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Background
The World Health Organization recommends universal distribution of iron supplementation or multiple micronutrient powders to all children living in settings where anaemia is prevalent. However, a critical recent concern has been the safety of iron supplementation to children living in settings where malaria and other infections are endemic, supported by large randomized controlled trials. While WHO guidelines are based on GRADE-based evaluations of evidence for pre-defined beneficial and harmful outcomes, these recommendations do not incorporate risk-benefit or economic analysis for these interventions. Previously attempted economic analyses of iron interventions have not attempted to incorporate any assessment of the costs of potential harms associated with iron. Furthermore, they have not used high quality evidence of effects of iron supplementation to inform expected effects sizes of modelled outcomes.

Formal assessment of the benefit-risk is required for implementation of new public health policies (for example, by NICE in the UK) and can provide policymakers and countries with a sophisticated quantification of the potential outcomes associated with an iron supplementation programme than is presently available within WHO guidelines. Together with economic analysis, this information can potentially guide programme managers and policy makers when selecting between various health priorities and public health interventions.

The age group in whom the risks of iron interventions have been most clearly demonstrated, but in whom the prevalence of anaemia is greatest and the putative consequences of iron deficiency most serious, is children <2 years of age (within the first ‘1000 days’). As such, this represents a critical group in whom to understand the benefit-risk of iron supplementation more clearly. It is essential to properly incorporate an appreciation of the putative benefits and risks of iron associated with iron interventions. Thus, we are undertaking a formal risk-benefit analysis of iron supplementation and related interventions when deployed in the public health context, to children under-2.

The group have met by teleconference monthly since July 2014, and convened face to face in Washington DC in May 2015.
Modelling approach
We are using a microsimulation approach, where a cohort of hypothetical individuals are generated and their individual trajectories followed over their lifetime. There are two main advantages of a microsimulation model: 1) it can incorporate a large number of patient characteristics in a dynamic manner, allowing characteristics to change as a result of major events, and enabling us to model the influence of various events on costs and outcomes; and 2) it can straightforwardly incorporate patient history in modelling costs and outcomes e.g. receiving an exposure at a given time affects behaviour and health outcomes later on. Examples of microsimulation models used to evaluate large scale policy interventions include the US Future Elderly Model (University of Southern California), The Population Health Model (Statistics Canada) and the Chronic Disease Policy Model 2.0 (OECD).

Methodology

- Country level approach. Thus, estimates will be generated for each included country.
- Modeling of net DALY averted or incurred from a policy of routine iron intervention to children living in a country.
- Modeling of net cost per DALY averted and financial benefit cost incorporating costs of intervention, cost of programme, cost of treating complications, and (if identified) any long term impact on future earnings.

Interventions to be considered:
As per WHO (Essential Nutrition Actions 2014):
Interventions will be modeled as being delivered within current WHO recommendations.

- Daily Iron supplementation.
- Daily multiple micronutrient powder home based fortification

Contexts to be considered:
- Countries where the prevalence of anaemia among children under-5 exceeds 40%, and hence where the prevalence of anaemia would be considered a ‘severe public health problem’:
  - Non-malaria endemic
  - Malaria endemic

Outputs
The model will be able to provide country specific information for iron interventions to children <2 years, comprising:
1. The net benefit from iron interventions (specifically, both iron supplements and multiple micronutrient powders) in terms of averted Disability Adjusted Life Years (DALYs).
2. The cost per DALY averted in each country, incorporating the costs of both the intervention and any excess of medical treatments required due to risks of iron.
3. The cost per DALY as a proportion of GDP in each country, enabling prioritization of these interventions where they are likely to be most cost effective and affordable.

The analysis will also highlight the knowledge gaps and hence research needs which would improve the model, thus directing resources towards addressing the most pressing needs.

A peer-reviewed report and publication in an international journal is planned for late 2016, together with a presentation to the Micronutrient Forum 2016 and International Congress of Nutrition in 2017.