

WHO evidence-informed global guidelines development

Rice Fortification



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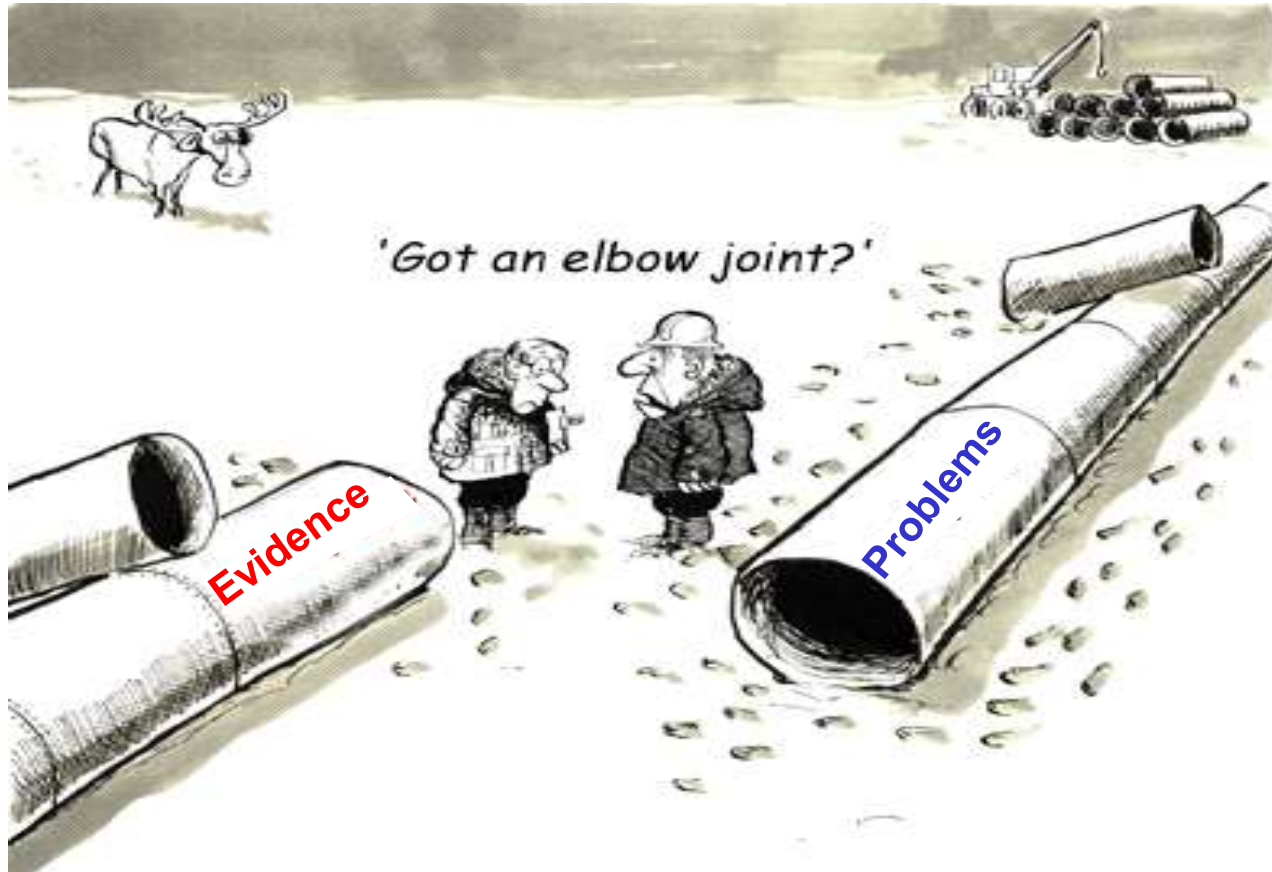
On behalf of WHO/HQ

Outline

- Why develop guidelines for rice fortification?
- Description of the WHO guideline development process
- Protocol for the Cochrane Review



Why develop guidelines for rice fortification?



Why develop guidelines for rice fortification?

- Vitamin and mineral deficiencies are important public health concerns world wide
- Food fortification represents an appealing intervention
- Rice represents a suitable vehicle for fortification
- No systematic assessment of benefits and harms of rice fortification has been conducted to inform policy making

Guidelines for rice fortification...

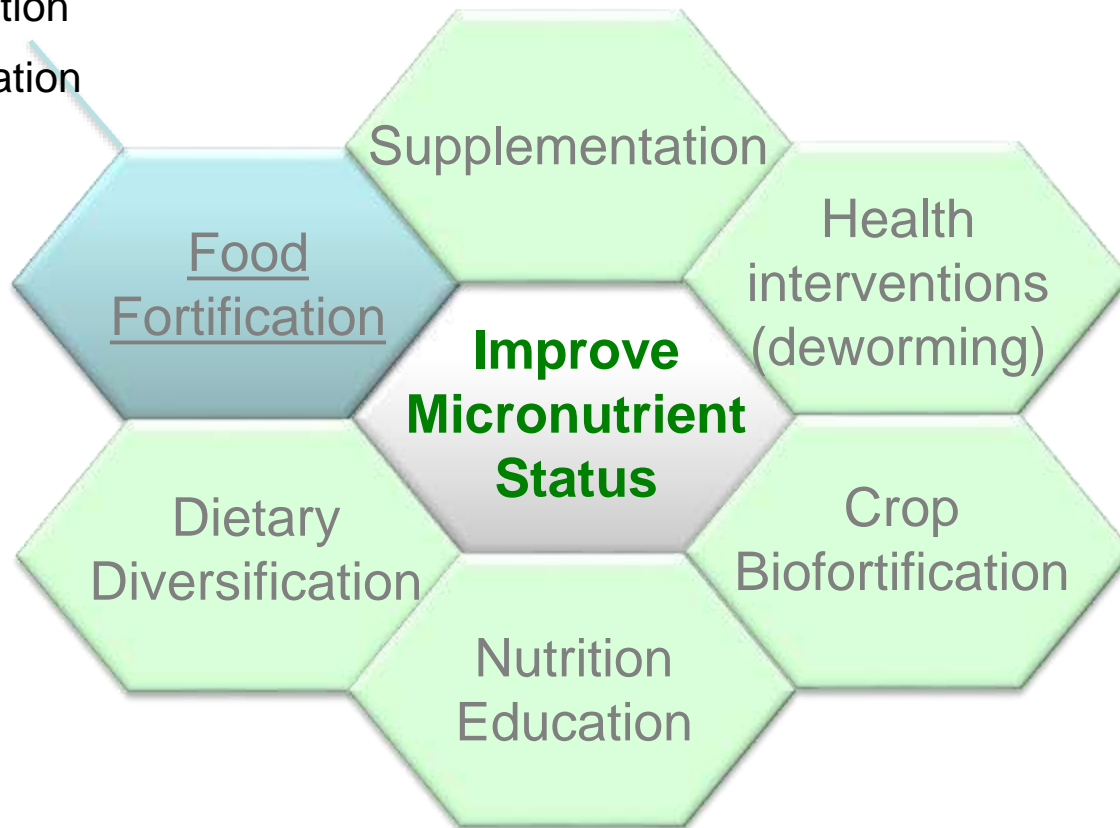
- ... as a **public health strategy**, rather than not a product to fortify under food regulations for *marketing purposes*.
- ...ensuing equitable access, especially for vulnerable populations



Interventions to address vitamin and mineral deficiencies

Point of use fortification

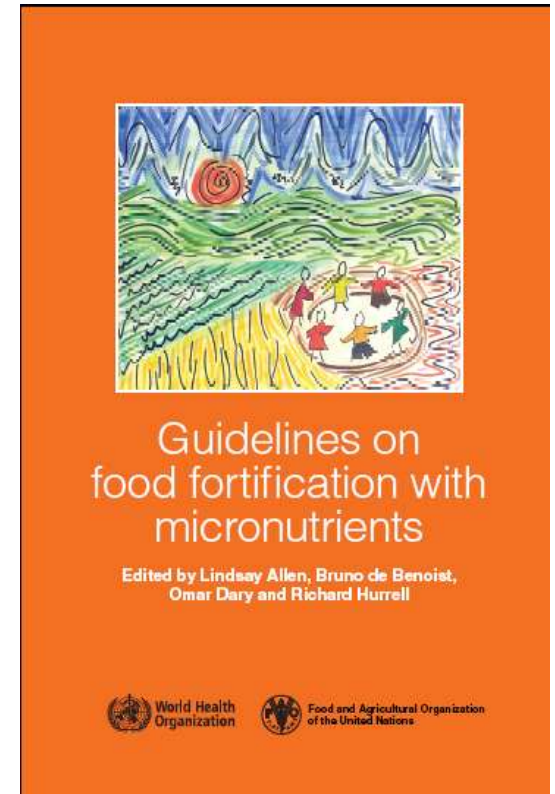
Point of use fortification



WHO FAO Guidelines on Food Fortification with Micronutrients

- Resource for governments and agencies implementing or considering food fortification
- Source of information for scientists, technologists and the food industry.
- General principles for effective fortification programs

- BUT: published prior to establishment of the *WHO evidence-informed guideline development process*



What is a WHO guideline?



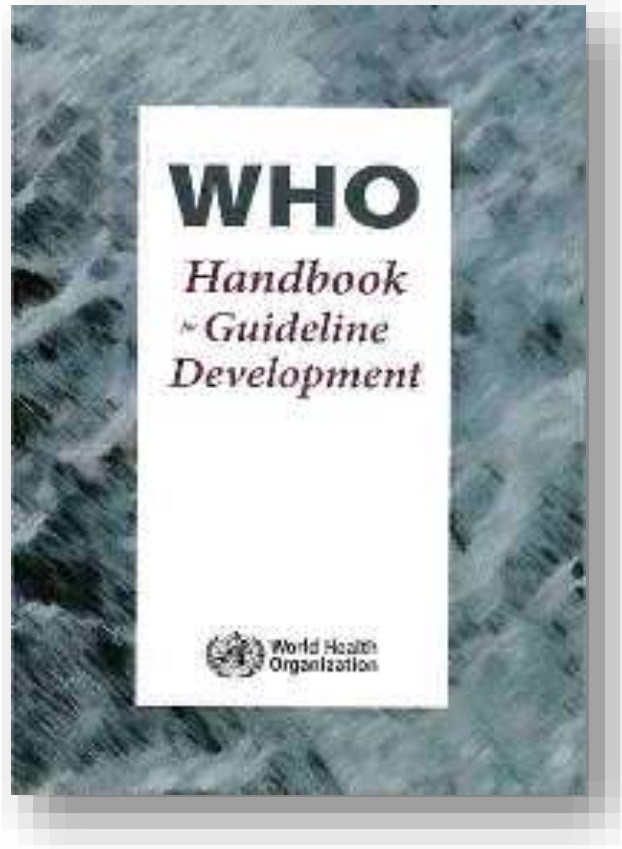
- Any document, whatever its title, containing WHO recommendations about health interventions, whether they be clinical, public health or policy interventions.
- A recommendation provides information about what policy-makers, health-care providers or patients should do. It implies a choice between different options that have an impact on health and that have ramifications for the use of resources.
- All publications containing WHO recommendations are approved by the WHO Guidelines Review Committee.



WHO core functions

1. Providing **leadership** on matters critical to health and engaging in partnerships where joint action is needed
2. Shaping the **research** agenda, and stimulating the generation, dissemination and application of valuable knowledge
3. Setting **norms and standards**, and promoting and monitoring their implementation
4. Articulating ethical and evidence-based **policy options**
5. Providing **technical support**, catalyzing change and building sustainable institutional capacity
6. **Monitoring** the health situation and assessing health trends

WHO evidence-informed guideline development process

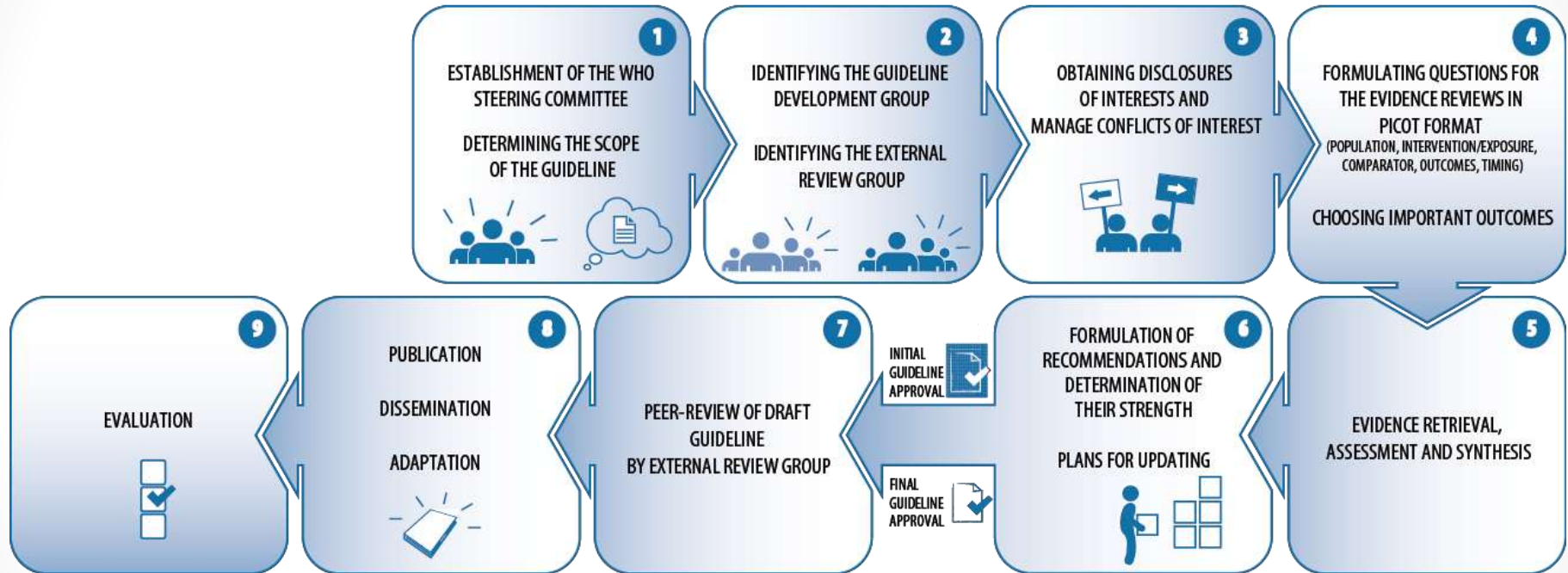


Guidance on effective nutrition interventions

- 25 WHO nutrition guidelines developed or updated in 2009-2013
- eLENA contains 88 nutrition actions.



WHO evidence-informed guideline development process



Steps 1-3: Setting up groups



Guideline Steering Committee

WHO Departments
Directors or alternate appointee



WHO guideline development group

geographic representation
multi disciplinary
17 members
9 Female, 8 Male



External review group

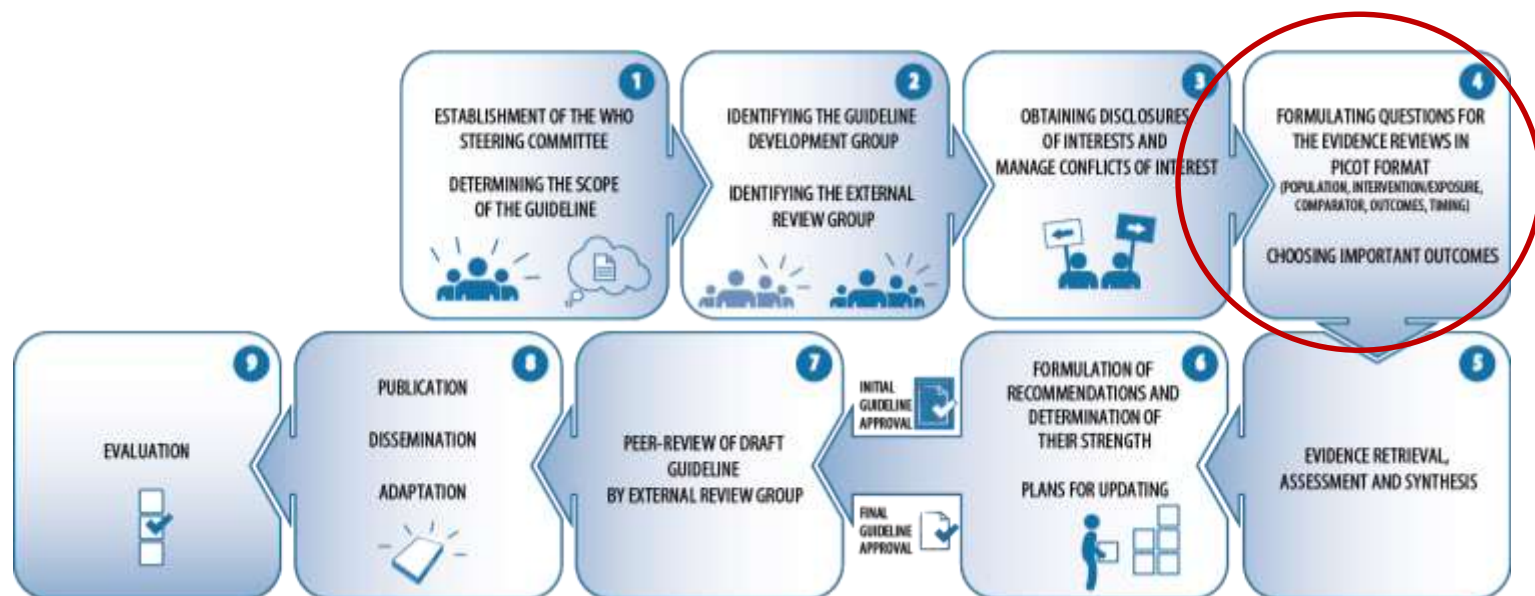
Stakeholders and experts

- Invited experts
- Open call for public comments

WHO Nutrition Guidelines Groups

- Members provide advice to WHO on:
 - The scope of the guidelines and priority questions for which systematic reviews of evidence will be commissioned
 - The choice of important outcomes for decision-making and developing recommendations
 - The interpretation of the evidence with explicit consideration of the overall balance of risks and benefits
 - The final drafting of formulating recommendations, taking into account existing evidence as well as diverse values and preferences

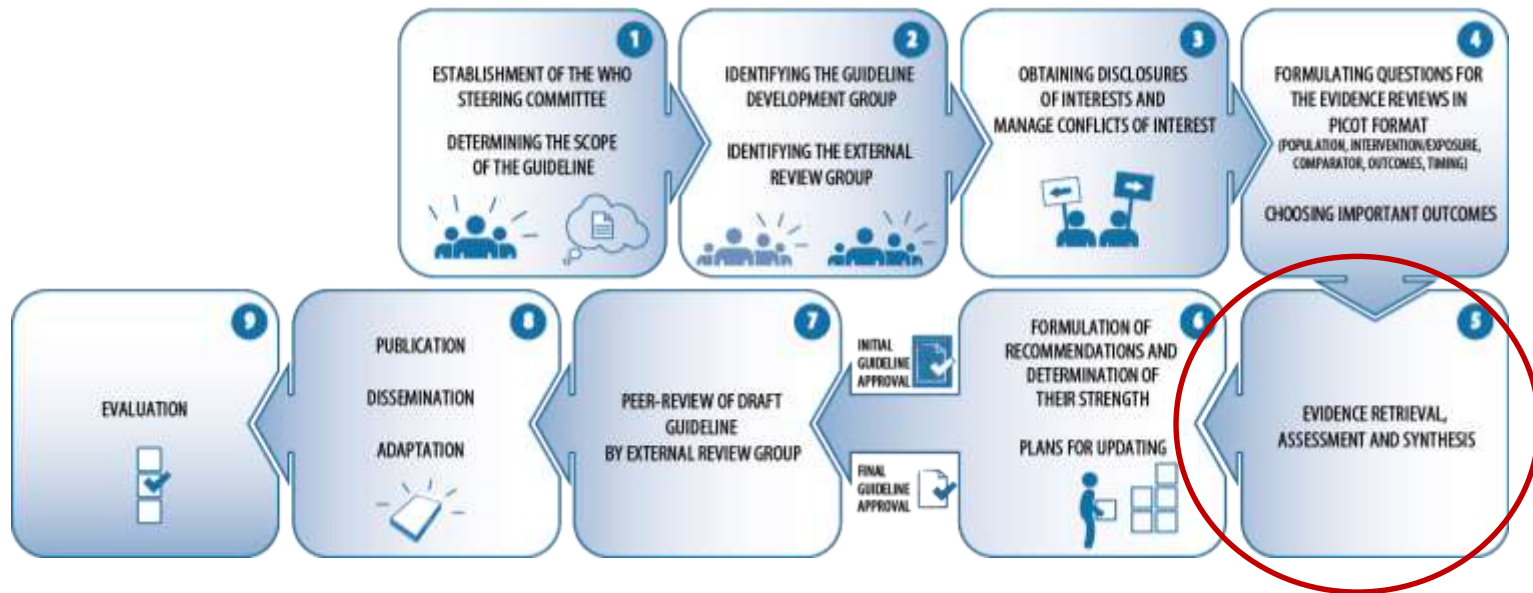
Step 4: Formulation of questions



Formulation of questions, e.g.

- Should rice be fortified with iron and other vitamins and minerals to:
 - Reduce the prevalence of anaemia in populations? 6-59 months), school-age children (5-12 years), and women of reproductive age (15-49 years)?
 - Improve iron status in populations? 6-59 months), school-age children (5-12 years), and women of reproductive age (15-49 years)?
 - Improve dietary intake of iron in populations? 6-59 months), school-age children (5-12 years), and women of reproductive age (15-49 years)?
 - If so, what iron compound(s) should be used and in what amounts?

Step 4: Formulation of questions



Protocol for the Cochrane Review

- Review attempts to evaluate the effectiveness of rice fortification as a public health intervention

**Fortification of rice with vitamins and minerals for addressing
micronutrient malnutrition (Protocol)**

Ashong J, Muthayya S, De-Regil LM, Laillou A, Guyondet C, Moench-Pfanner R, Burford BJ,
Peña-Rosas JP



Considerations

- Policies and legislation
- Production and supply
- Development of the delivery system
- Development and implementation of external and internal food quality control systems
- Development and implementation of strategies for IEC

Objectives of the review

- To determine the benefits and harms of rice fortification with vitamins and minerals (iron, vitamin A, zinc, folic acid) on micronutrient status and health-related outcomes.



Types of studies

- Randomized control trials
- Quasi-randomized control trials
- Non-randomized controlled trials
- Observational studies
 - Cohort studies
 - Controlled before and after studies
 - Interrupted time series

Types of interventions

- Rice has been fortified – with at least one MN or a combination (iron, folic acid, zinc, vitamin A or others)
- Fortified rice:
 - addition of a micronutrient premix to ordinary rice using any rice fortification technology



Comparisons

- Rice fortified with iron alone or in a combination with other MN versus unfortified rice
- Rice fortified with iron alone or in combination with other MN versus no intervention
- Rice fortified with vitamin A alone or in combination with other MN versus unfortified rice
- Rice fortified with vitamin A alone or in combination with other MN versus no intervention
- Rice fortified with zinc alone or in combination with other MN versus unfortified rice
- Rice fortified with zinc alone or in combination with other MN versus no intervention
- Rice fortified with folic acid alone or in combination with other MN versus unfortified rice
- Rice fortified with folic acid alone or in combination with other MN versus no intervention

Outcome measures: primary

Children (2 to 11.9 years of age)

1. Anaemia (defined as haemoglobin (Hb) below 110 g/L, adjusted for altitude as appropriate)
2. Iron deficiency (as defined by trialists, based on a biomarker of iron status)
3. Haemoglobin concentration (g/L)
4. Diarrhoea (three liquid stools in a single day)
5. Respiratory infections (as measured by trialists)
6. All-cause death
7. Serum or plasma folate (nmol/L)

Adolescent girls and boys (12 to 18.9 years of age)

1. Anaemia (defined as Hb below 115 g/L or 120 g/L, adjusted for altitude and smoking as appropriate)
2. Iron deficiency (as defined by trialists, based on a biomarker of iron status)
3. Haemoglobin concentration (g/L)
4. Vitamin A deficiency (as defined by trialists, by using a biomarker)
5. Serum or plasma folate (in nmol/L)

Outcome measures: primary

Pregnant women

1. Anaemia (defined as Hb below 110 g/L at any trimester of pregnancy, adjusted for altitude and smoking as appropriate)
2. Iron deficiency (as defined by trialists, based on a biomarker of iron status)
3. Haemoglobin concentration (in g/L)
4. Congenital anomalies (neural tube defect, cleft lip, cleft palate, congenital cardiovascular defects and others as reported by trialists)
5. Night blindness (defined as the reported inability to see after dusk by people who typically report having normal vision during the day)
6. Miscarriage
7. Serum or plasma folate (in nmol/L)

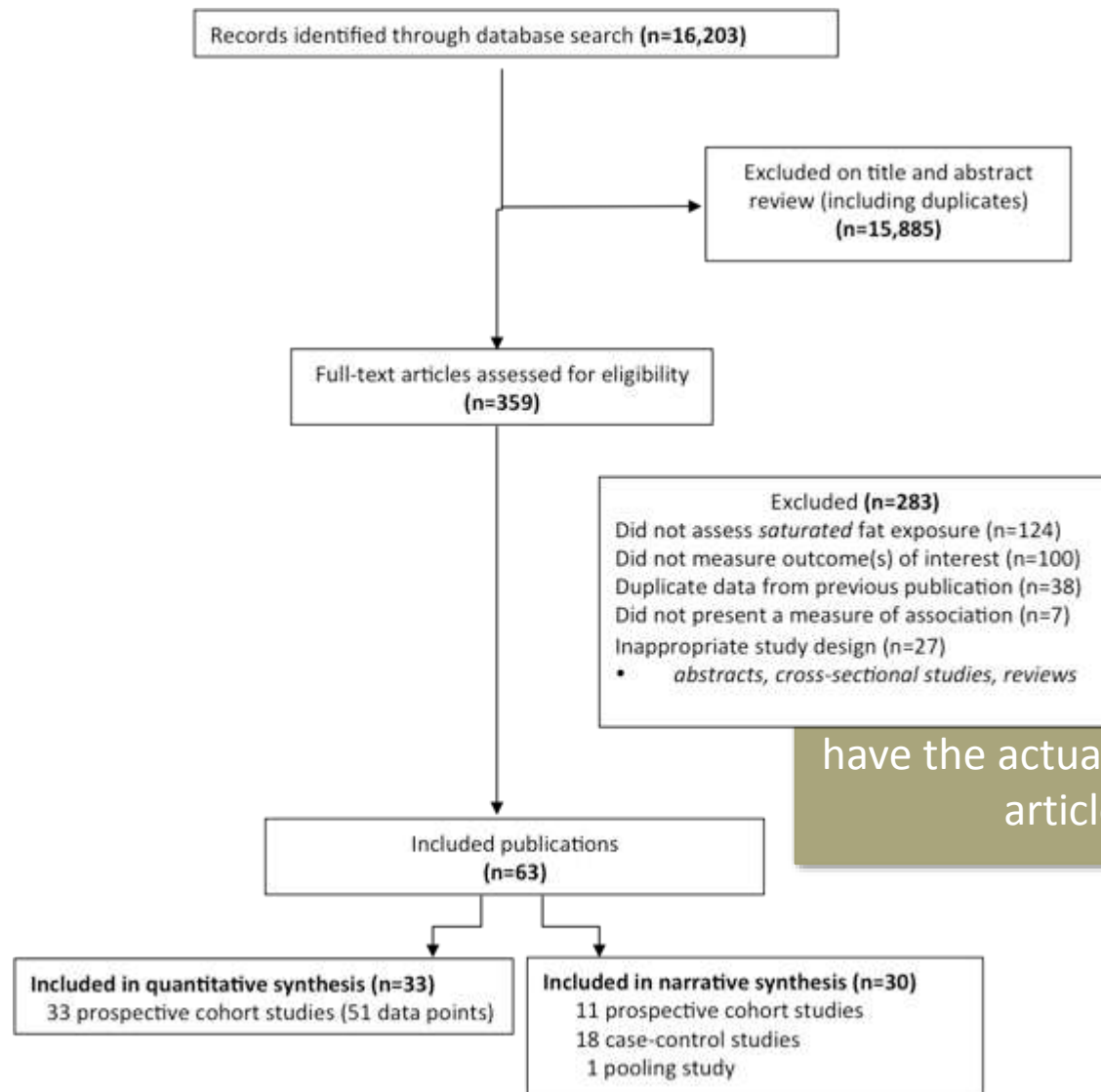
Adult males and females (19 years of age or older)

1. Anaemia (defined as Hb below 115 g/L or 120 g/L, adjusted for altitude and smoking as appropriate)
2. Iron deficiency (as defined by trialists, based on a biomarker of iron status)
3. Haemoglobin concentration (in g/L)
4. Serum/plasma folate (in nmol/L)
5. Vitamin A deficiency (as defined by trialists, by using a biomarker)

Outcome measures: secondary

1. Serum or plasma retinol ($\mu\text{mol/L}$).
2. Serum or plasma zinc ($\mu\text{mol/L}$).
3. Anthropometric measures (height-for-age Z-score and weight-for-height Z-score for children, body mass index (BMI) for adults).
4. Risk of iron overload (defined by serum ferritin higher than $150 \mu\text{g/L}$ in females and higher than $200 \mu\text{g/L}$ in men).
5. Clinical malarial (as defined by trialists).
6. Severe malaria (as defined by trialists).
7. Adverse side effects (including constipation, nausea, vomiting, heartburn).

Selection of articles (example)



What happens to
have the actual selection of
articles?



The *Grading of Recommendations Assessment, Development and Evaluation* approach

Clear separation of the two issues:

1) Quality of the evidence (high, moderate, low, very low)

- methodological quality of evidence
- likelihood of bias
- by outcome
- Ideally, people who grade evidence should have available to them systematic reviews of the evidence regarding the benefits and risks of the alternative management strategies they are considering.
- Better research gives better confidence in the evidence (and the following decisions)

The quality of the evidence

The extent to which one can be confident that an estimate of effect or association is correct.

High	Further research is very unlikely to change our confidence in the estimate of effect	⊕⊕⊕⊕
Moderate	Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.	⊕⊕⊕○
Low	Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate	⊕⊕○○
Very low	Any estimate of effect is very uncertain	⊕○○○



The *Grading of Recommendations Assessment, Development and Evaluation* approach

2) Two grades of recommendation: strong or conditional
(*for or against*)

- Quality of evidence only one factor
- Evidence alone is never sufficient to make a clinical or public health decision

A conditional recommendation

- When the guideline development group concludes that the desirable effects of adherence probably outweigh the undesirable effects, although the trade-offs are uncertain
- Implications
 - Patients: while many people in their situation would desire the recommended course of action, a considerable proportion would not.
 - Clinicians: they should help patients make a decision that is consistent with their values.
 - Policy-makers: there is a need for substantial debate and involvement from stakeholders before considering the adoption of the recommendation.
 - Funding agencies: the option may not represent an appropriate allocation of resources (i.e. alternative uses of resources may produce greater benefits).

A *strong* recommendation

- When the guideline development group is confident that the desirable effects of adherence outweigh the undesirable effects.
- Implications
 - Patients: most people in their situation would desire the recommended course of action and only a small proportion would not.
 - Clinicians: most patients should receive the recommended course of action, and adherence to this recommendation is a reasonable measure of good-quality care.
 - Policy-makers: it can be adapted as a policy in most situations
 - Funding agencies: it represents an appropriate allocation of resources (i.e. large net benefits relative to alternative allocation of resources).

Reality check

“...We have a problem. We need to make a decision. We can go either the practical way or we can use evidence. We would prefer, of course, making a decision informed by the evidence...”

Senior MOH Official



Guideline reporting template

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APPRAISAL OF GUIDELINES
FOR RESEARCH & EVALUATION



AGREE

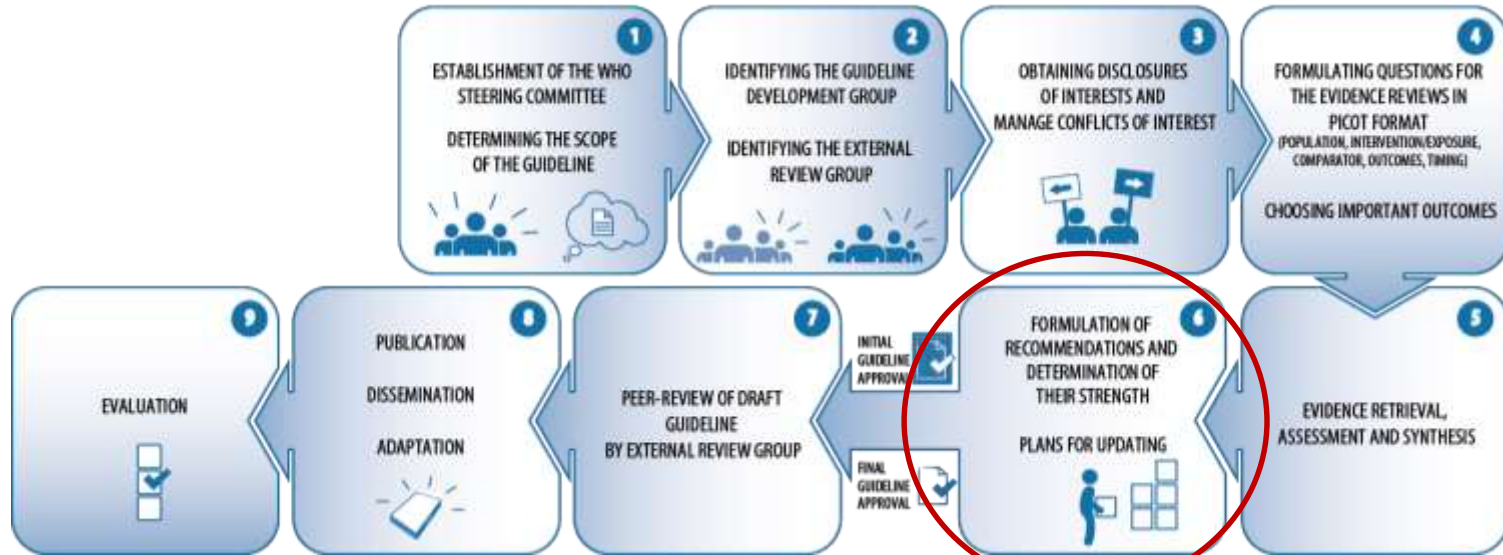
INSTRUMENT

TRAINING MANUAL

The AGREE Collaboration
January 2003

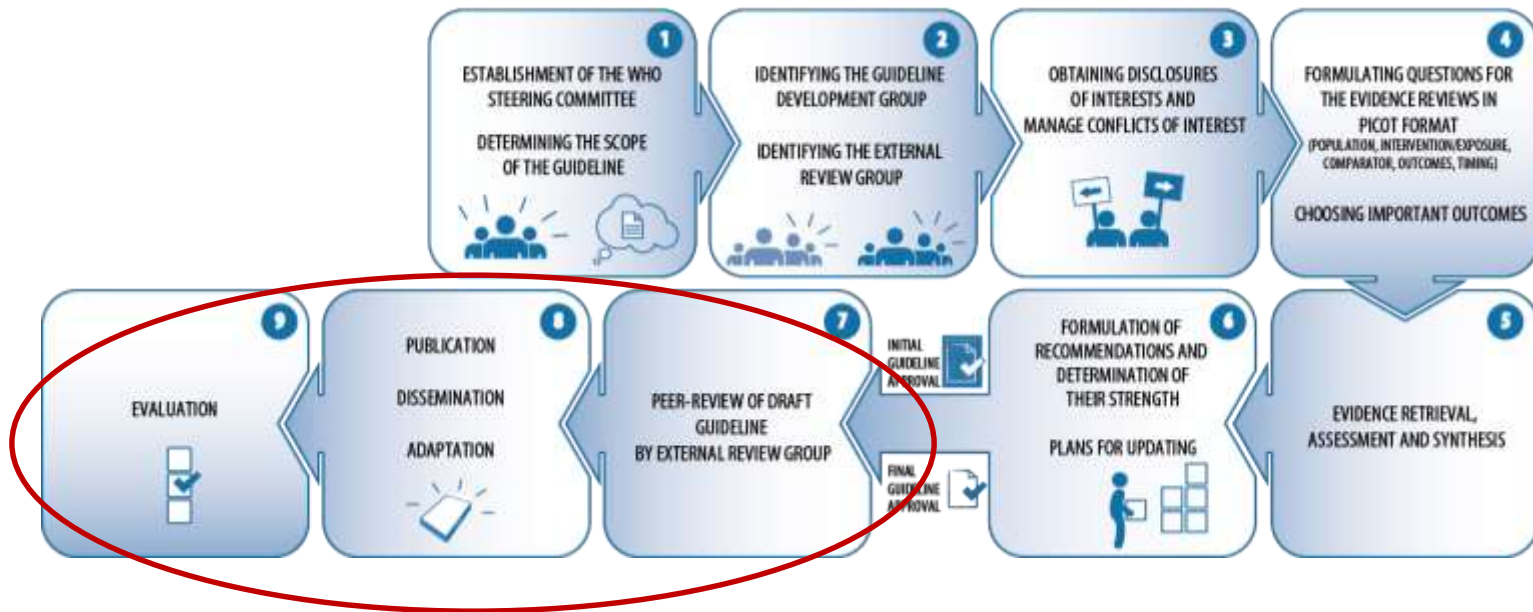


Moving to step 6



Nutrition Guideline Group will meet again on 3-4 November to formulate recommendations and determine their strength (GRADE tables)

A few more steps to go,...





Thank you for your attention