5th percentile and 25th percentile were of the same order of magnitude in each age group.

Table 5 gives an overview of the optimal fortification scenarios using the different optimization procedures for both an age-specific and a population-based approach.

Discussion

We present the use of a mathematical optimization model to fine-tune a fortification program to the specific needs of a population. An optimization method was developed and applied to the Belgian population for the development of the most effective vitamin D fortification scenario. The model allows the selection of both the optimal combination of food vehicles and the corresponding vitamin D fortification level.

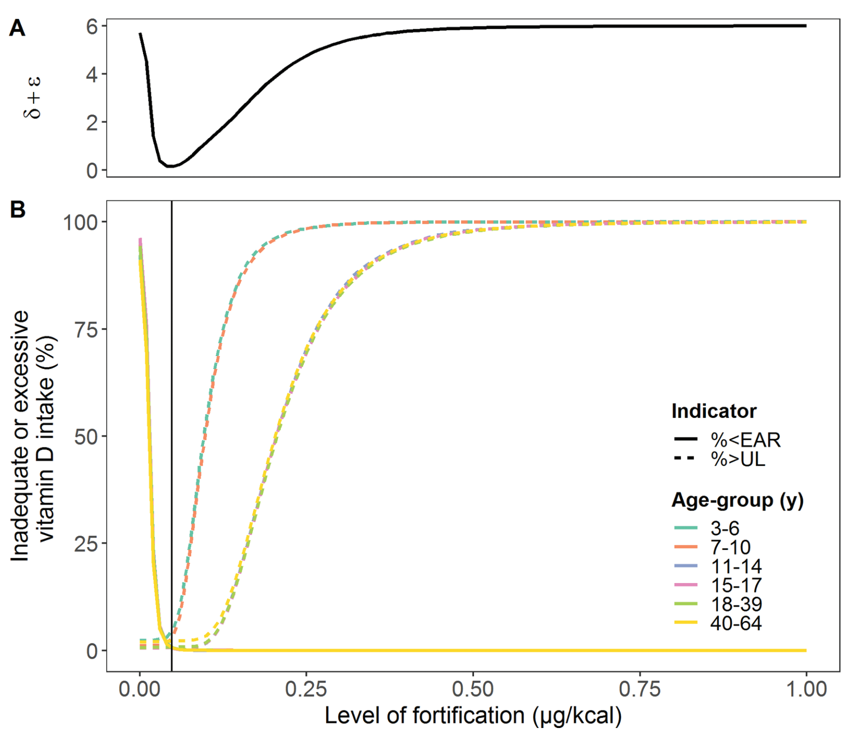

FIGURE 5 (A) Sum of the age-specific prevalence of inadequate (δ) and excessive (ϵ) vitamin D intake. (B) Prevalence of inadequate (solid lines) and excessive (dashed lines) vitamin D intake in different age groups of the Belgian population (ages 3–64 y) with increasing vitamin D fortification level (μg/kcal) for the combination of food vehicles including all food groups, namely "breakfast cereals" (BC), "milk and milk beverages" (MB), "fats and oils" (FO), "fruit juices" (FJ), "bread" (BR), and "yogurt and cream cheese" (YF). The vertical line indicates the optimal fortification level of 0.47 μg/kcal, corresponding to the point where the sum of the age-group–specific prevalence ($\delta + \epsilon$) is minimal (i.e., 0.15). EAR, estimated average requirement; UL, upper intake level.

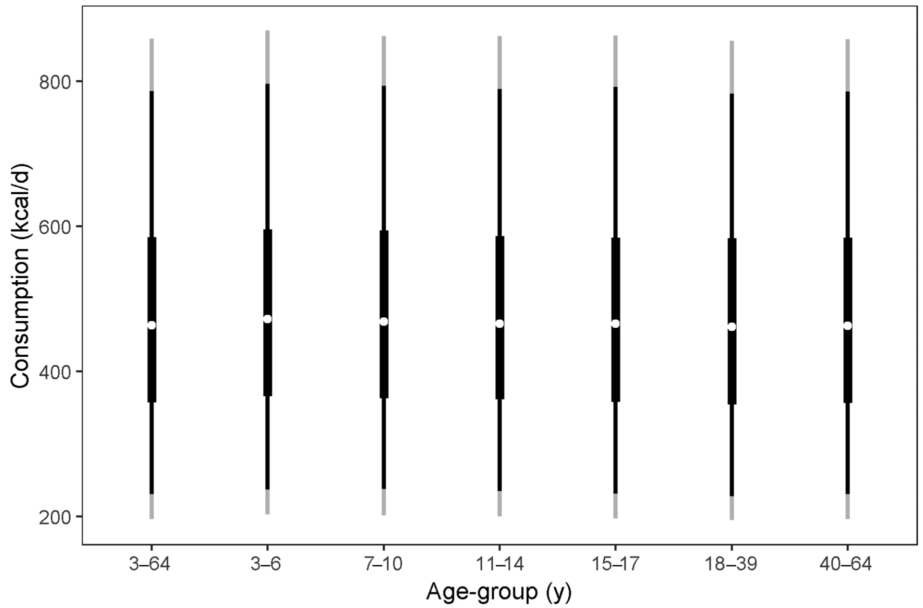

FIGURE 6 Usual consumption distribution of the combination of food vehicles including "breakfast cereals" (BC), "milk and milk beverages" (MB), "fats and oils" (FO), "fruit juices" (FJ), "bread" (BR), and "yogurt and cream cheese" (YF) (kcal/d) per age group of the Belgian population. White dots indicate the median consumption, black boxes the interquartile range [50% uncertainty interval (UI)], black lines the 5th and 95th percentiles (90% UI), and gray lines the 2.5th and 97.5th percentiles (95% UI).

Using an EAR of 10 μg/d and an age-specific approach, the optimal combination of food vehicles included the fortification of all relevant food groups, namely bread, milk and milk beverages, fats and oils, fruit juices, breakfast cereals, and yogurt and cream cheese, at a vitamin D fortification level of 0.047 μg/kcal.

To be efficient, a food fortification program should reach nearly all (97.5%) individuals within a population (sub)group at risk of deficiency and provide them with an adequate intake of the micronutrient without increased risk of excessive intake (12). The results of the model indicated that multiple combinations of food vehicles (top 30 combinations of the pyramid) were suitable to optimize the vitamin D intake within the Belgian population. Hence, inadequate vitamin D intake was almost completely eliminated in each of the population subgroups (from a prevalence of 92–96% to <2%). This allows policymakers to make a deliberate choice of the optimal combination of food vehicles taking account of other aspects such as the healthiness of the food vehicles, the feasibility of fortifying the food vehicle, production costs, and regulatory aspects. In nutrition policy priority should be given to the promotion of a healthy diet (38). Fortifying foods that are not contributing to a healthy diet would therefore militate against this goal and should be avoided. Following the WHO Europe nutrient-profiling model, specifically developed to support policymakers to restrict unhealthy food marketing to children, fruit juices and most breakfast cereals available on the Belgian market are not contributing to a healthy diet (39). The fortification of BR and MB at a level of 0.069 μg/kcal was therefore proposed as an optimal fortification scenario for the Belgian population. Due to the widespread consumption of bread and milk in the Belgian population, inadequate

TABLE 3 Median (P50) and 95th percentile (P95) of the distribution of vitamin D intake, and the prevalence of deficient and excessive vitamin D intake per age group of the Belgian population (ages 3–64 y) for the optimal vitamin D fortification scenario in case of an age-specific and a population-based approach using an EAR of 7.5 μg/d (34)[1]

	Age-specific approach[2]				Population-based approach[3]			
Age group (y)	P50 (μg/kcal)	P95 (μg/kcal)	% < EAR	% > UL[4]	P50 (μg/kcal)	P95 (μg/kcal)	% < EAR	% > UL[4]
3–6	24	42	2.0	2.6	21.5	41	0.8	2.0
7–10	23	40	0.1	1.6	23.6	42	0.3	2.0
11–14	23	39	0.3	0.5	24.6	44	0.2	9.0
15–17	23	39	0.2	0.5	25.1	43	0.2	5.0
18–39	23	40	0.3	1.1	26.6	47	0.1	1.7
40–64	22	42	0.4	1.7	28.3	47	0.2	1.3

[1] EAR, estimated average requirement; UL, upper intake limit.
[2] The optimal combination of food vehicles in case of an age-specific approach is "BCMBFOFJBR," including the fortification of "breakfast cereals" (BC), "milk and milk beverages" (MB), "fats and oils" (FO), "fruit juices" (FJ), and "bread" (BR).
[3] The optimal combination of food vehicles in case of a population-based approach is "BRYFFJFO," including the fortification of "bread" (BR), "yogurt and cream cheese" (YF), "fruit juices" (FJ), and "fats and oils" (FO).
[4] UL = 50 μg/d for children aged 3–10 y, = 100 μg/d for individuals aged 11–64 y (11).

TABLE 4 Fifth percentile (P5), median (P50), and 95th percentile (P95) of the distribution of vitamin D intake, and the prevalence of inadequate and excessive vitamin D intakes per age group of the Belgian population (ages 3–64 y) in the optimal fortification scenario found by minimizing the absolute value of the difference between AI and P50[1]

	Age-specific approach[2]				Population-based approach[3]			
Age group (y)	P5 (μg/kcal)	P50 (μg/kcal)	P95 (μg/kcal)	>UL[4] (%)	P5 (μg/kcal)	P50 (μg/kcal)	P95 (μg/kcal)	>UL[4] (%)
3–6	9	15	28	2	8.3	14	27	2
7–10	8	15	26	1	8.5	15	26	1
11–14	8	15	26	1	8.4	15	26	1
15–17	8	15	25	1	8.4	15	26	1
18–39	8	15	27	1	8.3	15	27	1
40–64	8	15	29	2	8.0	15	31	2

[1]Modeling is performed using an age-specific and a population-based approach and an AI of 15 μg/d (35). AI, Adequate Intake; UL, upper intake limit.
[2]The optimal combination of food vehicles in case of an age-specific approach is "BCMBFOFJBR," including the fortification of "breakfast cereals" (BC), "milk and milk beverages" (MB), "fats and oils" (FO), "fruit juices" (FJ), and "bread" (BR). The optimal fortification level for this scenario is 0.043 μg/d.
[3]The optimal combination of food vehicles in case of a population-based approach is "MBBR," including the fortification of "milk and milk beverages" (MB) and "bread" (BR). The optimal fortification level for this scenario is 0.015 μg/d.
[4]UL = 50 μg/d for children aged 3–10 y, = 100 μg/d for individuals aged 11–64 y (11).

vitamin D intake was thereby almost completely eliminated in each of the population subgroups (<2.5% below the EAR).

Some risk of excessive vitamin D intake remained in the top best combinations of food vehicles. This was because the model was constructed under the assumption that current fortification practices and supplement consumption remained the same. However, in the current situation (without a national fortification program) a minor risk for excessive vitamin D intake (0.5–2.5%) is already observed, especially in the younger age groups. This relates to the consumption of high-dose supplements and to nonuniform supplement recommendations (4). To exclude any risk of excessive vitamin D intake in the Belgian population, the implementation of a national vitamin D fortification program requires a simultaneous revision of the national regulations on maximum vitamin D levels in supplements and fortified foods as well as a revision and setting of uniform vitamin D supplement recommendations.

The results from the different approaches differed in their combination of food vehicles and in their vitamin D fortification levels. For each of these approaches the best results in terms of fortification utility and risk of excessive intakes were obtained when a staple food such as bread was included and when fortifying multiple foods with vitamin D. These results confirm the findings of Hirvonen et al. (20) and some other national food fortification studies (19, 30).

When using the population-based approach, inadequate and excessive intakes in adults weighed more than in children, due to the greater proportion of adults than children. However, the choice between the population-based approach and age-specific approach depends on the nutrient under study and the sensitivity for adverse health effects related to inadequate or excessive nutrient intakes in each of the life-stage groups. Because vitamin D participates in bone mineralization, adverse health effects of inadequate and excessive vitamin D intake affect people of all ages (40). However, due to the lower UL in children (ages 3–10 y) than in adults, children are at higher risk of excessive vitamin D intake (11). With respect to vitamin D, the age-specific approach is therefore recommended.

An advantage of this model is that it can inform risk managers and policymakers on the shape and variation of the intake distribution. When bringing the P50 close to the AI, the 95th percentile remained far below the UL in all age groups, whereas the 5th percentile was about half of the AI. The model is thus suitable to work with different types of reference values and can inform policymakers on the risk of unacceptably low or high vitamin D intakes for different combinations of food vehicles.

A strength of the current study is that the diversity in food consumption patterns of the majority of the population (ages 3–64 y) was taken into account. However, specific risk groups such as the elderly were omitted from the study. Before implementation of the fortification program the specific consumption patterns of these subgroups should be assessed to evaluate if they can also be reached within the proposed fortification scenario.

TABLE 5 Optimal combinations of food vehicles and vitamin D fortification levels for the optimal fortification scenario using different reference values and optimization approaches for the Belgian population (ages 3–64 y)[1]

Reference values used (μg/d)	Reference no.	Optimization approach	Optimal combination of food vehicles[2]	Fortification level (μg/kcal)
EAR = 7.5 andUL = 50/100[3]	(11, 34)	Age-specific	BCMBFOFJBR	0.043
		Population-based	BRYFFJFO	0.059
EAR = 10 andUL = 50/100	(11, 33)	Age-specific	BCMBFOFJBRYF	0.047
		Population-based	BRYFFJFO	0.069
AI = 15	(35)	Age-specific	BCMBFOFJBR	0.025
		Population-based	MBBR	0.034

[1]AI, Adequate Intake; EAR, estimated average requirement; UL, upper intake level.
[2]Combinations of food vehicles including "breakfast cereals" (BC), "bread" (BR), "fruit juices" (FJ), "fats and oils" (FO), "milk and milk beverages" (MB), and "yogurt and cream cheeses" (YF).
[3]UL = 50 μg/d for children aged 3–10 y, = 100 μg/d for individuals aged 11–64 y (11).

An important limitation of the study is that the optimization model was based only on food consumption data. Because sun-induced vitamin D synthesis is the major source of vitamin D, nationwide data on serum concentrations of 25-hydroxyvitamin D [25(OH)D] are needed to estimate the extent of vitamin D deficiency within the Belgian population and the additional vitamin D intake needed to obtain adequate status for almost the entire population (9). Ideally, meteorological data on UVB availability in Belgium coupled with serum 25(OH)D data are needed to fully understand the distribution of the vitamin D status of the Belgian population and investigate by which fortification level would improve vitamin D status (41).

The optimization model does not account for uncertainty or sampling error in the prevalence of inadequate and excessive intakes. In theory, this could be solved as follows: SPADE could generate the pseudo-people for different possible realizations of the models, taking into account sampling error. We could then apply our process of optimization to each set of pseudo-persons, and get different sets of answers, based on which we can determine CIs.

When computing the vitamin D intake, the assumption was made that all food items belonging to a specific food group are fortifiable. Following the European Union legislative framework 2013/461/EU on the application of the principle of mutual recognition it will not be possible to impose fortification on manufacturers importing their products into Belgium (42). Also, the potential overages of vitamin D in fortified foods and supplements to cover losses during storage/display were not taken into account. The vitamin D contents specified on food labels do not cover these overages (43). These factors will undeniably influence the fortification level and the choice of the food vehicles. However, information on market shares and estimates for overages could be easily implemented within the optimization model.

The optimization model presented allows nutrition policy-makers to make an evidence-based assessment of the most effective and safe fortification scenario taking account of the sensitivity of different population subgroups to adverse health effects. The model can be implemented in a dynamic way and allows a choice of food vehicles based on acceptable risks of low and excessive vitamin D intakes and other aspects such as feasibility and regulatory aspects.

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