Annex D
Estimation of the Impact of Iron Fortification on the Prevalence of Anemia

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To encourage countries to consider the fortification of flour with iron, it is useful to estimate the potential impact of flour fortification on the prevalence of anemia and iron deficiency. Many factors may affect the impact of iron-fortified flour on the prevalence of anemia and iron deficiency, including the following:

- average daily consumption of flour
- type of flour (e.g., wheat, corn)
- type of iron compound used
- incorporation of other micronutrients in the fortificant mix
- baseline levels of anemia and iron deficiency
- extraction rate (i.e., amount of bran removed from the wheat)
- diet (certain things may enhance or inhibit iron absorption)

The fortification of wheat flour with iron and other nutrients began in the United States in the 1940s. A number of other countries began similar fortification programs in the 1950s and later. While anecdotal information suggests that some of these fortification programs were associated with declines in anemia and/or iron deficiency, there has generally been no adequate baseline information to accurately estimate the impact of fortification or to assess whether declines in the prevalence might be due to other causes.

Few population-based studies have estimated the impact of iron-fortified foods on the prevalence of anemia or iron deficiency. Probably one of the best-studied situations was in Venezuela (Scrimshaw, 2001). In this study, a baseline survey was performed in 1992 and a follow-up survey in 1994. The prevalence of anemia in children from low socioeconomic strata was estimated to be 19% at baseline and declined to 9% in 1994. Likewise, iron deficiency dropped from 37% in 1992 to 16% in 1994. However, surveys in 1997, 1998, and 1999 found the prevalence of anemia to be 15%, 19%, and 17%, respectively; for iron deficiency, the prevalence estimates in these years were 14%, 11%, and 16%, respectively. (See Table D1.)

TABLE D1. Results from five surveys, showing the prevalence of anemia and iron deficiency in children from the low socioeconomic strata of the Venezuelan population

Survey Year	Population	Anemia (N)	Anemia (%)	Population	Iron Deficiency (N)	Iron Deficiency (%)
1992	282	51	19.0	282	105	36.6
1994	317	30	9.3	317	50	15.8
1997	590	86	14.6	571	80	14.0
1998	478	89	18.6	466	52	11.2
1999	545	93	17.1	537	83	15.5

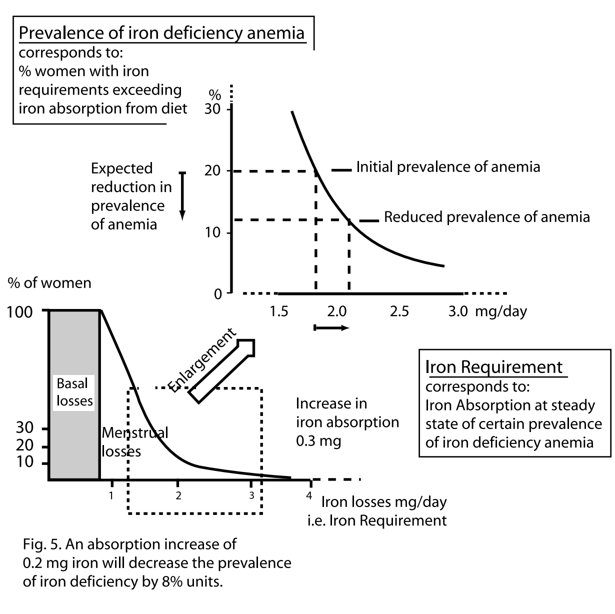
From Scrimshaw et al., 2001.

Many factors can cause anemia, iron deficiency being only one of them. So, in general, it would seem that iron-fortified foods have the potential to reduce the prevalence of anemia; however, the level of impact will depend upon the proportion of anemia in the population that is attributable to iron deficiency. Also, the impact of iron-fortified food products would be expected to be greater if measuring iron deficiency rather than anemia (i.e., hemoglobin). Unfortunately, very few studies have been done on the impact of iron supplements or iron-fortified foods on indicators of iron deficiency.

In our early attempts to estimate the impact, we used a manuscript by Leif Hallberg (1982). Hallberg depicted an estimated relationship between increased iron absorption and its impact on anemia (Figure D1). The population from which he drew his conclusions was made up of Swedish women. For the curvilinear relationship, the upper bound of the prevalence of anemia was 30%. In attempting to apply this curvilinear relationship to populations with higher prevalences (such as 50% or 60%), the model did not appear to predict very well.

We therefore decided to base estimates of the impact of iron fortification on the results of studies of iron supplementation, to estimate a relationship for lower daily intakes of iron.

FIGURE D1. Figure from publication by Hallberg, 1982



Methods

A review of iron supplement studies was used for this estimation process (Beaton and McCabe, 1999; see Figure D2). The data were limited to 19 studies of daily supplementation to compare the baseline prevalence of anemia with the final prevalence. The details of the studies are available in the appendices of Beaton and McCabe's document. In general, the age groups of the study groups varied: they included pregnant women or school-age children/adolescents (usually female only). The majority were based on 60mg iron/day and most included folate. A few studies provided other interventions simultaneously, such as deworming. The duration of the iron supplementation and the level of supervision of the supplement intake varied.

Because the amount of iron received daily from iron-fortified foods is generally less than the 60mg in a supplement, we assumed that the impact of lower amounts of iron on the prevalence of anemia was linear. For example, if a population had an initial prevalence of anemia of 50%, and it was estimated that a daily iron supplement of 60mg reduced the prevalence to 25%, then had only 30mg of iron been provided per day, the prevalence would be reduced to 37.5%.

Results

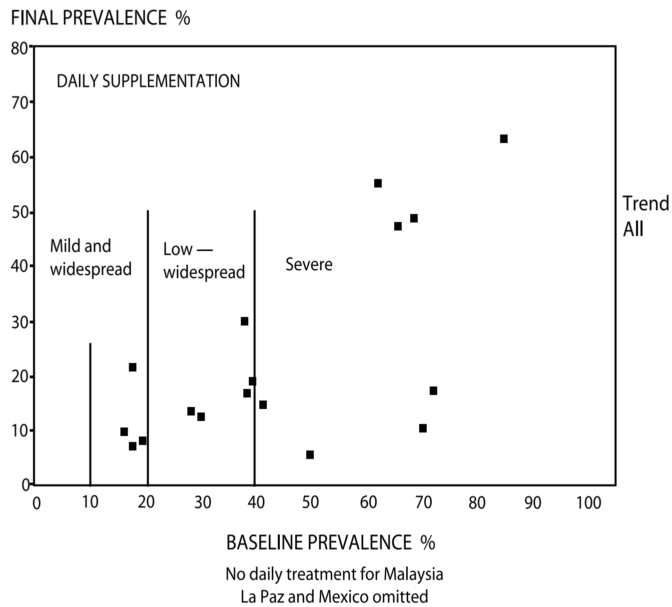
A number of features can be seen from Figure D2 (which is Figure 7.1 from Beaton and McCabe). First, there was variability between studies on the effectiveness of iron supp-lementation to reduce the prevalence of anemia. This level of variability was greatest in the "severe" baseline prevalence of anemia. The figure presents the regression line combining all studies. The intercept and slope of this graph were estimated as follows:

Final anemia prevalence = 1 + baseline anemia prevalence x (.467)

An example of using this formula is as follows. Assuming a population received 60 mg/day and the baseline prevalence was 50%, the final prevalence would be estimated as 24.4%:

24.4% = 1 + 50% x (.467)

FIGURE D2. Figure from publication by Beaton and McCabe, 1999



While most studies in Beaton and McCabe's analysis used 60mg iron supplements, there were a few that used slightly less or more iron. For our purposes, we assumed that all used 60mg iron.

To estimate the impact of less than 60mg iron/day, we used the following equation:

Predicted prevalence = baseline - ((baseline - (1 + (baseline x 0.467))) x (mg / 60))

"Predicted prevalence" is the predicted final anemia prevalence in percent; "baseline" is the baseline anemia prevalence in percent; and "mg" is the estimated daily intake of iron from the fortified product. For example, for a population with a baseline prevalence of anemia of 50% and an estimated daily intake of iron from a fortified product of 30mg:

Predicted prevalence = 50% - ((50% - (1 + (50% x 0.467))) x (30 / 60))

This would estimate a final anemia prevalence of 37.2%. Table D2 presents the predicted final anemia prevalence for a variety of baseline prevalences and iron intake.

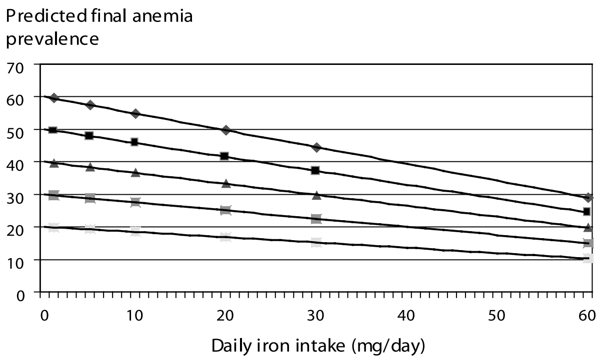
Figure D3 shows this data in graphical form.

TABLE D2. Estimates of predicted final anemia prevalence for various baseline anemia prevalence estimates and iron intake

Baseline Prevalence of Anemia (%)	Iron intake (mg/day) 1	5	10	20	30	60
60	59.5	57.4	54.8	49.7	44.5	29.0
50	49.6	47.9	45.7	41.5	37.2	24.4
40	39.7	38.3	36.6	33.2	29.8	19.7
30	29.8	28.8	27.5	25.0	22.5	15.0
20	19.8	19.2	18.5	16.8	15.2	10.3

Values presented in the table are the predicted final anemia prevalence estimates (%)

FIGURE D3. Estimates of the predicted final prevalence of anemia for vaious baseline prevalences; from top to bottom 60% baseline prevalence, 50%, 40%, 30% and 20%, for various daily intakes of iron



Conclusions

Ideally, estimates of the impact of iron-fortified foods should be based on randomized clinical trials, and the outcome should be the reduction of iron deficiency. Unfortunately, only sparse data are available, and therefore iron supplement studies were used in this document. It is possible that there is no linear relationship between daily iron dose and a reduction in the prevalence of anemia. The studies selected varied on a number of factors, such as age, duration of intervention, and perhaps quality of data collection/ supervision. Therefore, these results should be interpreted cautiously. It is hoped that others will perform more definitive clinical trials to improve the estimates of the impact of iron-fortified foods on reducing the prevalence of iron deficiency and anemia.

Issues

On the first page of this document a number of factors were listed that likely impact the effectiveness of iron fortification. Some other issues that might affect this document's estimation procedure are described below.

Reasons why the approach taken in this document might underestimate the effect of iron fortification:

- The curve might not be linear. There are data to suggest that around 50 mg of iron or more as a supplement might not affect, to any great extent, the final prevalence of anemia. This suggests that the "true" response curve may fall below those depicted in Figure D3, at least for the higher levels of daily iron intake.
- It has been suggested that small amounts of iron in fortified foods consumed daily over a long period of time may have a more beneficial effect than the curves presented in Figure D3. This might involve issues of pharmokinetics and cumulative dose.
- Using anemia as the endpoint likely understates the effect of iron fortification on iron deficiency.

Reasons why the approach taken in this document might overestimate the effect of iron fortification:

- Fortified foods are consumed with a meal that may include inhibitors that might reduce the impact of the iron.

Acknowledgements

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References

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