

Considerations for the safe and effective use of iron interventions in areas of malaria burden:

Interventions

Technical Working Group

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Intervention Strategies



Dietary modification?



Iron supplements?



Screen?



Home fortification?



Central fortification?



Delayed cord clamping?

Dietary Modification

- Increased iron bioavailability of traditional foods
 - Germination (50-64% reduction in phytate)
 - Microbial fermentation (up to 90% reduction in phytate)
 - Soaking (47-98% reduction in phytate)
 - Addition of ascorbic acid-containing foods
- Increased consumption of iron-rich foods.
- Use of iron cooking pots.



Is dietary modification effective and safe?

- Traditional food processing may increase Fe bioavailability, but does not sufficiently raise Fe intakes of young children.
- Dietary diversification, while important for overall dietary quality, is generally unsuccessful at closing the Fe gap for young children.
- Fe-rich animal source foods are expensive and often unavailable.
- Use of Fe pots has had limited success. Excess Fe content (e.g. fermented beverages) may be a risk.
- **In Summary:** It is unlikely that dietary modification strategies alone will be sufficient in most low-income populations.

Research priorities for dietary modification interventions

- Define the conditions under which dietary modification can be effective.
- Determine the safety of dietary strategies (e.g. use of Fe cooking pots) in areas with malaria.

Food Fortification

- Addition of Fe to commonly consumed foods, beverages, condiments.
 - *Centrally fortified food: Fe added at time of processing*
 - *Home or “point-of-use” fortification: Fe added to meals just before consumption*



Are centrally-processed iron-fortified foods effective and safe?

- With careful choice of the Fe compound and amount added, fortification can improve Fe status of all at-risk groups.
- However, products have not been developed for pregnant women and the higher Fe level needed may cause sensory changes.
- Although centrally processed fortified complementary foods are convenient, it is difficult to meet Fe needs for all children in the target age range with a single formulation.
- There is no evidence that centrally processed Fe-fortified foods are *not* safe, but no studies have focused on safety in malarial areas.
- There are few examples of widespread application of the approach in developing countries. The recent WHO food fortification guidelines should improve this situation.

Is home fortification effective and safe?

- Home fortification mixtures with appropriate amounts of absorbable Fe compounds can be formulated to improve or maintain the Fe status of infants, children, pregnant and non-pregnant women.
- In children, highly effective at reducing Fe deficiency (RR 0.44 [0.22, 0.86]) and anemia (RR 0.54 [0.46, 0.64]).
- There is no evidence that home fortification is *not* safe, but no studies have focused on safety in malaria-endemic areas.

Research priorities for food fortification (central or home-based) in areas of malaria

- Conduct studies in malaria-endemic areas to establish the safety of Fe administration through food fortification.
- Evaluate efficacy of fortified foods in populations with high disease prevalence, given that malaria and other infections may reduce Fe absorption.

Iron Supplementation

- Delivery of medicinal Fe orally in the form of pills or liquids, usually consumed in the absence of food.



Is iron supplementation effective and safe?

- Fe supplementation prevents and ameliorates nutritional Fe-deficiency in children and pregnant women.
- However, providing Fe supplements in liquid or tablet form may increase the incidence, and possibly the severity, of malaria (and other infections) among Fe-replete children.
- In pregnant women, increased placental malaria has been demonstrated with intravenous infusions and is suspected with Fe supplements but has not been demonstrated in the few studies available.

Research priorities for iron supplementation

- Evaluate the safety and efficacy of administering Fe supplements with food rather than between meals.
- Develop a slow release Fe supplement. This assumes that adverse effects are due to a mechanism related to increased non-transferrin-bound iron (NTBI), and that Fe absorbed over a longer period of time would reduce NTBI.
 - Re-visit the viability and feasibility of the Gastric Delivery System

Delayed cord clamping

- Delay clamping of the umbilical cord by 2 to 3 minutes.
- Results in a greater transfusion of placental blood to the infant.
- Increases the total body Fe content of the infant at birth (+ ~75 mg Fe), which helps to prevent Fe deficiency during the first year of life.



Is delayed cord clamping effective and safe?

- Reduces the risk of anemia (relative risk 0.53; 95% CI=0.40, 0.70) at 2-6 months of age.
- Increases indices of Fe status:
 - ferritin concentration (+17.9 ug/L; 95% CI=16.6, 19.2)
 - Stored Fe (+19.9 mg; 95% CI =7.7, 32.1)
- Guidelines have been developed for implementation and uptake of this strategy in low-resource settings.
- There are no data on safety in the context of malaria.

Research priorities for delayed cord clamping

- Evaluate the safety and efficacy of delayed cord clamping in malaria-endemic areas, including the impact of the mother's Fe status on outcomes.
- Evaluate the risk of jaundice as a result of delayed cord clamping in populations with a high prevalence of glucose-6-phosphate dehydrogenase deficiency.

Cochrane Review: Iron supplementation and malaria

- Ojukwu et al. 2009: 'Oral iron supplementation for preventing or treating anemia among children in malaria-endemic areas'
- Most comprehensive meta-analysis to date
- Consistent with the findings of the:
 - Pemba trial
 - Joint recommendation statement by the WHO/UNICEF
 - Previously published reviews
 - Conclusions of the Iron and Malaria Technical Report

TWG conclusions from the Cochrane review

- When health care is insufficient there is an increased risk of malaria with Fe supplementation
- When there is comprehensive surveillance and prompt malaria diagnosis and treatment there is no increased risk
 - Adequate malaria surveillance may not be practiced in all settings and inequalities may exist between communities and within families.
 - Thus, the safety of Fe supplementation (particularly pills/liquids) remains a concern.

The TWG identified two of the Cochrane review research gaps as priorities.

- Timing of providing iron Fe a malaria attack
- New meta-analyses based on raw datasets

Overall Conclusions

- At this time, the provision of Fe via tablets or liquids requires caution and may be the least desirable approach in malaria endemic areas.
- Fortified foods may be the most viable alternative intervention. This includes Fe fortification (central or home) of complementary foods for infants and young children and of staple foods or condiments for women and older children.
- Assuming that the Fe from these foods is absorbed more slowly than Fe from supplements, and that this leads to little or no excess NTBI formation or associated harmful effects, Fe-fortified foods are expected to be safe in such areas.