

## Invited Commentary

# Flour fortification as a strategy to prevent anaemia

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National wheat flour fortification programmes were introduced in the USA and Europe in the 1940s as a way to combat deficiencies of Fe and certain B vitamins. At that time, Fe deficiency (ID) was the major cause of anaemia and Fe-fortified wheat flour was introduced as a preventive measure. Since then, about eighty countries worldwide have introduced national wheat flour fortification programmes with Fe and a range of other micronutrients. However, none of the national wheat flour fortification programmes has been rigorously evaluated with respect to their impact on Fe status and anaemia, and although Fe-deficiency anaemia (IDA) levels are now low in the USA and Europe, this could be due to an increased consumption of animal tissue foods as the populations became more prosperous. Additionally, as new research findings on Fe fortification have emerged, there is now uncertainty concerning the effectiveness of national wheat flour fortification programmes<sup>(1)</sup>. In 2009, the WHO<sup>(2)</sup> recommended Fe compounds and fortification levels for flour fortification based on published research findings. The new evidence included results from well-controlled efficacy studies<sup>(1)</sup> showing improvements in the Fe status of women and children consuming Fe-fortified foods for at least 6 months, expected flour consumption patterns in individual countries, and the reported bioavailability of Fe compounds in humans. The early wheat flour fortification programmes were based on the restoration of the Fe level in low-extraction white flour to that in wholegrain flour. Unlike the current recommendations, the defined fortification level did not take into account the amount of Fe lacking in the diet, the bioavailability of the selected Fe compound, or the daily flour consumption. When the current national Fe fortification programmes were evaluated with respect to the new WHO recommendations, it was concluded that only nine of the seventy-eight wheat flour fortification programmes would be expected to improve the Fe status<sup>(1)</sup>.

Barkley *et al.*<sup>(3)</sup> used the national data on anaemia prevalence in non-pregnant women in selected countries fortifying flour to address the concern over the impact of national flour fortification programmes on anaemia prevalence. They have now provided for the first time good evidence that anaemia prevalence can be reduced in countries fortifying flour. The authors compared the national data on anaemia prevalence in twelve countries before and at least 2 years after the introduction of wheat or maize flour fortification programmes. After adjusting for the Human Development Index and malaria, they showed that each year of consuming flour fortified with Fe, folic acid, vitamin A and vitamin B<sub>12</sub> was associated with a 2.4% decrease in the odds of anaemia

prevalence. Although all the four micronutrients can influence Hb concentrations, Fe would be expected to have had the major impact on anaemia prevalence. Folic acid, vitamin A and vitamin B<sub>12</sub> are not added to flour to prevent anaemia but are added to flour to prevent the more specific deficiency symptoms linked to lack of these micronutrients. The authors also evaluated anaemia prevalence in non-pregnant women in a further twenty countries that have never introduced fortified flour programmes, and reported no decrease in the odds of anaemia prevalence over a similar time period.

These findings are very encouraging as they confirm that Fe-fortified flour is a useful public health intervention; however, they need to be interpreted carefully as they only confirm that Fe-fortified flour programmes can decrease IDA prevalence at the national level, provided the programmes follow the WHO recommendations on Fe fortification compounds<sup>(2)</sup> and follow general recommendations on setting up Fe fortification programmes<sup>(4)</sup>. It should be noted that Fe fortification of foods is technically difficult<sup>(4)</sup>, and there are further hurdles to overcome if Fe-fortified flour is to successfully prevent IDA on a broader international scale. The main problem of adding Fe to flour is unacceptable sensory changes to the flour. These can develop during storage if water-soluble (more bioavailable) Fe fortification compounds catalyse the oxidation of flour lipids. Water-soluble Fe compounds can also cause unacceptable colour changes to some foods prepared from the fortified flour. Another major hurdle is that cereal flours are rich in phytic acid, a potent inhibitor of Fe absorption, and its presence must be taken into account when defining Fe fortification levels. The WHO-recommended Fe compounds for fortification are ferrous sulphate, ferrous fumarate, sodium EDTA (NaFeEDTA) and electrolytic Fe powder. NaFeEDTA is the preferred compound as it is the only Fe fortificant that can overcome the inhibition of phytic acid on Fe absorption; however, it is the most expensive of the recommended compounds. Because of its higher bioavailability, it is recommended to add half as much Fe from NaFeEDTA as from sulphate or fumarate. Conversely, owing to the lower absorption of electrolytic Fe powder, the recommendation is to add twice as much Fe from electrolytic Fe powder as from sulphate or fumarate.

Millers have generally preferred to add Fe powders to cereal flours as they cause little or no sensory changes and are the least expensive. Today, a major concern with national wheat flour fortification programmes is that many millers are fortifying with low levels of non-recommended, poorly

absorbed Fe powders. This practice is permitted by the national legislation, which was made before the new WHO recommendations and is not yet updated. The use of different elemental Fe powders originated from the USA, where the regulations do not stipulate the type of elemental Fe powder to be added. Currently, five elemental Fe powders (electrolytic, H-reduced, CO-reduced, carbonyl and atomised), manufactured by different processes, are available for flour fortification. Of these powders, atomised and H-reduced are commonly used. They are less expensive than electrolytic Fe powder, but have lower bioavailability and have not been demonstrated to effectively improve the Fe status in women or children.

A closer look at flour fortification programmes in the countries evaluated by Barkley *et al.*<sup>(3)</sup> shows that they were mostly mandatory and that most, but not all, programmes followed the WHO recommendations on Fe fortification of flour<sup>(2)</sup>. Mandatory programmes are considered more likely to succeed than voluntary programmes<sup>(4)</sup>. Of the twelve countries, eight evaluated fortified flour with the WHO-recommended Fe compounds. Bolivia, Costa Rica, Honduras, Nicaragua and Senegal use fumarate; Jordan and Mexico use sulphate; and Indonesia uses electrolytic Fe powder<sup>(1)</sup>. Fiji and the Philippines permit H-reduced Fe powder, and Peru and Uzbekistan do not specify the Fe compound. The recommended fortification levels are also more or less respected. However, wheat flour consumption in the Central American countries, Mexico and Indonesia is relatively low, indicating that other food vehicles may also be needed for Fe fortification if the Fe status of at-risk populations is to be improved nationally. For example, Costa Rica replaced H-reduced Fe with fumarate in wheat flour in 2002 and, about the same time, fortified maize flour and powdered milk with ferrous bisglycinate. Anaemia prevalence in Costa Rica between 1996 and 2009 has recently been reported to have decreased from 18 to 10% in women and from 19 to 4% in children<sup>(5)</sup>.

Another important issue that needs to be considered is that Barkley *et al.*<sup>(3)</sup> used Hb and anaemia prevalence as the measures of Fe status. This is only valid if ID is the cause of anaemia, and ID is responsible for only about half of the global anaemia burden<sup>(6)</sup>. Anaemia has up to seventeen different aetiologies, the most important being ID due to insufficient dietary Fe absorption, haemoglobinopathies, and inflammation and blood loss due to infections in tropical countries<sup>(6)</sup>. Infections such as malaria, hookworm and schistosomiasis can be as important as ID as a cause of anaemia in some countries in sub-Saharan Africa and Asia. The anaemia of infection can only be prevented by infection control and not by Fe fortification. Many individuals in tropical countries may have anaemia due to more than one cause, and this anaemia can only be prevented or treated by combining interventions targeting both infections and ID. In the evaluation by Barkley *et al.*<sup>(3)</sup>, many more of the control non-fortification countries, than of the fortification countries, would be expected to have anaemia caused by malaria and other infections. For example, the twenty non-fortification countries included eight Sub-Saharan countries, Madagascar and Cambodia, where the risk of malaria is high. In contrast,

only one of the eight fortification countries (Senegal) would be expected to have similar levels of infections.

In conclusion, wheat flour fortification with Fe is technically difficult and to have an impact on the Fe status, programmes must be carefully set up and rigorously monitored, with mandatory programmes more likely to succeed than voluntary programmes. Until the evaluation of Barkley *et al.*<sup>(3)</sup>, we have had little proof that national flour fortification programmes can improve the Fe status, and that they can be usefully used as a public health measure to prevent IDA. However, it should be noted that they cannot prevent or treat anaemia caused by infections and inflammation, which are common in tropical countries. As the fortification countries evaluated by Barkley *et al.*<sup>(3)</sup> mostly conformed to the WHO recommendations on Fe fortification of flour, the study confirms that if these WHO recommendations are followed, the prevalence of IDA can decrease. However, as most of the other eighty countries that fortified flour did not follow the WHO recommendations, many of these national flour fortification programmes would be expected to have little or no effect on the Fe status or IDA prevalence in their populations. Therefore, there is an urgent need for many countries (including the UK) to update antiquated national flour fortification legislation to conform to the more recent WHO recommendations on Fe compounds and fortification levels.

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