WHO-EM/NUT/313/E

Summary report on the

Consultation on the development of regional guidelines on vitamin D supplementation for the WHO Eastern Mediterranean Region

Beirut, Lebanon
15–16 May 2023

World Health Organization
Eastern Mediterranean Region

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1. Introduction

The countries of the WHO Eastern Mediterranean Region face the double burden of malnutrition – where undernutrition co-exists with increasingly common overweight and obesity. Many communities face the challenges of overweight and obesity at the same time as the "hidden hunger" of vitamin and mineral deficiencies. Improving access to, and consumption of, healthy, diversified diets is the best way to ensure adequate micronutrient intake. Still, where it cannot be achieved soon enough, other strategies including micronutrient supplementation and food fortification must be employed.

Vitamin D is important for maintaining normal blood levels of calcium and phosphate, which are needed for general cell functioning in all cells of the body, but especially for bone health. Vitamin D is a fat-soluble vitamin that is mainly produced by the human body from exposure to sunlight. However, it can also be consumed from a few foods such as fish-liver oils, fatty fish, mushrooms, egg yolks and liver. Estimation of dietary intake and dermal synthesis of vitamin D is not a simple task, mainly due to the lack of accurate food composition data for vitamin D and the many factors influencing skin synthesis, including skin pigmentation and the efficiency of direct sun exposure affected by clothing style, older age and sunscreen use. Groups at risk of severe vitamin D deficiency include children, adolescents, pregnant women and older people. In pregnancy, vitamin D deficiency is implicated in the development of pre-eclampsia, gestational diabetes, preterm birth and low birthweight.

At the global level, vitamin D supplementation is not recommended for children or adults. In a recent review of the latest evidence for updated WHO recommendations on antenatal oral vitamin D supplements, the WHO concluded that oral vitamin D supplementation is also not recommended for all pregnant women to improve maternal and

perinatal outcomes.[1] Pregnant women should be advised that sunlight is the most important source of vitamin D and encouraged to receive adequate nutrition through a healthy balanced diet.

Population-based data on vitamin D status are rare, and interpretation of results is complicated by use of different (non-standardized) laboratory methods and the lack of a globally agreed cut-off for vitamin D deficiency or insufficiency. Different cut-offs of the relevant biomarker – serum 25-hydroxy vitamin D (25(OH)D) levels – are used, which create challenges for the implementation of public health programmes and surveillance.

Studies on vitamin D status have been conducted in countries in the Eastern Mediterranean Region that suggest the prevalence of vitamin D deficiency can be particularly high in Middle Eastern countries despite abundant sunshine.[2] Prevalence has been suggested to range from 30% to 90%, depending on the type of study, country, age group and analytical method used. There is also evidence that patterns of vitamin D status among populations in the Region may differ from those in Europe and North America, where existing guidelines relating to vitamin D have been published. Given these concerns about vitamin D status, regional guidance on vitamin D would be useful for WHO's Member States in the Region.

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[1] WHO antenatal care recommendations for a positive pregnancy experience. Nutritional interventions update: vitamin D supplements during pregnancy. Geneva: World Health Organization; 2020 (https://www.who.int/publications/i/item/9789240008120).

[2] Lips P, Cashman K, Lamberg-Allardt C, Bischoff-Ferrari HA, Obermayer-Pietsch B, Bianchi ML et al. Current vitamin D status in European and Middle East countries and strategies to prevent vitamin D deficiency: a position statement of the European Calcified Tissue Society. Eur J Endocrinol. 2019;180(4):23–54. doi:10.1530/EJE-18-0736.

In November 2022, the American University of Beirut (AUB) published vitamin D guidelines for Lebanon.[1] These guidelines comprise recommendations for vitamin D screening and supplementation for the adult population in the country. The guidelines, along with the process used for their development and other initiatives within the Region, could usefully inform the development of regional guidelines.

To inform country actions to improve vitamin D status and to further explore the potential development of regional guidelines on vitamin D, the WHO Regional Office for the Eastern Mediterranean held an expert consultation in Beirut, Lebanon, on 15–16 May 2023. Participants in the hybrid meeting included invited experts and officials from selected countries.

The objectives of the meeting were to:

- provide a summary of global guidance relating to vitamin D;
- disseminate the Lebanese vitamin D guidelines and discuss their applicability to the countries of the Eastern Mediterranean Region; and
- identify research and data gaps on vitamin D nutrition as well as appropriate methodology for obtaining the necessary data.

2. Summary of discussions

Vitamin D status in the Eastern Mediterranean Region

Despite abundant, year-long sunshine in much of the Region, available data suggest that vitamin D deficiency and insufficiency are prevalent due to traditional clothing styles covering most of the body and lack of foods rich in, or fortified with, vitamin D.

[1] The Lebanese vitamin D guidelines. Beirut: American University of Beirut Medical Centre; 2022.

As noted above, the use of different cut-offs in studies conducted in the countries of the Eastern Mediterranean Region affects the credibility and comparability of results. Despite these concerns, available data were presented at the meeting. Data from a small number of countries suggest vitamin D insufficiency amongst pre-school children ranging from 23% to 64%, with deficiency ranging from 6% to 28%. Among school-age children, there is very little data: the Islamic Republic of Iran reports 62% combined vitamin D insufficiency and deficiency; Jordan reports 53% insufficiency and 44% deficiency; and Morocco reports 27% vitamin D insufficiency and 3% deficiency. Among women of reproductive age, vitamin D deficiency levels ranging from 16% to 74% were reported from surveys in seven countries. While the prevalence of vitamin D deficiency among pregnant women was reported as 19% in Sudan and 25% in Pakistan (along with 56% insufficiency).

Among adults over 15 years of age, the prevalence of deficiency was reported to be 41% in males and 63% in females in Saudi Arabia and 33% in males and 17% in women in Kuwait. There was no breakdown of prevalence by age. In the Islamic Republic of Iran, 59% of adults aged between 50 and 60 years were reported to be vitamin D deficient (no breakdown by gender).

The meeting learned that studies in Saudi Arabia and the United Arab Emirates had separately identified that – contrary to the patterns in Europe and North America – vitamin D deficiency is higher in summer than in winter months. A potential explanation is that people spend more time outdoors in the winter months because of the extreme temperatures experienced in Gulf countries during July and August.

The Lebanese vitamin D guidelines

In November 2022, following an extensive guideline development process, the AUB Medical Center published The Lebanese vitamin D guidelines. These guidelines, and the methodology for their development, were presented to the meeting by Dr Ghada El-Hajj Fuleihan, Dr Elie Akl and Dr Marlene Chakhtoura, all from the AUB Medical Center.

The guidelines were drawn up by an Executive Committee from AUB and a guidelines panel, consisting of international and national experts. The process included systematic reviews and meta-analyses conducted by AUB, and use of the Grading of Recommendations, Assessment, Development and Evaluations (GRADE) framework for developing and presenting summaries of evidence and systematically making recommendations. The selected outcome for the reviews was reducing fractures in community-dwelling and institutionalized individuals.

The guideline recommendations are set out below.

Vitamin D alone

There was consistent evidence for the lack of a beneficial effect of vitamin D alone in reducing fractures, for both community-dwelling and institutionalized individuals.

Vitamin D with calcium

Question 1: Should testing for vitamin D deficiency vs. no testing be implemented in adults in Lebanon?

Community-dwelling individuals: The panel suggests no screening for vitamin D deficiency, over screening for vitamin D deficiency, in the community-dwelling Lebanese adult population* (conditional recommendation, based on very low certainty evidence).

Institutionalized individuals: The panel suggests no screening for vitamin D deficiency, over screening for vitamin D deficiency, in institutionalized Lebanese adult population* (conditional recommendation, based on very low certainty evidence).

Question 2: Should vitamin D supplementation (with or without calcium) vs. no supplementation be used in adults in Lebanon?

Community-dwelling individuals: The panel suggests no supplementation with calcium and vitamin D (Ca/D), over supplementation with Ca/D, in the community-dwelling Lebanese adult population* (conditional recommendation, based on moderate certainty evidence).

Institutionalized individuals: The panel suggests supplementation with Ca/D, over no supplementation with Ca/D, in the institutionalized Lebanese adult population (conditional recommendation, based on moderate certainty evidence).

Question 3: What is the optimal vitamin D supplementation dose, if recommended, to specific adult sub-populations?

In the community-dwelling Lebanese adult population for whom there is a decision to supplement with Ca/D, the panel suggests supplementation with the vitamin D daily equivalent of 600–2000 IU, as compared to higher doses > 2000 IU* (conditional recommendation, based on very low certainty evidence).

In the institutionalized Lebanese adult population for whom there is a decision to supplement with Ca/D, the panel suggests supplementation with the vitamin D daily equivalent of 600–2000 IU as compared to higher doses > 2000 IU (conditional recommendation, based on very low certainty evidence).

* Subgroups more/most likely to benefit:

- individuals at high risk of low vitamin D levels (obesity, bariatric surgery, malabsorption, malnutrition, biliary disease, concealed clothing style, dark skin pigmentation, pollution, lactose intolerance, gluten enteropathy, biliary disease, oldest old age);
- individuals with osteoporosis or osteomalacia; and
- individuals on drugs that affect vitamin D metabolism (such as glucocorticoids and anti-epileptics).

Since the launch in November 2022 of the guidelines, a dissemination plan has been enacted. This includes dissemination to the Ministry of Public Health, the scientific community at national and regional levels, health insurers, nongovernmental organizations and the general public. There is also a plan for implementation of the guidelines in the country's 292 primary health care centres. The long-term subsidization protocol – the country's reimbursement programme – will be revised, along with other primary care guidelines, to align with the vitamin D guidelines for adults. In addition, there will be capacity-building for primary health care staff, and compliance with the vitamin D guidelines will be monitored through the administrative registration system.

In discussion, it was noted that because of the gaps in the evidence, the recommendations were presented as conditional – rather than strong – recommendations. It was suggested that this language is problematic for policy-makers and that it can be difficult to take strong policy action based on a conditional recommendation. The reality, however, is that data are sparse and there remains a need to develop much stronger evidence, so the recommendations have to be conditional. At the same time, it is important to use the dissemination of guidelines to highlight the huge evidence gap and stimulate further research.

There was some discussion of the impact of genetic polymorphisms and vitamin D metabolism, but it was suggested that the impact of such genetic differences is fairly small compared to lifestyle factors (diet and sun exposure).

It was noted that the evidence base is dominated by studies on Caucasian populations. There is a need to further develop the evidence, with studies on multiple skin types and different ethnic populations, to be able to develop guidelines that better address entire populations and specific ethnic groups.

It was also suggested that, when considering the development of regional guidelines, it is important to take into account some important differences across the Region. The climate in Lebanon, for example, is very different from that in the Gulf countries. It was suggested that a regional framework for guidelines could be developed, and then adapted to different national contexts.

The importance of distinguishing between guidelines that relate to individuals and population-level guidelines was highlighted. It was suggested that further clarity would be needed about the recommendations relating to supplementation and "institutionalized individuals". The question of whether this relates to everyone in institutions was raised and whether it extends to older people more generally – further clarity is needed on this.

The fact that these guidelines relate to adults (and institutionalized adults) was raised, and the importance of conducting a similar exercise for different population groups – such as infants, children, and pregnant and lactating women – was highlighted.

It was suggested that the guidelines placed insufficient emphasis on diet as a source of vitamin D. It was clarified that this is addressed in the executive summary. It was suggested that more prominent messaging on the importance of diet would be advisable in any regional or other national guidelines.

It was agreed that the guidelines, and the work to prepare them, are extremely welcome and are valuable to countries throughout the Region. There is a need for further work on specific population groups and for each country to contextualize the data – in collaboration with national experts and civil society – to define an appropriate context-specific approach.

Vitamin D guidance in the Eastern Mediterranean Region: Experience from Saudi Arabia, Kuwait and United Arab Emirates

The meeting heard from representatives of different Member States on the vitamin D status in their countries and national approaches to address vitamin D deficiency.

In Saudi Arabia, vitamin D deficiency continues to be an important health problem, although the prevalence of deficiency does seem to be decreasing. There are high levels of public awareness of the importance of vitamin D for bone health and cutaneous synthesis. Taking vitamin D supplements is becoming increasingly common. Seasonal variation in vitamin D deficiency has been observed, with deficiency more common in summer months – and there has been some suggestion that supplementation during summer months could be considered as a recommendation. Modelling results suggest that increasing everyone's serum 25(OH)D levels to a level of 30 nmol/L or above could lead to considerable reductions in the risk of cardiovascular diseases.

A consensus for the assessment and management of vitamin D deficiency for the Gulf Cooperation Council (GCC) countries was published in 2020. This consensus was developed by a group of experts, representing all six GCC Member States. The experts agreed that the prevalence of vitamin D deficiency appears to be higher in the Middle East than in Western or Eastern countries. The group reached a consensus that the cut-off for deficiency should be < 50 nmol/L serum 25(OH)D, with sufficiency for the general population at > 50 nmol/L, but > 75 nmol/L should be the target for frail, osteoporotic and older individuals. The experts concluded that widescale testing is not justified in practical and economic terms, and the consensus does not endorse population-based screening and only recommends limited testing for the populations at highest risk. The consensus recommended that all

laboratories should be accredited for standardized vitamin D measurement. In addition, the consensus contains recommendations on the ideal times of the day for sun exposure in summer (9–10.30 am and 2–3 pm) and winter (10 am–2 pm) and highlights dietary sources. In addition, it recommends the doses for supplementation, where required, in different age groups.

Recent surveys in Kuwait have identified risk factors for having lower levels of serum 25(OH)D. These include gender (being female), lower parental education, higher BMI, not walking to and from school, more time spent indoors, wearing sunscreen and staying in the shade. For older adults, low duration of sun exposure was identified as a risk factor. The Kuwait Osteoporosis Society has issued some recommendations for monitoring vitamin D status and management of vitamin D deficiency. This includes recommendations for frequency of testing of at-risk individuals, to reduce over-frequent prescribing of testing.

Vitamin D levels in the United Arab Emirates are the lowest among the GCC countries and, as in Saudi Arabia, vitamin D levels were higher in winter than in summer. Dr Afrozul Haq and colleagues issued clinical guidelines for vitamin D in United Arab Emirates in 2018, intended for use by physicians in the United Arab Emirates and GCC Member States.[1]

Recommending Vitamin D intake requirements

An overview of current recommended vitamin D intakes was presented to the meeting, along with an outline of an approach to estimating intake requirements from serum 25(OH)D levels based on individual study participant data. Estimated vitamin D intake requirements are based on

[1] Haq A, Wimalawansa SJ, Pludowski P, Al Anouti F. Clinical practice guidelines for vitamin D in the United Arab Emirates. J Steroid Biochem Mol Biol. 2018;175: 4–11. doi:10.1016/j.jsbmb.2016.09.021.

the dose–response relationship between total vitamin D intake (dietary intake and supplements) and serum 25(OH)D levels. The method based on individual participant data enables the variability between individuals, in terms of their response to a particular intake of vitamin D, to be fully taken into account.

Based on work by Dr Kevin Cashman and colleagues in 2017 that drew on individual participant data from seven randomized controlled trials (RCTs), 97.5% of the population would require a total vitamin D intake of 26 or 28 µg/day, depending on age, to have a serum 25(OH)D level of 50 nmol/L or over (or 13 µg/day for 30 nmol/L of 25(OH)D). This is considerably higher than, for example, the estimates of 15 µg/day to achieve 50 nmol/L serum 25(OH)D by the United States' Institute of Medicine (for those under 70 years only) and the European Food Safety Agency. The seven RCTs used for this work were largely conducted on light-skinned populations and further work has estimated that the equivalent intakes in dark-skinned populations would be much higher.

There was clarification that all the data shown were collected using a standardized methodology. Further work done in this area must also be done, wherever possible, using standardized data to eliminate any differences due to methodology. This can be done by contacting the original study authors and, if blood samples remain available, having the samples reanalysed by an accredited laboratory.

There was also clarification that the studies from which these data were obtained were conducted in winter in North America or Europe, so there would be little or no contribution of sun exposure to vitamin D levels. This means that the recommended intakes may not be needed in situations where there is greater sun exposure. For the Eastern Mediterranean Region, if a similar exercise were to be conducted it

would need to take into account the high levels of UVB and the uncertainties about sun exposure and seasonal variation.

Draft action plan and way forward on vitamin D guidelines at the regional level

In discussion, the importance of involving a wide range of stakeholders in taking forward work on vitamin D in the Region was emphasized, as was the need to adopt a multisectoral approach. National champions for action on vitamin D (or micronutrients in general) were identified as being an important asset. The need to engage political leaders was also underlined.

The importance of issuing guidance that is clear and not open to misinterpretation and misrepresentation was noted. The need for a clear distinction between clinical guidelines and public health guidance was highlighted, as was the need for consensus and clarity on cut-offs for vitamin D deficiency/insufficiency and sufficiency.

It was noted that setting a "trigger point" for vitamin D deficiency at the community level (the prevalence rate that necessitates action from policy-makers) can be useful, and that any number equal to or above 50% warrants immediate action, no matter what the criterion may be.

It was observed that calcium and vitamin D co-supplementation can be justified only in those without adequate calcium intake. There are dietary sources to obtain enough calcium but not for vitamin D (at least in many food cultures). Taking more calcium than the body needs through pills can be harmful in the long term.

The importance of food systems transformation, to ensure access to healthy diets and to promote dietary diversity, was pointed out. The role of staple food fortification was also raised.

There was a clear call that governments receive WHO support and expert advice on the most appropriate actions to take for vitamin D. The value of Member State collaboration, with WHO support, was underlined. The experience with food composition databases was given as a positive example of such cooperation within the Region, which has been a very fruitful area of collaboration.

3. Conclusions

- Meeting participants congratulated the American University of Beirut and Lebanon for the development of the national guidelines on vitamin D.
- Food systems transformation to deliver affordable healthy diets is central to the work of the United Nations system, including supporting agri-food businesses, farmers and food value chains to provide healthy foods.
- There is an urgent need for evidence-based guidance on both public health and clinical practices on vitamin D deficiency in the Eastern Mediterranean Region.
- There is a great need for population-specific studies in the Eastern Mediterranean Region to focus on the physiology, regulatory mechanisms and significant thresholds for vitamin D.
- Vitamin D levels in patients should be well thought-out and be interpreted from the perspective of the overall clinical picture and the individual’s risk of deficiency.

4. Recommendations

To Member States

1. Raise awareness and promote behaviour change among key stakeholders to promote diet diversification (e.g. to promote the supply of mushrooms which are rich in both protein and vitamin D).
2. Promote reasonable sun exposure as a cheap source of vitamin D to encourage healthy eating habits and enforce fortification with vitamin D within safe margins.
3. Only test symptomatic or persons at risk for vitamin D deficiency, in accordance with current guidelines.
4. No recommendations for population-wide screening for vitamin D insufficiency and deficiency using 25(OH)D are advised.
5. Specific recommendation to Lebanon: The participatory, multisectoral and multi-ministerial approach is key for addressing micronutrient deficiencies.

To WHO

6. Share Lebanon's national guidelines on vitamin D with other countries in the Eastern Mediterranean Region.
7. Develop regional guidelines on vitamin D, targeting all age groups, to avoid duplication of efforts and build on existing resources in different Member States.
8. To advance the prevention and treatment of vitamin D deficiency in the Region:
   - conduct a mapping exercise for interested stakeholders;
   - define the scope of work (set the agenda); and
   - collaborate on primary research and the development of guidelines.

9. Create a shared folder that includes the meeting's PowerPoint presentations and technical documents, and all WHO resources relating to vitamin D (both global and regional).
10. Move forward with the development of a regional technical guide on vitamin D, focusing on cut-offs, management goals, method standardization, fortification and other dietary strategies. Invite meeting participants and other experts to contribute to the development of the technical guide, with support from WHO. A provisional outline for the technical guide is proposed:
    - vitamin D nutritional survey;
    - vitamin D food fortification;
    - vitamin D quality assurance programmes for assay standardization and fortification monitoring; and
    - vitamin D guidelines: the framework and paradigm.
11. Establish a regional network on vitamin D, including research centres, academia and governments.
12. Provide guidance that is clear for both policy-makers and technical experts and covers all age groups.
13. Work with other United Nations agencies to support national ministries of health to develop a fortification project at the national level, based on the results of national surveys (which should be planned this year).

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