GUIDELINE: 1 FORTIFICATION OF RICE WITH VITAMINS AND MINERALS AS A PUBLIC HEALTH STRATEGY

EXECUTIVE SUMMARY

Fortification of staple foods, when appropriately implemented, can be an efficient, simple and inexpensive strategy for supplying additional vitamins and minerals to the diets of large segments of the population. Rice is cultivated in many parts of the world, as it grows in diverse climates. Industrial fortification of rice with vitamins and minerals has been practised for many years in several countries in the World Health Organization (WHO) Eastern Mediterranean Region, Western Pacific Region and Region of the Americas, where rice is a staple consumed regularly in the preparation of many common local dishes.

Decisions about the types and amounts of nutrients to add to fortified rice are commonly based on the nutritional needs and gaps in dietary intake of the target populations; the usual level of consumption of rice; the sensory and physical effects of the fortificant on the rice kernels; the fortification processing used in the production of the fortified kernels; the availability and coverage of fortification of other staple food vehicles; the population consumption of vitamin and mineral supplements; the costs; the feasibility of implementation; and the acceptability to the consumers.

Rice kernels can be fortified with several micronutrients, such as iron, folic acid and other B-complex vitamins,² vitamin A and zinc – some are used for restitution of the intrinsic nutritional contents prior to milling and others are used for fortification purposes. Their bioavailability will depend, importantly, on the processing used in the production of the fortified kernels.

PURPOSE OF THE GUIDELINE

This guideline provides global, evidence-informed recommendations on the fortification of rice with micronutrients, as a strategy to improve the health status of populations.

It aims to help Member States and their partners to make informed decisions on the appropriate nutrition actions to achieve the 2030 <u>Sustainable Development Goals</u>³ and the global targets set in the <u>Comprehensive implementation plan on maternal, infant and young child nutrition</u>.⁴

The recommendations in this guideline are intended for a wide audience, including policy-makers, their expert advisers, and technical and programme staff in ministries and organizations involved in the design, implementation and scaling up of nutrition actions for public health.

The guideline complements the WHO/FAO (Food and Agriculture Organization of the United Nations) <u>Guidelines on food fortification with micronutrients</u>⁵ and the Pan American Health Organization document, <u>Iron compounds for food fortification: guidelines for Latin America and the Caribbean 2002</u>.⁶

This publication is a World Health Organization (WHO) guideline. A WHO guideline is any document, whatever its title, containing WHO recommendations about health interventions, whether they be clinical, public health or policy interventions. A recommendation provides information about what policy-makers, health-care providers or patients should do. It implies a choice between different interventions that have an impact on health and that have ramifications for the use of resources. All publications containing WHO recommendations are approved by the WHO Guidelines Review Committee.

² The B-complex vitamins include B₁, thiamine; B₂, riboflavin; B₃, niacin; B₆, pyridoxine; B₉, folate; and B₁₂, cyanocobalamin. Thiamine, riboflavin, niacin and folic acid are commonly referred to by name, and their names are used throughout this document; the others are referred to by vitamin number.

³ Sustainable Knowledge Development Platform. Sustainable Development Goals (https://sustainabledevelopment.un.org/sdgs).

Comprehensive implementation plan on maternal, infant and young child nutrition. Geneva: World Health Organization; 2014 (WHO/NMH/NHD/14.1; http://apps.who.int/iris/bitstream/handle/10665/113048/WHO_NMH_NHD_14.1_eng.pdf?sequence=1).

⁵ Allen L, de Benoist B, Dary O, Hurrell R, editors. Guidelines on food fortification with micronutrients. Geneva: World Health Organization and Food and Agriculture Organization of the United Nations; 2006 (http://apps.who.int/iris/bitstream/handle/10665/43412/9241594012 eng.pdf?sequence=1).

⁶ Dary O, Freire W, Kim S. Iron compounds for food fortification: guidelines for Latin America and the Caribbean 2002. Nutr Rev. 2002;60(7):550–61. doi:10.1301/002966402320285218.

SUMMARY OF THE EVIDENCE

A Cochrane systematic review on fortification of rice with vitamins and minerals for addressing micronutrient malnutrition included 16 studies (14 267 participants). The search strategy was conducted in 2012 and updated in 2017. Twelve were randomized controlled trials (5167 participants) with 10 involving children in urban and rural settings and two studies involving non-pregnant non-lactating women. Four studies were controlled before-and-after studies (9100 participants). The 16 selected studies reported fortification with iron. Of these, six studies fortified rice with iron only; in 10 studies, other micronutrients were added (iron, zinc and vitamin A, and folic acid). Five studies provided other B-complex vitamins. The control for all trials was unfortified rice. The iron content ranged from 0.2 mg to 112.8 mg/100 g uncooked rice, given for a period varying from 2 weeks to 48 months.

The review showed that the provision of rice fortified with vitamins and minerals including iron, when compared with unfortified rice, probably improves iron status by reducing the risk of iron deficiency by 35% and increasing the average concentration of haemoglobin by almost 2 g/L, but may not make a difference to the risk of anaemia in the general population of those aged over 2 years. When the fortification of rice includes vitamin A, it may reduce both iron deficiency and vitamin A deficiency. When fortification includes folic acid, fortified rice may slightly increase serum folate concentrations.

In addition to the direct and indirect evidence (vitamins and minerals delivered using food vehicles other than rice) and its overall quality, other considerations were taken into account by the guideline development group, to define the direction and strength of the recommendations. They included values and preferences of the populations related to fortification of rice in different settings; trade-off between benefits and harms; costs; and feasibility.

For developing the recommendations, the guideline development group considered the certainty of the existing evidence, values and preferences, costs, baseline prevalence of anaemia and/or other nutritional deficiencies, equity, and the feasibility of implementation.

The Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach defines the overall rating of confidence in the body of evidence from systematic reviews as the extent to which one can be confident of the effect estimates across all outcomes considered critical to the recommendation. Each of the critical outcomes had a confidence rating based on certainty of evidence – high, moderate, low or very low. High-certainty evidence indicates confidence that the true effect lies close to that of the estimate of the effect. Moderate-certainty evidence indicates moderate confidence in the effect estimate and that the true estimate is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different. Low-certainty evidence indicates that confidence in the effect estimate is limited and the true effect may be substantially different from the estimate of the effect. Very low-certainty evidence indicates very little confidence in the effect estimate and the true effect is likely to be substantially different from the estimate of effect.

RECOMMENDATIONS

- Fortification of rice with iron is recommended as a public health strategy to improve the iron status of populations, in settings where rice is a staple food (strong recommendation, moderate-certainty evidence).
- Fortification of rice with vitamin A may be used as a public health strategy to improve the iron status and vitamin A nutrition of populations (conditional recommendation, low-certainty evidence).
- Fortification of rice with folic acid may be used as a public health strategy to improve the folate nutritional status of populations (conditional recommendation, very low-certainty evidence).

REMARKS

The remarks in this section are intended to give some considerations for implementation of the recommendations, based on the discussion of the guideline development group.

- The number and amounts of nutrients should be adapted according to the needs of the
 country. If other fortification programmes with other food vehicles (i.e. wheat flour, maize
 flour or corn meal) and other micronutrient interventions are jointly implemented effectively,
 these suggested fortification levels need to be adjusted downwards as necessary. A combined
 fortification strategy using multiple vehicles appears to be a suitably effective option for
 reaching all segments of the population.
- There are several methods available for the fortification of rice. The method chosen depends
 on the local technology available, costs and other preferences. The process of adding nutrients
 to rice through dusting reduces the number of nutrients consumed in settings where rice is
 commonly washed before cooking. In particular, washing and cooking practices among
 a population are important considerations in selecting a method for fortification of rice. For
 example, rinse-resistant methods to ensure that nutrients are retained after washing will be
 important if rice is commonly washed before cooking.
- Rice milling results in the loss of a significant proportion of B vitamins and minerals that are
 found predominately in the outer germ and bran layers. Nutrient losses during milling can be
 minimized by a process called parboiling, in which raw rice is soaked in water and partially
 steamed before drying and milling, resulting in some of the B vitamins migrating further into
 the grain.
- Since some of the fat- and micronutrient-rich bran layers are removed during rice milling, the
 restoration of thiamine, niacin and riboflavin in the fortification profile should remain a regular
 practice in fortification.

A staple food, or simply a staple, is a food that is consumed regularly and provides an important proportion of the energy (calories) and nutrient requirements. Its preparation is variable in different contexts and is closely linked to the most available foods in each place.

A strong recommendation is one for which the guideline development group is confident that the desirable effects of adherence outweigh the undesirable effects. Implications of a strong recommendation are that most people in these settings would desire the recommended fortification of rice with iron and only a small proportion would not. For policy-makers, a strong recommendation indicates that the recommendation can be adopted as policy in most situations.

³ A conditional recommendation is one for which the guideline development group concludes that the desirable effects of adherence probably outweigh the undesirable effects, although the trade-offs are uncertain. Implications of a conditional recommendation for populations are that while many people would desire fortification of rice with vitamins and minerals, a considerable proportion would not. With regard to policy-makers, a conditional recommendation means that there is a need for substantial debate and involvement from stakeholders before considering the adoption of fortification of rice with these vitamins and minerals in each setting.

- The prevalence of depletion and deficiency of vitamin B_{12} is high in all age groups, reaching 50% in some countries. The inclusion of vitamin B_{12} is recommended when staples are fortified with folic acid, to avoid the masking effect of folic acid on vitamin B_{12} deficiency.
- Fortification of rice with iron has been a challenge, since most of the bioavailable iron powders used in food fortification are coloured, which produces changes in the aspect of fortified kernels compared to unfortified ones. Ferric pyrophosphate been the choice for rice fortification because it is a white powder, although its bioavailability is low.¹ In human absorption studies, the addition of enhancing compounds such as citric acid/trisodium citrate mixtures has been linked to an increase in iron absorption from ferric pyrophosphate.²
- Mandatory rice-fortification programmes can only be effective if they are properly implemented and legislation enforced.
- Food fortification should be guided by national standards, with quality-assurance and quality-control systems to ensure quality fortification. Continuous programme monitoring should be in place, as part of a process to ensure high-quality implementation. Monitoring of consumption patterns and evaluation of micronutrient status in the population can inform adjustment of fortification levels over time.
- Rice fortification on a national scale requires a large, cost-effective and sustainable supply of fortified kernels.
- In malaria-endemic areas, the provision of iron through rice fortification as a public health strategy should be done in conjunction with public health measures to prevent, diagnose and treat malaria.
- Behaviour-change communication strategies may be necessary for overcoming barriers and creating and maintaining demand for fortified rice.

RESEARCH PRIORITIES

During discussions in the WHO technical meeting on rice fortification, the WHO guideline development groups and the external review group highlighted the limited evidence available in some knowledge areas, meriting further research on the fortification of rice, particularly in the following areas:

- the bioavailability of different iron compounds for use in food fortification, including mixtures of different compounds and the development of bioavailable iron compounds that do not change the colour of the rice grain;
- · the effects of different phytate contents on the absorption of iron from the premix formulation;
- the efficacy and effectiveness of rice fortification with nutrients other than iron in country/ programme settings, and for different age and sex groups;

Moretti D, Zimmermann MB, Wegmüller R, Walczyk T, Zeder C, Hurrell RF. Iron status and food matrix strongly affect the relative bioavailability of ferric pyrophosphate in humans. Am J Clin Nutr. 2006;83(3):632–8. doi:10.1093/ajcn.83.3.632.

Hackl L, Cercamondi C, Zeder C, Wild D, Adelmann H, Zimmermann M et al. Cofortification of ferric pyrophosphate and citric acid/trisodium citrate into extruded rice grains doubles iron bioavailability through in situ generation of soluble ferric pyrophosphate citrate complexes. Am J Clin Nutr. 2016;103(5):1252–9. doi:10.3945/aicn.115.128173.

- determination of appropriate levels and combinations of nutrients and their interactions, the stability of micronutrient compounds, and their physical properties and acceptability to consumers;
- the stability of different micronutrients and compounds in different cooking processes that are context specific;
- the relative bioavailability among different chemical forms of various micronutrients that can be used in rice fortification, including nutrient–nutrient interactions;
- the acceptability of changes, if any, in organoleptic characteristics with different micronutrient combinations for different fortified-rice preparations and cooking methods;
- the most appropriate delivery platforms for reaching the intended target population;
- the effectiveness of different methods for fortification of rice in different contexts;
- validated assays for measuring the vitamin and mineral content in fortified rice.

GUIDELINE DEVELOPMENT METHODOLOGY

WHO developed the present evidence-informed recommendations using the procedures outlined in the <u>WHO handbook for guideline development</u>.¹ The steps in this process included: (i) identification of priority questions and outcomes; (ii) retrieval of the evidence; (iii) assessment and synthesis of the evidence; (iv) formulation of recommendations, including research priorities; and planning for (v) dissemination; (vi) equity, human rights, implementation, regulatory and ethical considerations; as well as (vii) impact evaluation and updating of the guideline. The Grading of Recommendations Assessment, Development and Evaluation (<u>GRADE</u>) methodology was followed, to prepare evidence profiles related to preselected topics, based on up-to-date systematic reviews and other narrative synthesis of the evidence.

The guideline development groups consisted of content experts, methodologists and representatives of potential stakeholders and beneficiaries. For developing this guideline, one guideline group participated in a meeting held in Geneva, Switzerland on 22–25 February 2010, where the guideline was scoped. A second guideline group participated in a meeting held in Cancun, Mexico, on 3–6 November 2014, to discuss the evidence and finalize the recommendations. Additionally, WHO convened a non-normative dialogue with stakeholders, to discuss technical considerations for rice fortification in public health, on 9 and 10 October 2012, in Geneva, Switzerland. The objective of this dialogue was to review the industrial and regulatory technical considerations in rice fortification, as well as the considerations for implementing it as a public health strategy and assuring equitable access and universal coverage. External experts, as resource persons, assisted the guideline development group during the guideline development process, in presenting the evidence and identifying research priorities. Four technical experts were invited to peer-review the draft guideline.

WHO handbook for guideline development, second edition. Geneva: World Health Organization; 2014 (http://apps.who.int/medicinedocs/documents/s22083en.pdf).

PLANS FOR UPDATING THE GUIDELINE

The WHO steering group will continue to follow research developments in the area of rice fortification, particularly for areas in which the evidence was limited and its certainty was found to be low or very low. If the guideline merits an update, or if there are concerns about the validity of the guideline, the Department of Nutrition for Health and Development, in collaboration with other WHO departments or programmes, will coordinate the guideline update, following the formal procedures of the WHO handbook for guideline development.

As the guideline nears the 10-year review period, the Department of Nutrition for Health and Development at the WHO headquarters in Geneva, Switzerland, along with its internal partners, will be responsible for conducting a search for appropriate new evidence.

WHO handbook for guideline development, second edition. Geneva: World Health Organization; 2014 (http://apps.who.int/medicinedocs/documents/s22083en.pdf).