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Weighing the risks of insufficient vs high intake from multiple iron intervention programs

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Special Issue: *Risk of Excessive Intake of Vitamins and Minerals*
REVIEW

Weighing the risks of high intakes of selected micronutrients compared with the risks of deficiencies

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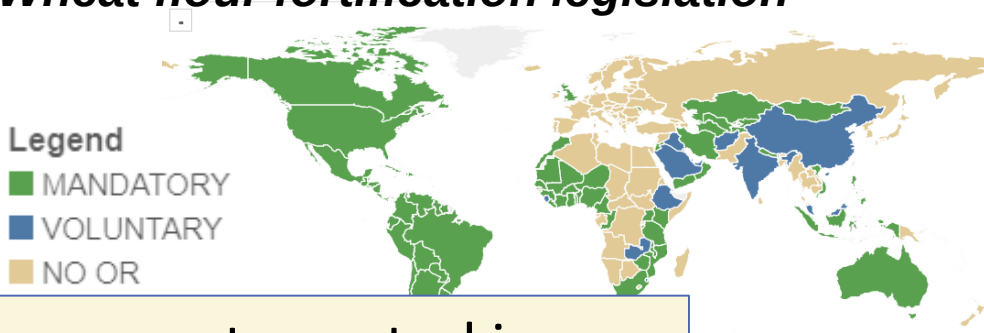
Context: Changing food supply and programmatic environment

Scaling up iron programs

Wheat flour fortification legislation



tion Data Exchange
fortificationdata.org)

The challenge for programs to control iron deficiency anemia:
Is there a risk of "too much of a good thing"?
How can any potential risks be managed?

Voluntary fortification

Understanding "environmental" micronutrients

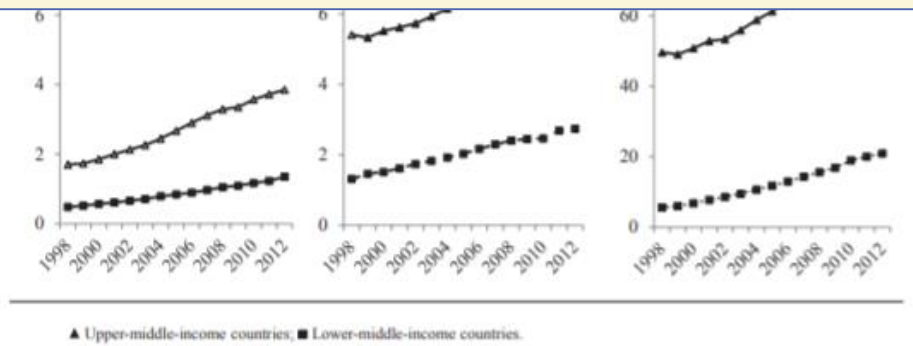


Figure 3 Per capita retail sales of selected ultra-processed products in lower- and upper-middle-income countries (1998–2012).

Monteiro et al., Obesity Reviews, 2013

50% REDUCTION
OF ANAEMIA IN WOMEN OF
REPRODUCTIVE AGE

Outline

*Focus on iron interventions among **nonpregnant** women*

- How do we assess iron excess?
- Are current programs contributing to high iron intakes?
  - Literature review and simulation studies: prevalence of high intake and major dietary iron sources
- What tools can help us plan to address deficiency while avoiding high intakes?

Assessing excess

Biomarkers of excessive intake/status

- Not well characterized for most micronutrients
- For iron, can consider serum/plasma ferritin, but concentrations are affected by inflammation

Intakes above the tolerable upper intake level (UL)

- Most common way to assess risk of high micronutrient intakes
- Requires appropriate methods of data collection and analysis to capture usual dietary intake from ALL sources

Interpretation of intakes above the UL

Purpose of the UL

"the highest average daily nutrient intake level that is likely to pose no risk of adverse health effects to almost all individuals in the general population. As intake increases, the potential risk of adverse effects may increase." – US IOM

- Intentionally conservative
- Based on limited data (no dose-response available)
- Does not specifically account for bioavailability

No specific guidance on to interpret intakes above the UL in settings with:

1) High prevalence of deficiency, and/or

2) High prevalence of infectious disease (or other characteristics not present in the populations used to define the UL)?

How common is iron intake above the UL?

Most data from high-income settings → quality data needed in LMICs!

Prevalence of iron intake above the UL was generally low or 0 for children and adults

- Includes national surveys in South Africa, Philippines, Cameroon, Uganda
- Exceptions: Ethiopia (64% > UL, extrinsic iron in food?), regions of Bangladesh (groundwater)

Sources contributing to exceeding the UL:

- 0-4% > UL among consumers of **fortified breakfast cereal**
  - 4% Canadian women, 2% Irish adults, <1% US children
- 7-14% > UL among adult **supplement users**
  - 7% US women & Chinese women, 12% US men, 14% Mexican women
- Did not find evidence that current staple food fortification programs are associated with high iron intakes

Barr et al., 2013; Galvin et al., 2002; Berner et al., 2014
Bailey et al., 2011; Mejia-Rodriguez et al., 2007; Zhao et al., 2016

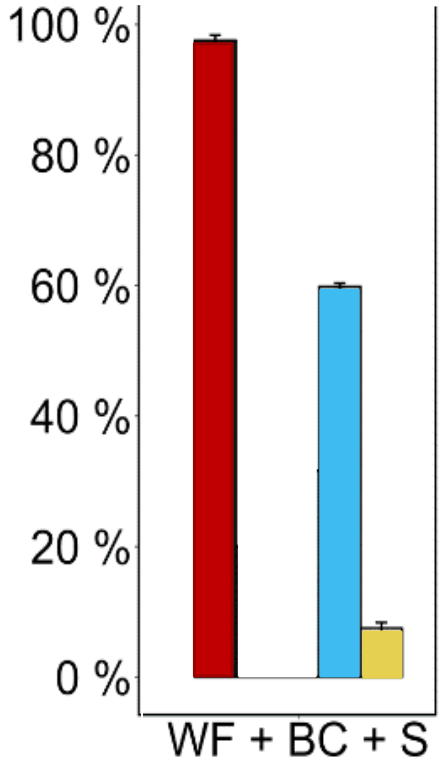
Hypothetical simulation of overlapping iron programs for women in northern Cameroon:

Wheat flour (WF), bouillon cube (BC), and supplementation (S)

% reached by any program

% who received at least 7.4 mg iron per day

% with intake > UL



Implications for monitoring risk:
Counting programs is not sufficient.
Need to know 1) reach of the program, and 2) performance of the program (how much iron will actually be delivered?)

Luo et al., 2019 (unpublished; do not cite)

Considerations for anemia control programs

- **Risk of excess will decrease if programs are targeted well**
  - Understanding anemia etiology by region/subgroup (where will iron solve the problem?)
  - Future role for point-of-care testing of individuals?
- Who is not targeted but still affected? (e.g., staple food fortification)
- What other nutrients are being delivered? (e.g., MNP)

- **Monitoring data are critical to understand actual program impact**
- But remember that not all sources of dietary iron are delivered through programs!

- **Consider the context**
- Are malaria control programs in place and working well?
- Is the health system accessible and well-equipped?

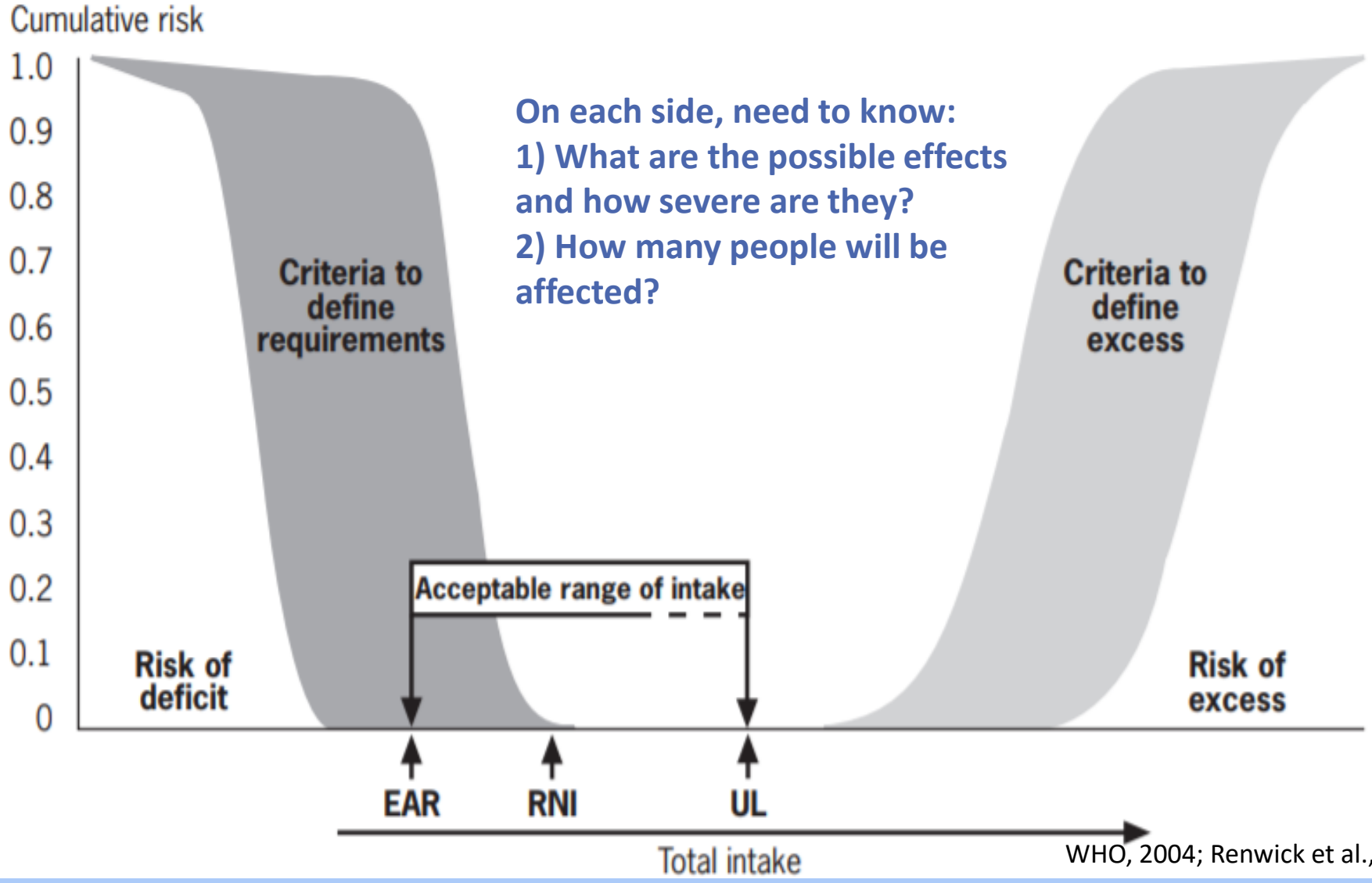
Interpreting data on diets, status, and programs: **Weighing risks of inadequacy vs excess**

Typically, programs aim to minimize both deficiency and excess

But, sometimes tradeoffs between low and high intakes may be unavoidable…

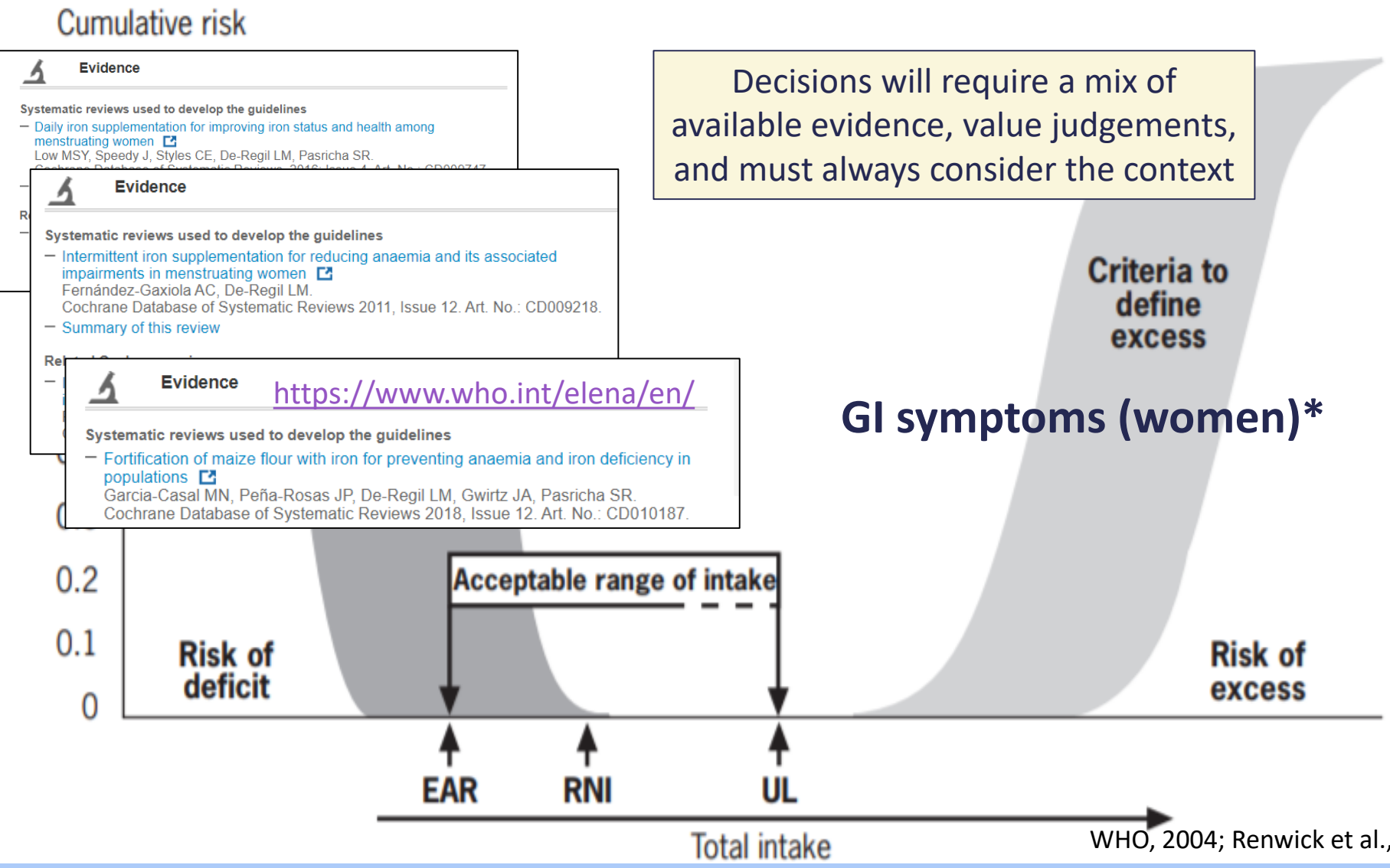
In this case, how to quantify and compare the **severity** of deficiency vs high intake?

Comparing low and high intakes: information needs



WHO, 2004; Renwick et al., 2004

Comparing low and high intakes: More information available on deficiency



WHO, 2004; Renwick et al., 2004

*Evidence differs for children

Tools to help inform decision-making

Can risks and hazards on both sides be quantified in a single metric, such as DALYs?

(Hoekstra et al., Food and Chemical Toxicology, 2008)

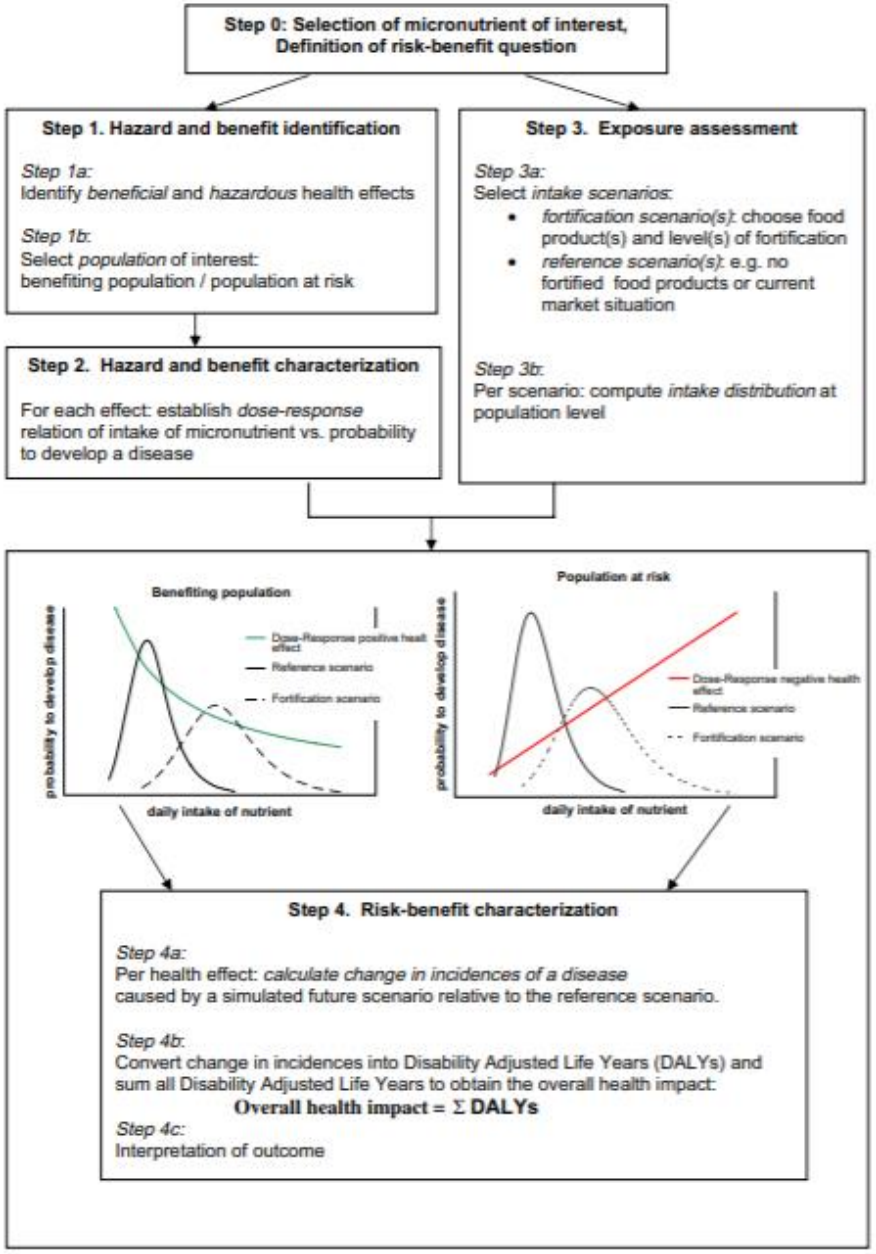
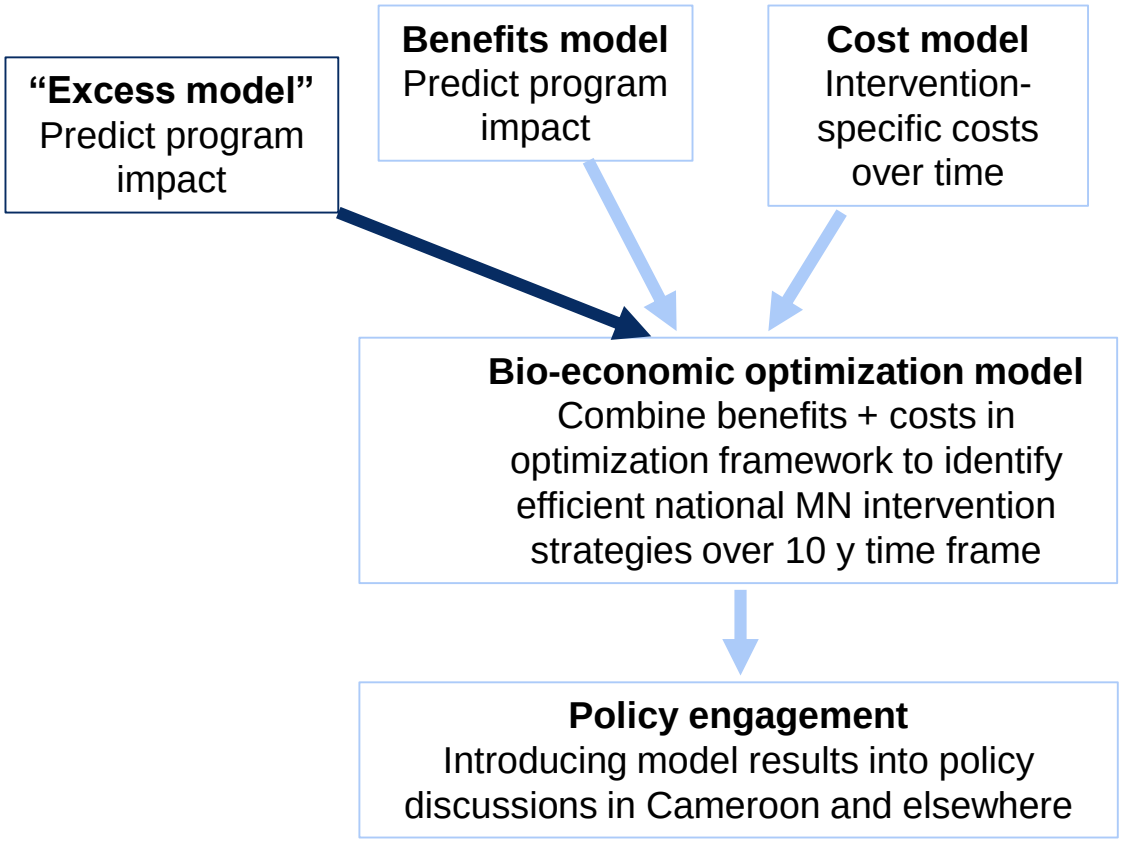


Fig. 1. Integrated risk–benefit model for micronutrients.

Economic optimization modeling: A framework for decision-making



Predict program impact on

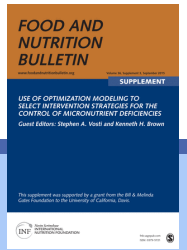
1) inadequate intakes,

2) high intakes,

3) where possible - functional outcomes of inadequacy (or excess)

Micronutrient Intervention Modeling project (MINIMOD)

Methods described in Food Nutrition Bulletin special issue, 2015



https://minimod.ucdavis.edu/

Conclusions

- Maternal anemia remains a public health priority globally; intervention programs are needed
- Measured and modeled dietary intakes suggest that exceeding the UL for iron is rare from diet but may occur occasionally from supplements or specific fortified products
  - Health consequences of high intakes are uncertain but appear minor for women (more complex for children)
- Models exist to help inform decisions to balance deficiency and high intake
  - Data to populate them are limited, but framework can still be useful
- What can we do going forward?
  - Ensure that programs are addressing a need and are targeted appropriately
  - Collect (and use!) program monitoring data
  - Advocate for collection of data on ALL potential sources of iron intake
  - Implement iron interventions along with malaria control measures (see WHO guidelines)

Thank you!

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