



Evidence & Programme Guidance

# Fortification of maize flour and corn meal with vitamins and minerals in public health

**Maria Nieves Garcia-Casal**

Senior Consultant

Evidence and Programme Guidance Unit

World Health Organization

November 2014

# Systematic review



Garcia-Casal MN, Peña-Rosas JP, De-Regil LM, Gwirtz JA, Pasricha S-R.  
Fortification of maize flour with iron for preventing anaemia and iron  
deficiency in populations. Cochrane Database of Systematic Reviews 2012 ,  
Issue 11 . Art. No.: CD010187. DOI: 10.1002/14651858.CD010187

# Objective



To determine the benefits and harms of iron fortification of maize flour, corn meal and fortified maize flour products on anaemia and iron status among the general population.

# Types of studies



- RCT with randomisation at either individual or cluster level;
- quasi-randomised trials, non-randomised controlled studies;
- observational studies that are prospective and have a control group;
- cohort studies (prospective and retrospective);
- controlled before and after studies;
- interrupted time series with at least three measurement points both before and after intervention.

# Types of studies



- We did not pool results from RCT with those from non-randomised studies in meta-analysis; instead using separate meta-analysis estimates for different study designs.
- Before and after studies without a control group were also considered for inclusion in this review (presented as separate table).

# Types of participants



General population older than 2 years of age (including pregnant women), from any country.

# Types of interventions

- Interventions in which maize flours and/or maize sub-products have been fortified with iron alone or iron plus other vitamins/minerals.
- Composite flours that contain more than 50% maize.
- Maize flour products include all products derived from fortified corn meal and flour (e.g. breads, cereals, polenta, porridges, grits, arepas).
- Fortification of the maize flour or corn meal must have occurred during flour production for the study to have been included.

# Exclusion criteria



- Studies evaluating products derived from wet milling of maize, including corn starch (which is often called 'corn flour' in the United Kingdom and Australia) and products that are fortified after recomposition of the flour.
- Maize fortification versus other forms of micronutrient interventions: iron supplementation, point-of-use fortification of maize products with micronutrients powders or lipid-based spreads, biofortification or fortification of wheat flour with iron or folic acid.
- Studies of interventions targeted toward participants with a critical illness or severe co-morbidities.



# Comparisons



1. maize flour or maize flour products fortified with iron alone versus no intervention;
2. maize flour or maize flour products fortified with iron plus other vitamins and minerals versus no intervention;
3. maize flour or maize flour products fortified with iron alone versus unfortified maize flours or maize flour products (not containing iron nor any other vitamin and minerals);
4. maize flour or maize flour products fortified with iron plus other vitamins and minerals versus unfortified maize flours or maize flour products (not containing iron nor any other vitamin and minerals).

# Primary outcomes

- Anaemia
- Iron deficiency
- Haemoglobin concentration
- Iron status (as reported: ferritin, transferrin saturation, soluble transferrin receptor, soluble transferrin receptor-ferritin index, total iron binding capacity, serum iron).
- Adverse side effects (including constipation, nausea, vomiting, heartburn or diarrhoea, as measured by trialists).



# Secondary outcomes

- Iron deficiency anaemia (as defined by trialists).
- Cognitive development (as defined by trialists).
- Motor skill development (as defined by trialists).
- Premature birth (less than 37 weeks).
- Very premature birth (less than 34 weeks).
- Low birth weight (less than 2500 g).
- Congenital anomalies (including neural tube defect, cleft lip, cleft palate, congenital cardiovascular defects and other birth defects as reported by trialists).
- Growth: height-for-age (z-scores).
- Growth: weight-for-height (z-scores).
- Work capacity (as defined by trialists).
- High ferritin concentrations (defined as more than 150 mg/L).
- Malaria severity (only for malaria settings).
- Malaria incidence (only for malaria settings).

# Search



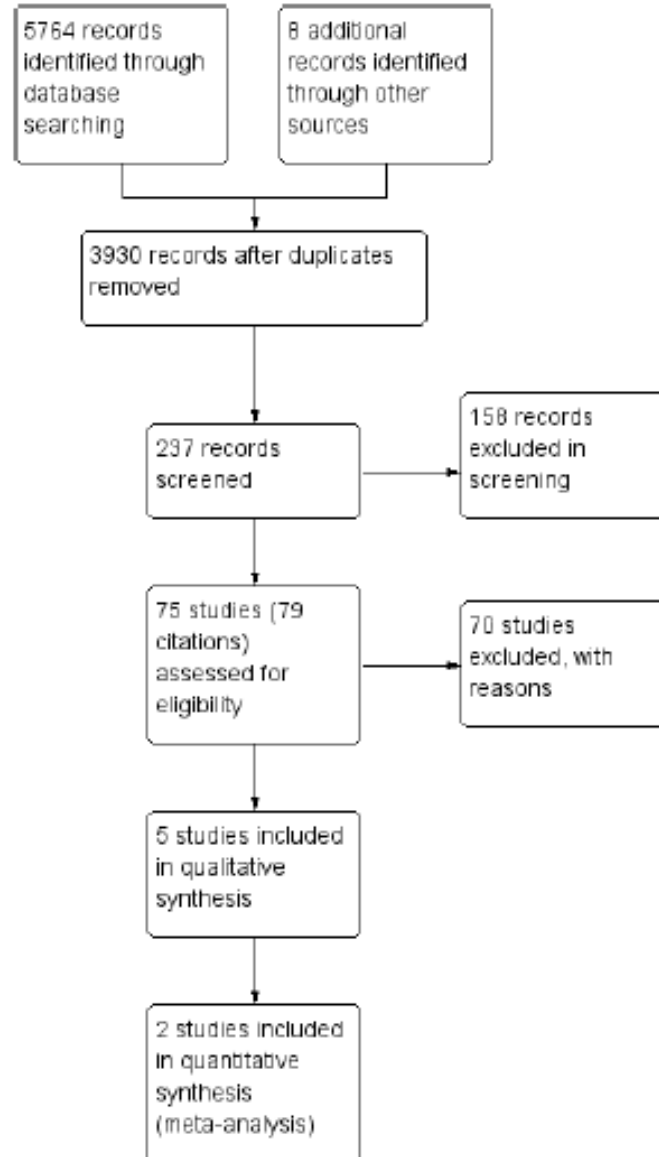
- **International databases**
- 1. Cochrane Central Register of Controlled Trials (CENTRAL) (21/5/15)
- 2. MEDLINE (OVID) (21/5/15)
- 3. MEDLINE (R) In Process (OVID) (21/5/15)
- 4. EMBASE (OVID) (21/5/15)
- 5. Web of Science (both the Social Science Citation Index and the Science Citation Index) (ISI) (22/5/15)
- 6. CINAHL (Ebsco) (21/5/15)
- 7. POPLINE (22/5/15)
- 8. AGRICOLA (<http://agricola.nal.usda.gov/>) (22/5/15)
- 9. BIOSIS (ISI) (22/5/15)
- **Regional databases**
- 1. IBECs (<http://ibecs.isciii.es/>) (21/5/15)
- 2. Scielo (<http://www.scielo.br/>) (21/5/15)
- 3. Global Index Medicus - AFRO (includes African Index Medicus); EMRO (includes Index Medicus for the Eastern Mediterranean Region) (24/5/15)
- 4. LILACS (22/5/15)
- 5. PAHO (Pan American Health Library) (22/5/15)
- 6. WHOLIS (WHO Library) (22/5/15)
- 7. WPRO (includes Western Pacific Region Index Medicus) (27/09 2012)
- 8. IMSEAR, Index Medicus for the South-East Asian Region (24/5/15)
- 9. IndMED, Indian medical journals (<http://indmed.nic.in/>) (24/5/15)
- 10. Native Health Research Database (<https://hcssl.unm.edu/nhd/>) (24/5/15)

# Search



- International Clinical Trials Registry Platform (ICTRP) was searched for any ongoing or planned studies and contacted authors of such studies to obtain further information or eligible data if available.
- Relevant international organizations and agencies working in food fortification for assistance in identifying ongoing or unpublished studies.

# Results



# Results



- From 5 selected studies:
- 3 were randomised trials involving 2610 participants
- 2 were pre and post interventions without a control group involving 849 participants.
- In comparison with unfortified maize flour, fortification of maize flour or corn meals with iron and other vitamins and minerals reduced the risk of iron deficiency in children (risk ratio (RR) 0.53, 95% CI 0.40 to 0.69; 2 studies; 1277 participants; very low-quality evidence)

# Results



- The intervention had no effect on **anaemia** (risk ratio (RR) 0.89, 95% CI 0.57 to 1.39; 2 studies; 1359 participants; very low-quality evidence), **haemoglobin** (mean difference (MD) 0.42 g/L, 95% confidence interval (CI) -2.47 to 3.31 g/L; 2 studies; 1325 participants; very low-quality evidence) or **ferritin** (mean difference (MD) 0.00 µg/L, 95% confidence interval (CI) -0.27 to 0.27 µg/L; 2 studies; 758 participants; very low-quality evidence).
- None of the studies reported on adverse side effects.



# Summary of findings table

Patient or population: Children (2 to 11.9 years of age)			
Setting: all settings			
Intervention: maize flour or maize flour products fortified with iron plus other vitamins and minerals			
Comparison: unfortified maize flours or maize flour products (not containing iron nor any other vitamin and minerals)			
Outcomes	Relative effect (95% CI)	№ of participants (studies)	Quality of the evidence (GRADE)
Anaemia in children (defined as haemoglobin (Hb) below 110 g/L or 115 g/L, adjusted for altitude as appropriate)	RR 0.89 (0.57 to 1.39)	1359 (2 RCTs)	⊕⊕⊕⊕ VERY LOW <sup>1, 2, 3</sup>
Iron deficiency in children (as defined by trialists, based on a biomarker of iron status).	RR 0.53 (0.40 to 0.69)	1277 (2 RCTs)	⊕⊕⊕⊕ VERY LOW <sup>1, 3</sup>
Haemoglobin concentration in children (in g/L)	-	1325 (2 RCTs)	⊕⊕⊕⊕ VERY LOW <sup>1, 2, 3</sup>
Ferritin in children (in µg/L)	-	758 (1 RCT)	⊕⊕⊕⊕ LOW <sup>1, 4</sup>
Iron deficiency anaemia in children (as defined by trialists)	RR 1.04 (0.58 to 1.88)	515 (1 RCT)	⊕⊕⊕⊕ LOW <sup>2,4</sup>
Any adverse side effects in children (including constipation, nausea, vomiting, heartburn or diarrhoea, as measured by trialists)	No reported	(0 RCTs)	No estimable
*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).			
CI: Confidence interval; RR: Risk ratio; OR: Odds ratio;			
GRADE Working Group grades of evidence			
High quality: We are very confident that the true effect lies close to that of the estimate of the effect			
Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different			
Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect			
Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect			

# Simultaneous maize and corn flour fortification

Reference	Country	Design	Population	Pre-fortification			Post-fortification		
				n	Hb concentration (g/L)	Anaemia prevalence (%)	n	Hb concentration (g/L)	Anaemia prevalence (%)
<a href="#">Abreu 2009</a>	Brazil	Pre- post study without control. Based on records.	Pregnant women	384	124.6 ± 14.3	14.3	384	125.3 ± 11.7	8.07
<a href="#">Assuncao 2007a</a>	Brazil	Pre- post study without control. Based on records.	Preschool children	453	113 ± 28	-	923	113 ± 25	-
<a href="#">Assuncao 2012</a>	Brazil	Pre- post study without control. Based on records.	Preschool children	507	-	28.5	799	-	31.3
<a href="#">da Silva 2012</a>	Brazil	Retrospective cross-sectional analysis from secondary data.	Pregnant women	391	116.6 ± 10.0	40.3	387	119.7 ± 10.5	28.8
<a href="#">de Souza 2011</a>	Brazil	Retrospective cross-sectional analysis from secondary data.	Pregnant women	427	117 ± 12	-	427	124 ± 13	-
<a href="#">Fujimori 2011</a>	Brazil	Retrospective cross-sectional analysis from secondary data.	Pregnant women	6062	118 ± 13	-	6057	129 ± 12	-
<a href="#">Layrisse 1996</a>	Venezuela	Pre and post study Venezuelan fortification programme.	Children and adolescents	282		19	317		9.3
<a href="#">Sato 2008</a>	Brazil	Retrospective cross-sectional analysis from secondary data.	Pregnant women	390	123.5 ± 10	-	360	123.9 ± 11	-
<a href="#">Sato 2011</a>	Brazil	Retrospective cross-sectional analysis from secondary data.	Pregnant women	12119		25	12119		20

# Conclusions



- Fortification of maize flour with iron and other vitamins and minerals in comparison to unfortified maize flour reduces the risk of iron deficiency in children.
- Lack of published evidence that this intervention has an effect on reducing the risk of anaemia or improving haemoglobin concentrations in adolescents and adult women.
- There are no results data in pregnant women and adult men. None of the studies reported on adverse side effects.