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

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Flour Fortification Monitoring and Surveillance: Process and Possibilities
Acknowledgements

Gabrielle Fanning-Dowdell
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.

Porta 2008
Countries that mandate wheat flour fortification with iron and/or folic acid

December 2012: 75 countries require iron and/or folic acid in wheat flour
**Recommendations on wheat and maize flour fortification**

<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)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>&lt;75(^2) 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>NR(^3)</td>
</tr>
<tr>
<td></td>
<td>High</td>
<td>NaFeEDTA</td>
<td>40</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Folic Acid</td>
<td>5.0</td>
</tr>
<tr>
<td>Folic Acid</td>
<td>Low or High</td>
<td>Folic Acid</td>
<td>5.0</td>
</tr>
<tr>
<td>Vitamin B(_{12})</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(^4)</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
Serum folate

Serum Folate (nmol/L): Pre and Post Fortification with Folic Acid

Prefortification mean or median  Postfortification mean or median

6 mo

5 y

Children 2-15 y

Middle age and elderly

All ages and genders

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)

Children  Women of childbearing age  Men

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

Hemoglobin (g/L): Pre and Post Fortification

<table>
<thead>
<tr>
<th>Prefortification hemoglobin (g/L)</th>
<th>Postfortification hemoglobin (g/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Children</td>
<td>Men</td>
</tr>
<tr>
<td>Children</td>
<td>Women of childbearing age</td>
</tr>
</tbody>
</table>

FFI review 2013. Nutrients added to flour were iron, zinc, folic acid (B9), thiamin (B1), riboflavin (B2), niacin (B3), pyridoxine (B6), and vitamin A
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.
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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Flour Fortification Initiative:
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LinkedIn.com
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


Serum folate

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All ages and genders

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

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