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Food Fortification or Individual Supplementation? Commentary on the Slovenian Guidelines for Adequate Vitamin D Status (2025)

Obogatitev živil z vitaminom D ali individualno dodajanje? Komentar na slovenske smernice za zadostno preskrbljenost z vitaminom D (2025)

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Abstract

Background: This study critically reviews the recently published "Slovenian guidelines for adequate vitamin D status (2025)", focusing on the chapter titled *Cost assessment of selected recommendations in the Slovenian guidelines for adequate vitamin D provision*. Several methodological weaknesses were identified in the economic evaluation, which may lead to inefficient and inequitable public health decisions.

Methods: A secondary analysis of the guideline's cost-assessment methodology was performed, together with an independent cost comparison of vitamin D sources.

Results and discussion: The guideline's cost-effectiveness analysis for reducing acute respiratory infections (ARI) in older adults (>65 years) with serum 25(OH)D <25 nmol/L is based on a subgroup meta-analysis in which >80% of participants were children, making extrapolation to older adults questionable. The model also assumes unrealistically high adherence to vitamin D supplementation. In contrast, population-wide food fortification is proven effective, minimizes adherence problems, is cost-effective, and ensures equitable access. Estimated annual costs for providing 20 µg vitamin D_3 daily to the total population aged ≥1 year (2.1 million people) were: 26.1 million EUR for prescription medicines; 37.3 million EUR for prescription medicines including a yearly short physician visit; 112.1 million EUR for over-the-counter medicines; 30.4 million EUR for food supplements; and 0.4 million EUR for food fortification.

Conclusions: Given its demonstrated effectiveness, low cost, and ability to reduce health inequities, population-wide food fortification represents the most realistic strategy for preventing vitamin D deficiency in the entire population.

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Izvleček

Izhodišča: Raziskava kritično ocenjuje nedavno objavljene "Slovenske smernice za zadostno preskrbljenost z vitaminom D(2025)" s posebnim poudarkom na poglavju *Stroškovno ovrednotenje nekaterih priporočil v slovenskih smernicah za zadostno preskrbljenost z vitaminom D*. Ekonomska ocena je ugotovila več metodoloških pomanjkljivosti, ki lahko vodijo do neučinkovitih javnozdravstvenih odločitev in do povečanja neenakosti v zdravju.

Metode: Izvedli smo sekundarno analizo metodologije ocenjevanja stroškov v smernicah ter opravili neodvisno primerjavo stroškov za različne vire vitamina D.

Rezultati in razpravljanje: Analiza stroškovne učinkovitosti smernic pri zmanjševanju akutnih respiracijskih okužb (ARI) pri starejših odraslih (> 65 let) s serumskim 25(OH)D <25 nmol/L temelji na metaanalizi podskupine, v kateri je bilo > 80 % udeležencev otrok. Posploševanje teh rezultatov na populacijo starejših odraslih je metodološko vprašljivo. Model predpostavlja tudi nerealno visoko adherenco pri dodajanju vitamina D. Nasprotno pa je obogatitev živil za celotno populacijo dokazano učinkovita, zmanjšuje težave glede adherence, je stroškovno učinkovita in zagotavlja enakopraven dostop za celotno populacijo. Ocenjeni letni stroški zagotavljanja 20 µg vitamina D_3 dnevno za vse osebe, stare ≥1 leto (2,1 milijona ljudi), so znašali: 26,1 milijona EUR za zdravila na recept; 37,3 milijona EUR za zdravila na recept s kratkim obiskom zdravnika; 112,1 milijona EUR za zdravila brez recepta; 30,4 milijona EUR za prehranska dopolnila; in 0,4 milijona EUR za obogatitev živil.

Zaključki: Glede na dokazani učinek, nizke stroške in sposobnost zmanjševanja neenakosti je obogatitev živil za celotno populacijo najbolj realistična strategija za preprečevanje pomanjkanja vitamina D.

1 Introduction

We comment on the recently published Slovenian guidelines for adequate vitamin D status, with particular focus on the chapter "Cost assessment of selected recommendations in the Slovenian guidelines for adequate vitamin D provision" (1).

The prevalence of vitamin D deficiency in Slovenia is high across all population groups. In a nationally representative study the prevalence of vitamin D deficiency (25(OH)D <50 nmol/L) was 58% in adults and 63% in older adults (65-74 years) (2).

Given the major implications for population health and public expenditure in Slovenia, cost assessments must be based on data from comparable populations and accurately interpreted. We have identified several issues that may lead to inefficient and inequitable public health decisions.

2 Materials and methods

This study is based on secondary analysis of published data. We analysed the methodology and input data used for calculations by Pfeifer et al. (1) in their cost-effectiveness analysis of vitamin D supplementation for preventing acute respiratory infections (ARI). We conducted a detailed, critical appraisal of the evidence from the meta-analysis by Martineau et al. (3) on vitamin D supplementation for preventing acute respiratory infections (ARI). Particular attention was given to the subgroup with baseline 25(OH)D <25 nmol/L to assess the applicability of the observed effects to older adults.

A cost comparison of an annual supply of 20 µg vitamin D_3 from different sources was conducted for the Slovenian population aged ≥1 year. Population data for 2025 were obtained from the Statistical Office of the Republic of Slovenia (4). Cost inputs for food fortification were taken from Vičič et al. (5) and revalorised to account for inflation (6). The cost of a short physician visit was sourced from the Health Insurance Institute of Slovenia (5.31 EUR), and we assumed one visit per year (7). We conducted a pragmatic, non-systematic online search to identify the lowest-cost vitamin D over-the-counter medicine and food supplement. The lowest-cost over-the-counter vitamin D medicine (18.16 EUR for 100 tablets containing 2500 µg D_3) (8) and food supplement (2.95 EUR for 60 soft capsules containing 1500 µg D_3) were used (9). The price of the lowest-cost prescription vitamin D medicine was retrieved from the central medicines database (CBZ) (7.61 EUR for a 12.5 mL bottle containing 4500 µg D_3) (10). A daily dose of 20 µg vitamin D_3 was used for comparison across sources. It must be noted that, in fortification, the typical target dose is lower (11).

Endocrine Society cut-off values were applied to

classify serum total 25(OH)D concentrations: optimal vitamin D status was defined as 75–125 nmol/L, insufficiency as 50–75 nmol/L, and deficiency as <50 nmol/L (12,13).

3 Results and discussion

We address four key concerns: 1. absence of guidelines for fortification of staple foods with vitamin D, 2. lack of consideration of adherence, 3. methodological issues, and 4. increasing health inequities.

3.1 Absence of guidelines for fortification of staple foods with vitamin D

Public health problems should be addressed with public health measures. Extensive evidence shows that fortifying staple foods with vitamin D can eliminate severe vitamin D deficiency and reduce its prevalence (14-16). The success of Finnish vitamin D fortification is demonstrated by the documented increase in population serum 25(OH)D (16). A successful example of food fortification in Slovenia is iodine fortification of salt, which began in 1953 and became mandatory in 1999. Salt iodisation has been shown to be safe and effective (17). In stark contrast, recommendations for individual supplementation with prescription or over-the-counter medicines or food supplements have never achieved results even remotely comparable to those at the population level.

In cost calculation of vitamin D supplementation in older adults (>65 years) (1), the following data were omitted or not adequately considered: 1. food fortification as a more cost-effective option, 2. the costs of individual physician visits required to prescribe vitamin D medication, 3. prescription medication costs were applied to the entire population aged >65 years, even though such prescription coverage is not universally available and 4. over-the-counter products are substantially more costly (Figure 1).

The goal of food fortification is to eradicate severe vitamin D deficiency (25(OH)D <30 nmol/L) and prevent vitamin D deficiency (25(OH)D <50 nmol/L) in the majority of the population. The target vitamin D intake that can be safely provided through foods is usually around 10 µg (400 IU) per day (11). To achieve optimal serum concentrations (>75 nmol/L), vitamin D supplementation via medicines or food supplements will still be necessary. Food fortification, therefore, neither excludes nor fully replaces individual vitamin D

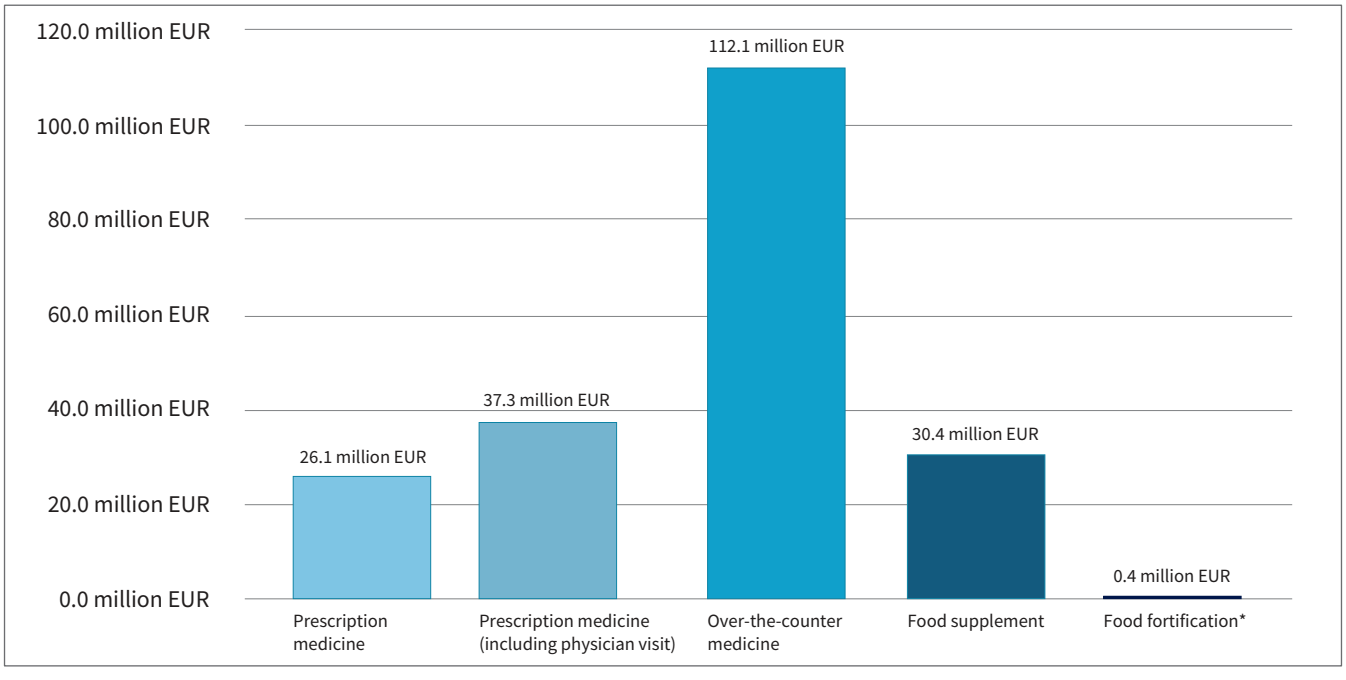

Figure 1: Cost comparison of an annual supply of 20 µg vitamin D_3 from different sources for the Slovenian population aged ≥1 year (2.1 M). Only the lowest-cost prescription medicine, over-the-counter medicine, food supplement, and food fortification were used.

* A daily dose of 20 µg vitamin D_3 was used for comparison across sources. Typical target dose for food fortification is ~10 µg (11).

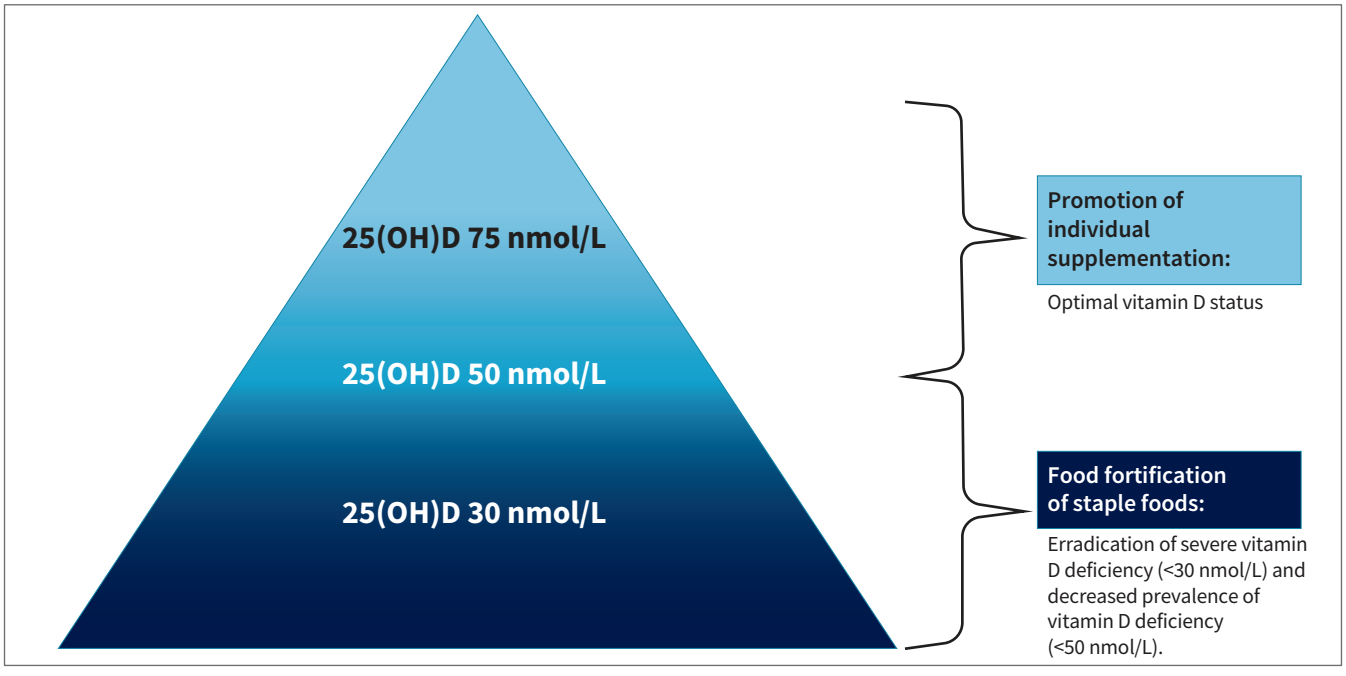

Figure 2: Integration of food fortification and individual supplementation to improve 25(OH)D levels in Slovenian population. Black and dark grey indicate the levels that could be achieved by vitamin D food fortification, while lighter grey represents the additional effect attained through individual supplementation. Conceptual illustration; not to scale and not based on quantitative data.

supplementation with medicines or food supplements (18) (Figure 2). The fortification - direct addition of vitamin D to foods is already permitted in the EU; however, it is insufficiently implemented due to the absence of clear national guidelines (5).

3.2 Lack of consideration of adherence

We suggest that all calculations should be improved by realistic adherence data, as currently, 100% adherence is assumed. In a meta-analysis of 11 studies, the authors examined adherence to vitamin D supplementation in children under 5 years in Europe, the USA, and Canada. Adherence ranged from 11.3% to 95.6%, with 6 of the studies reporting low adherence (19). In Finland, vitamin D supplementation is recommended and promoted through public health campaigns, resulting in a 41% of the population supplementing with vitamin D (14). In a Slovenian study of women aged 44-65 years, subjects were provided with 25(OH)D measurements and asked whether they supplemented vitamin D. 20 months after initial measurement only 70% of those who supplemented vitamin D were still supplementing (18).

The Danish Health Authority recommended supplementation with 20 µg vitamin D and 800–1000 mg calcium for all residents of Danish nursing homes. A cross-sectional survey of 50 nursing homes revealed poor adherence to the guideline, despite respondents having a high level of knowledge of the recommendations. Low adherence (≤40% of residents taking both supplements) was observed in 35% of nursing homes, whereas only 8% of facilities achieved high adherence (>80% of residents taking both supplements) (20). For institutionalised populations, a more effective intervention could be the use of fortified foods. A Romanian intervention study demonstrated that daily consumption of bread fortified with vitamin D_3 and calcium was both safe and effective for nursing home residents (21). A higher prevalence of deficiency was found in institutionalized older adults who do not supplement vitamin D (22). In the absence of UV exposure, a similar vitamin D status is expected in any institutionalized population, including prisoners (23) and psychiatric patients (24). The benefits of population-wide fortification extend to institutionalized populations, as demonstrated by the mandatory enrichment of bread in Australia, which also reduced thiamin deficiency among hospitalized patients and led to a 40% decrease in the incidence of acute Wernicke encephalopathy and Korsakoff syndrome (25).

3.3 Increasing health inequities

The chapter evaluates the benefits of vitamin D supplementation only in the population of older adults (>65 years), despite most Slovenian studies showing a high prevalence of vitamin D deficiency in adults (<65 years). In the Slovenian NUTRIHEALTH study, conducted between November and April (2017–2018), 40.8% of adults (<65 years) and 34.6% of older adults (65-75 years) had severe vitamin D deficiency - serum 25(OH)D <30 nmol/L (2). Similarly, a study conducted during the COVID-19 pandemic found lower levels of 25(OH)D in older premenopausal compared with postmenopausal women (11).

Given the low adherence to vitamin D supplements and medications, it is unrealistic to prevent deficiency (<50 nmol/L) in the entire population through individual supplementation (18). Such a strategy fails to reach those at highest risk of deficiency, as supplement intake is positively associated with a healthier lifestyle and higher socioeconomic status (15). Numerous studies also report a higher risk of vitamin D deficiency associated with lower socioeconomic status (26-29). Relying only on individual supplementation will deepen health inequalities, as only a small proportion of the population with higher socioeconomic status and education will consistently supplement vitamin D.

A Czech study revealed a significant positive association between vitamin D supplementation and both education and income level. Individuals holding a bachelor's degree or higher demonstrated significantly higher odds of supplementation (OR = 2.18). Similarly, higher income was significantly associated with increased odds of supplementation (OR = 1.87). The prevalence of consistent year-round supplementation was 13.5%, while 51.5% never supplemented (26). A similar effect of folic acid supplementation is observed in the Slovenian population of pregnant women, who are universally advised to supplement with 400 µg/day folic acid; this advice is followed by only 32% of women with elementary education, compared with >90% of women with at least high school education. Odds of taking folic acid supplements for women with a university degree were 8 times higher compared to those with an elementary school degree (30). Fortification programs also have limitations, such as in Finland, where vitamin D fortification has limited impact among immigrants with low consumption of fortified foods (31).

3.4 Methodological issues

The authors (1) evaluated the cost-effectiveness of daily vitamin D supplementation (20 µg/day) for preventing acute respiratory infections (ARI) in older adults (>65 years), using data from the meta-analysis by Martineau et al. (3). For the first subgroup 34.6% of the population of Slovenian older adults (>65 years) with 25(OH)D <30 nmol/L they (1) used aOR 0.30 and for the second subgroup, 65.4% of the population of Slovenian older adults (>65 years) with 25(OH)D >30 nmol/L they used aOR 0.75.

The first subgroup analysis of daily or weekly supplementation in participants with baseline 25(OH)D <25 nmol/L included six highly heterogeneous studies that differed in populations, ages, vitamin D doses, and baseline vitamin D status. Of the 243 participants (2.2% of total meta-analysis participants) (3) with baseline 25(OH)D <25 nmol/L, 192 were third/fourth grade schoolchildren from Mongolia (32) (Table 1). Therefore, the observed strong protective effect (aOR 0.30; NNT = 4) may be driven predominantly by data from children. While this demonstrates a benefit in a specific pediatric population, extrapolating this effect to older adults (>65 years) is biologically and methodologically questionable (32).

The second subgroup analysis of daily or weekly supplementation in participants with baseline 25(OH)D >25 nmol/L included 1603 participants across six studies (3), which indicates that most vitamin D supplementation studies are conducted in developed countries with mandatory or widespread voluntary food fortification. Among Slovenian adults (<65 years), the prevalence of severe vitamin D deficiency (<30 nmol/L) is 40.8% (2), whereas in a US study by Li-Ng et al. (33), only 2% had 25(OH)D <25 nmol/L, reflecting the impact of mandatory fortification.

To this day, there are still no published studies examining the effect of daily vitamin D supplementation on ARI risk in healthy older adults (>65 years). In April 2025, an updated meta-analysis including 37 studies was published, concluding that vitamin D supplementation did not provide statistically significant protection against ARI (38). This conclusion is not surprising, as most studies are conducted in countries with mandatory or widespread vitamin D fortification.

Only one study has investigated healthy, non-institutionalised, free-living older adults (>65 years), using monthly vitamin D boluses of 0.75 mg and 1.5 mg

Table 1: Characteristics of first subgroup of studies (25(OH)D <25 nmol/L) used for cost assessment analysis of vitamin D supplementation (20 µg/day) for preventing acute respiratory infections (ARI) in older adults (>65 years) by Pfeifer et al. (1). Six studies using daily or weekly supplementation, each with at least one participant with a baseline 25(OH)D level below 25 nmol/L, were manually selected from the meta-analysis Martineau et al., (3).

Population / Age Group	Country	Dose	Age (years mean ± SD)	Intervention: Control (n)	25(OH) D baseline concentration <25 nmol/L n ()	Reference
Healthy adults	USA	50 µg/day	57.9 ± 13.6	84 : 78	3 (2%)	Li-Ng et al. (33)
Children with asthma	Japan	20 µg/day	9.9 ± 2.3	54 : 35	1 (1.1%)	Tachimoto et al. (34)
Third/fourth grade schoolchildren	Mongolia	7.5 µg/day	10.0 ± 0.9	143 : 104	192 (78.4%)	Camargo et al. (32)
Adults with increased ARI susceptibility	Sweden	100 µg/day	53.1 ± 13.1	70 : 70	15 (11.5%)	Bergman et al. (35)
Italian children with recurrent acute otitis media	Italy	25 µg/day	2.8 ± 1.0	58 : 58	2 (1.7%)	Marchisio et al. (36)
Pregnant women and their offspring	New Zealand	Mothers 25–50 µg/day Offspring 10–20 µg/day	Mothers: ND Infants: 0-18 months	173 : 87 (mothers) 164 : 85 (offspring)	30 (total) (15%)	Grant et al. (37)
Intervention: Control (n) Total (n)				746 : 517 1263	243* (19.2%)	Martineau et al., (3)

* The final number of participants in meta-analysis Martineau et al. (3) was n=234. There is no data on which participants were excluded.

rather than daily supplementation. The group that received 1.5 mg of D_3 had a statistically nonsignificant lower rate of antibiotic prescriptions (RR: 0.72; 95% CI: 0.48, 1.07) compared with the placebo group (39). This study was not included in the previously mentioned subgroup analysis (3). In the meta-analysis, only one study of daily vitamin D supplementation (50 µg) in healthy participants was included. It reported that after 12 weeks of follow-up, vitamin D supplementation had no statistically significant effect on the incidence of respiratory infections (33).

3.5 Study limitations and future research

Our analysis has several limitations: 1. The fortification cost estimate excludes implementation-related expenses, including product reformulation, quality control, and regulatory monitoring. Moreover, the successful promotion of both voluntary fortification and/or supplementation would likely require large-scale media campaigns. Although difficult to quantify, these would almost certainly amount to several million EUR and would remain cost-effective when compared with alternative strategies for vitamin D intake. 2. Consumers and prescribing physicians do not always select the lowest-cost food supplement or prescription medicine per µg of vitamin D. Ideally, analyses should include a sensitivity analysis considering the lowest, highest, and median costs; however, market data on the market share of supplements and the potential cost of media campaigns to promote vitamin D-fortified food were not available to us. 3. The cost comparison also does not specify the payer: costs may be borne by the healthcare system (prescription medicines), by citizens directly (food supplements, over-the-counter medicines), or indirectly through the purchase of fortified foods. 4. Our critique of the data from the meta-analysis by Martineau et al. (3) also has limitations. We manually selected six studies for subset analysis based on reported participant characteristics. However, because the original study was an individual participant data (IPD) meta-analysis that excluded certain participants, and

we lacked access to the raw data, we could not independently verify the final composition of the analysed subgroup, as noted in the footnote to Table 1.

4 Conclusions

The publishing of Slovenian guidelines for adequate vitamin D status is commendable. However, the cost assessment in the Slovenian vitamin D guidelines should be corrected. Recommendations for individual supplementation through prescription or over-the-counter medicines or food supplements alone, based on adherence data from similar interventions, will not be sufficiently effective in improving vitamin D status in the Slovenian population. Additional steps are needed to align these recommendations with effective and equitable public health strategies. Given its proven success, cost-effectiveness, and capacity to reduce health inequities, population-wide food fortification is the most realistic strategy for preventing vitamin D deficiency in the entire population. It is important to note that individual supplementation will still be necessary, as food fortification would primarily prevent severe vitamin D deficiency and only a proportion of overall deficiency; achieving optimal vitamin D status would therefore continue to require individual supplementation.

Conflict of interest

The author declares that no conflicts of interest exist.

Funding

The study received no funding.

Ethical approval

Ethical approval was not required for this methodological and economic analysis.

Availability of data and materials

The datasets supporting this study are derived from publicly available sources cited in the references. Further details are available from the corresponding author upon request.

Use of generative AI

AI technologies have been used only to improve the language and readability of text (Instatext, Deepseek), not to generate concepts, insights, data analysing or to create any conclusions.

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