Review of the public-health evidence of flour fortification impacting serum folate, neural tube defects, serum ferritin, and hemoglobin

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Cost Benefit Analysis training in Dar –es-Salaam
Acknowledgements

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Study types

**EFFICACY**
“The extent to which a specific intervention, procedure, regimen, or service produces a beneficial result under ideal conditions … Ideally, the determination of efficacy is based on the results of a randomized controlled trial.”

**EFFECTIVENESS**
“…it is a measure of the extent to which a specific intervention, procedure, regimen, or service, when deployed in the field in the usual circumstances, does what it is intended to do for a specified population. A measure of the extent to which a health care intervention fulfills its objectives in practice.”

This presentation will summarize results from effectiveness trials, conducted before and after fortification programs were initiated in countries. None of these results are from efficacy trials.
Wheat Availability and Fortification Legislation

- 75 or more grams available per person per day
- Less than 75 grams available per person per day
- Mandatory fortification legislation *
  78 countries
- No availability or legislation data

* Legislation has effect of mandating grain fortification with at least iron or folic acid; does not reflect how much grain is available.
Grain availability data from the Food and Agriculture Organization (2009).
Legislation status from the Flour Fortification Initiative (www.FFInetwork.org) November 2013
Rice Availability and Fortification Legislation

75 or more grams available per person per day

Less than 75 grams available per person per day

Mandatory fortification legislation *

5 countries

No availability or legislation data

* Legislation has effect of mandating grain fortification with at least iron or folic acid; does not reflect how much grain is available.
Grain availability data from the Food and Agriculture Organization (2009).
Legislation status from the Flour Fortification Initiative (www.FFInetwork.org) November 2013
Maize Availability and Fortification Legislation

- **75 or more grams available per person per day**
- **Less than 75 grams available per person per day**
- **Mandatory fortification legislation** *12 countries*
- **No availability or legislation data**

* Legislation has effect of mandating grain fortification with at least iron or folic acid; does not reflect how much grain is available.

Grain availability data from the Food and Agriculture Organization (2009).
Legislation status from the Flour Fortification Initiative ([www.FFInetwork.org](http://www.FFInetwork.org)) November 2013
Recommendations on wheat and maize flour fortification

Table 1. Average levels of nutrients to consider adding to fortified wheat flour based on extraction, fortificant compound, and estimated per capita flour availability

<table>
<thead>
<tr>
<th>Nutrient</th>
<th>Flour Extraction Rate</th>
<th>Compound</th>
<th>Level of nutrient to be added in parts per million (ppm) by estimated average per capita wheat flour availability (g/day)¹</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>&lt;75² g/day</td>
</tr>
<tr>
<td>Iron</td>
<td>Low</td>
<td>NaFeEDTA</td>
<td>40</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Ferrous Sulfate</td>
<td>60</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Ferrous Fumarate</td>
<td>60</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Electrolytic Iron</td>
<td>NR³</td>
</tr>
<tr>
<td></td>
<td>High</td>
<td>NaFeEDTA</td>
<td>40</td>
</tr>
<tr>
<td>Folic Acid</td>
<td>Low or High</td>
<td>Folic Acid</td>
<td>5.0</td>
</tr>
<tr>
<td>Vitamin B₁₂</td>
<td>Low or High</td>
<td>Cyanocobalamin</td>
<td>0.04</td>
</tr>
<tr>
<td>Vitamin A</td>
<td>Low or High</td>
<td>Vitamin A Palmitate</td>
<td>5.9</td>
</tr>
<tr>
<td>Zinc</td>
<td>Low</td>
<td>Zinc Oxide</td>
<td>95</td>
</tr>
<tr>
<td></td>
<td>High</td>
<td>Zinc Oxide</td>
<td>100</td>
</tr>
</tbody>
</table>

WHO and partners 2009
FFI review 2013. Folic acid in flour ranged from 1.2-2.2 mg/kg.
Neural tube defects

Neural Tube Defects (per 10,000): Pre and Post Fortification with Folic Acid

Prefortification NTD per 10,000
Postfortification NTD per 10,000

Brazil, Canada, Chile, Costa Rica, Iran, Jordan, Peru, Saudi Arabia, South Africa, USA

Adapted from FFI 2013

Folic acid in flour ranged from 1.2-2.2 mg/kg.
Iron deficiency vs anemia vs iron-deficiency anemia

Causes of iron deficiency:
- Deficient iron intake
- Excessive iron loss

Biological marker:
- Serum ferritin

Causes of anemia:
- Deficiency of iron, vitamin B12, folate, vitamin A
- Hemoglobinopathies
- Infections

Biological marker:
- Hemoglobin

Causes of iron-deficiency anemia:
- Iron deficiency

Biological marker:
- Serum ferritin & hemoglobin

Zimmermann 2008; Gleason 2007; Scott 2007; West 2007; Cameron 2011
Serum ferritin

Serum ferritin (mcg/L): Pre and Post Fortification with Iron

Prefortification serum ferritin (mcg/L)  Postfortification serum ferritin (mcg/L)

FFI review 2013. Iron in flour ranged from 30-60 mg/kg. Iron compounds used were ferrous sulfate, ferrous fumarate, elemental iron, and electrolytic iron.
Hemoglobin (g/L): Pre and Post Fortification

FFI review 2013. Nutrients added to flour were iron, zinc, folic acid (B9), thiamin (B1), riboflavin (B2), niacin (B3), pyridoxine (B6), and vitamin A
Effectiveness of National Flour Fortification Programs

<table>
<thead>
<tr>
<th>Country</th>
<th>Risk Group</th>
<th>Condition</th>
<th>Pre</th>
<th>Post</th>
<th>% Reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Venezuela</td>
<td>Children &gt; 5yrs</td>
<td>Iron Deficiency</td>
<td>37.2%</td>
<td>15.5%</td>
<td>58.3%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Anemia</td>
<td>18.1%</td>
<td>17.1%</td>
<td>5.5%</td>
</tr>
<tr>
<td>Costa Rica</td>
<td>Adult Women</td>
<td>Anemia</td>
<td>18.4%</td>
<td>10.2%</td>
<td>45%</td>
</tr>
<tr>
<td>Kuwait</td>
<td>Pregnant Women</td>
<td>Anemia</td>
<td>33%</td>
<td>24%</td>
<td>27%</td>
</tr>
<tr>
<td>Oman</td>
<td>Pregnant Women</td>
<td></td>
<td>49%</td>
<td>31%</td>
<td>37%</td>
</tr>
</tbody>
</table>
# Summary

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Favorable Result (n)*</th>
<th>Total Evaluated (n)**</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum folate</td>
<td>18</td>
<td>19</td>
</tr>
<tr>
<td>Neural tube defects (NTDs)</td>
<td>19</td>
<td>20</td>
</tr>
<tr>
<td>Serum ferritin</td>
<td>9</td>
<td>11</td>
</tr>
<tr>
<td>Hemoglobin</td>
<td>11</td>
<td>23</td>
</tr>
</tbody>
</table>

* Favorable result (increased folate, ferritin, hemoglobin; decreased NTDs) in sub-group analyses
** Total number of sub-groups analyzed

FFI review 2013.
**Prevalence of Vitamin A Deficiency**
*(Serum Retinol < 0.70 umol/l)*

<table>
<thead>
<tr>
<th></th>
<th>Pre</th>
<th>Post</th>
<th>% Reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pregnant Women</td>
<td>24.5%</td>
<td>23.2%</td>
<td>5%</td>
</tr>
<tr>
<td>School Age Children</td>
<td>34.5%</td>
<td>18.7%</td>
<td>46%</td>
</tr>
<tr>
<td>Adolescent Girls</td>
<td>30.1%</td>
<td>12.5%</td>
<td>58%</td>
</tr>
<tr>
<td>Pre-School Children</td>
<td>26.5%</td>
<td>22.5%</td>
<td>15%</td>
</tr>
</tbody>
</table>
Conclusions

Effectiveness studies of wheat and maize flour fortification programs reveal:

- Folic-acid fortification *increases* serum *folate* levels
- Folic-acid fortification *decreases* risk of neural tube defects (NTDs)
- Iron fortification *increases* serum *ferritin* levels
- Effect of fortification with one or multiple nutrients on *hemoglobin* levels is *equivocal*
For more information

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References for download

http://www.sph.emory.edu/~hpacho2/
References for slides 3, 5, and 8

Miquel Porta, Dictionary of Epidemiology, 2008.  
http://jpkc.fudan.edu.cn/picture/article/189/c4/24/81c086374fd8a31d9be7208bbb80/eb7e72b0-3b41-4b6b-8b23-168950e0e794.pdf


References for serum folate (1)


References for serum folate (2)


References for neural tube defects (1)


References for neural tube defects (2)


References for serum ferritin


References for hemoglobin (1)


References for hemoglobin

