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# Interventions to reduce anaemia in low- and middle-income countries

## An evidence gap map

May 2024

Evidence  
Gap Map  
Report 33

Health



International  
Initiative for  
Impact Evaluation

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## About this evidence gap map

This report presents the findings of a systematic search to identify and map the evidence base of impact evaluations and systematic reviews of interventions for reducing anaemia. The online EGM is available [here](#). All content in this report is the sole responsibility of the authors and does not represent the opinions of Nutrition International and 3ie, including its donors or its Board of Commissioners. Any errors and omissions are also the sole responsibility of the authors. Please direct any comments or queries to the corresponding author, Ashiqun Nabi [anabi@3ieimpact.org](mailto:anabi@3ieimpact.org). All figures, charts, graphs, and tables in this report do not contain alternative text.

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## **Evidence Gap Map Report 33**

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## Summary

Anaemia affects about one-quarter of the world's population. Characterized by low red blood cell count or haemoglobin levels, anaemia is linked to a host of negative health consequences and death. Anaemia slows development and increases susceptibility to illness in children, reduces quality of life and productivity for adults, and causes health complications for women during pregnancy or childbirth. Food insecurity, conflict and socio-economic disadvantage are relevant factors, and some low- and middle-income countries (L&MICs) with high anaemia prevalence have weak economic growth. The loss of human potential from anaemia can perpetuate a vicious cycle of poverty.

Evidence about interventions to tackle the myriad causes of anaemia is growing. Previous evidence mapping has focused on a subset of relevant factors, interventions, or populations. This evidence gap map (EGM) considers a broad range of multi-sectoral factors, programs, and diverse populations. By compiling the relevant rigorous evidence, we aim to inform decision-making and facilitate the use of resources across multiple fronts to reduce the global anaemia burden.

We included:

- **2,196 impact evaluations (IEs)**
- **57 systematic reviews (SRs)** that we rated as high or medium confidence, and 15 ongoing SRs

We mapped the evidence across 46 intervention categories under 13 sub-domains and 21 health outcome categories. The interventions address **direct causes** of anaemia, such as nutrient intake, disease burden, and gynecological, obstetric and other health conditions; **intermediate risk factors**, including food insecurity, maternal and newborn care, family planning, knowledge, and services access; and **underlying risk factors** such as education, poverty, cultural norms, and health policies.

Most IEs focused on direct causes through *supplementation* of preventative and therapeutic micronutrients or *anti-malaria programs*. *Anaemia prevalence* and *haemoglobin levels* were the most frequently measured outcomes. Far fewer studies focused on interventions to address underlying risk factors of anaemia, such as *poverty*.

Reflective of trends in anaemia prevalence, most IEs took place in Africa and South-East Asia. However, **we identified a lower volume of studies for some countries with high anaemia prevalence**, including Mali, Zambia and Togo. When considering high anaemia prevalence, particularly for children under five and women of reproductive age, we identified a very low number of studies in countries such as Yemen, Mali, and Benin.

Of 180 eligible SRs, we assessed 57 as high or medium confidence.<sup>1</sup> Results were often inconclusive, inconsistent, or directly contradictory. Variations in population characteristics reviewed by SRs may contribute to conflicting findings about whether populations crossed the threshold of having anaemia. For example, populations covered by each SR may have differed with respect to underlying causes of anaemia, or baseline and endline haemoglobin levels. Although results should be interpreted with caution,

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<sup>1</sup> We assessed the remaining 123 SRs as low confidence as they did not utilize gold standard synthesis methodology. These were not included in the map or analysis.

findings from high- and medium-confidence SRs suggest the following interventions appear promising:

- Infants and children:
  - Iron fortification to increase haemoglobin levels
  - Multiple micronutrient fortification and the provision of specialized foods to increase haemoglobin levels and reduce anaemia prevalence
  - Intermittent preventative treatment against malaria
- Pregnant women:
  - Iron supplementation, sometimes combined with folic acid, to reduce maternal anaemia
  - Vitamin D supplementation to increase vitamin D levels

**Synthesis opportunities exist for future SRs, or to update existing SRs, for interventions that address:**

- Direct causes of anaemia:
  - Biofortification, HIV programs, and anti-parasite programs (other than malaria and helminths)
  - Point-of-use fortification, targeted fortification and dietary enhancement
- Intermediate risk factors:
  - Preventative care such as annual check-ups and adult immunization
  - Resources for health facilities, anaemia education and habit support, and other nutrition education activities

The EGM aims to facilitate the utilization of evidence for policy decisions, further evidence production, and the development of future interventions in L&MICs. Establishing a robust policy environment and extensive stakeholder support is crucial to facilitate the successful prevention and management of anaemia.

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## Acronyms

3ie	International Initiative for Impact Evaluation
AGP	$\alpha$ -1-acid glycoprotein
CRP	C-reactive protein
EGM	Evidence Gap Map
FCDO/DFID	Foreign, Commonwealth & Development Office of the UK, former DFID
HICs	High-income Countries
HKI	Helen Keller International
ICDDR,B	International Centre for Diarrhoeal Disease Research, Bangladesh
IE	Impact Evaluation
IFPRI	International Food Policy Research Institute
IYCF	Infant and Young Child Feeding
L&MICs	Low- and Middle-Income Countries
MAPS	Multi-Sector Anaemia Platform Strengthening
NI	Nutrition International
NIH	National Institutes of Health
SR	Systematic Review
SURE	Specialist Unit for Review Evidence
UNESCWA	United Nations Economic and Social Commission for Western Asia
UNSCN	United Nations System Standing Committee on Nutrition
WASH	Water, Sanitation, and Hygiene
WHO	World Health Organization
WRA	Women of Reproductive Age

# 1. Background

## 1.1 Anaemia is a global concern that disproportionately affects women and children

Anaemia is a health condition characterized by a below-normal quantity of red blood cells and a low concentration of haemoglobin in the blood.<sup>2</sup> Reduced haemoglobin volume **decreases oxygen circulating in the blood, causing fatigue, weakness, and reduced cognitive functionality**. Anaemia in children can permanently inhibit physical and mental development, increasing susceptibility to infectious and chronic diseases (Larson et al. 2019; Scott et al. 2014). Anaemia during pregnancy can result in adverse maternal and birth outcomes (Young et al. 2019; World Health Organization 2017; Jung et al. 2019).<sup>3</sup> In adulthood, anaemia reduces quality of life and productivity, **perpetuating a vicious cycle of poverty and anaemia** (Gardner et al. 2023; Balarajan et al. 2011; Horton and Ross 2003; Haas and Brownlie 2001).<sup>4</sup>

Anaemia is a major public health concern at a global scale, **affecting about one-quarter of the world's population** in 2021.<sup>5</sup> Children under five and women 15-49 are at particularly high risk of anaemia (Gardner et al. 2023; Stevens et al. 2022).<sup>6</sup> Rates of anaemia decreased from 1990 to 2021; however, the rate of progress plateaued in recent years (Gardner et al. 2023). There was essentially no change in the global prevalence of anaemia among women 15-49 years old from 2012 to 2019, the last year with available data for this demographic group (28.5% to 29.9%; FAO, IFAD, UNICEF, WFP, WHO and UNESCWA 2023). As such, **we are not on track to achieve the Sustainable Development Goal** of ending all forms of malnutrition by 2030 or the World Health Assembly's goal of reducing anaemia in women 15-49 by 50% by 2025 (World Health Organization 2020; United Nations 2020).<sup>7</sup> In response, the international community is taking action, with the launch of a **new comprehensive framework for anaemia action** (World Health Organization 2023a).

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<sup>2</sup> The current cut-offs for different age, sex and pregnancy status are defined by the World Health Organization (2017).

<sup>3</sup> Direct impacts of anaemia among pregnant women and their infants include preterm labor, postpartum haemorrhage, and low birth weight, among other complications, endangering both the mother and the child (Jung et al. 2019; Young et al. 2019).

<sup>4</sup> Adults, particularly older adults, commonly suffer from fatigue, loss of work productivity, and poorer health outcomes including increased hospitalization and mortality (Gardner et al. 2023; Haas and Brownlie 2001).

<sup>5</sup> According to the GBD data, 1.9 billion people (24.3% of the global population) across all ages were living with anaemia in 2021. The prevalence figure for 2021 decreased from 28.2% in 1990. However, the total number of people with anaemia increased from 1.5 billion to 1.9 billion, mainly due to population growth (Gardner et al. 2023).

<sup>6</sup> Estimates vary with Gardner and colleagues (2023) reporting prevalences of 41% in children under five, 34% in females 15-49, and 11% in males 15-49 for comparison. Stevens and colleagues (2022) report that 40% (269 million) of children 6–59 months of age, 37% (32 million) of pregnant women, and 30% (571 million) of women 15–49 years of age are affected by anaemia.

<sup>7</sup> In 2012, the 65<sup>th</sup> World Health Assembly set the target of reducing anaemia for women of reproductive age by 50% by 2025 (World Health Organization 2014).

## 1.2 Anaemia is a complex public health challenge

Its complex aetiology makes reducing the prevalence of anaemia challenging. Although anaemia is most commonly associated with iron and other nutrient deficiency (World Health Organization 2023b), infections and chronic diseases are also **direct causes** of anaemia (Hess et al. 2023; Chaparro and Suchdev 2019; World Health Organization 2017). Food insecurity and inadequate maternal and child care, family planning, access to health and nutrition services and knowledge are **intermediate risk factors**, increasing the likelihood that people experience the direct causes of anaemia (Hess et al. 2023; Sagalova et al. 2021). These risk factors are themselves affected by poverty, education, cultural norms, and health policies, which make people more vulnerable to anaemia and represent **underlying risk factors** (Gardner et al. 2023; Mitchinson et al. 2019). Finally, all of these risk factors are **fundamentally driven** by politics, the economy, ecology, inequity, climate, and geography, making anaemia a complex interdisciplinary challenge (Wilson et al. 2023; World Health Organization 2023a).

Because of this complex aetiology, **anaemia needs to be addressed through cross sectoral interventions that go beyond the direct causes of anaemia, to focus on the intermediate risk factors, underlying risk factors, and fundamental drivers.**

These complex interventions expand beyond the purview of the health sector, require multi-sectoral approaches, and must be supported by broad political and financial commitments (Wilson et al. 2023). A 2017 estimation by Shekhar and colleagues (2017) called for a substantial investment of US\$12.9 billion over 10 years to reach the global goal of a 50% reduction in anaemia in women 15-49 years. Given that limited progress has been made since that time, larger financial commitments will be needed to reduce the global anaemia burden.

## 1.3 Rationale for the EGM: decisionmakers need to know what works, for whom, and at what cost

To break the stagnation in progress towards anaemia reduction goals, impactful interventions must be identified, resources must be used efficiently, and robust political commitment and effective delivery platforms must be established. In response, WHO, with support from a range of stakeholders,<sup>8</sup> developed a 'comprehensive framework for integrated action on the prevention, diagnosis, and management of anaemia' in 2023. The framework launched a renewed global effort which prioritizes contextualized, multi-sectoral strategies and encourages the synchronized implementation of actions to address the various determinants of anaemia (World Health Organization 2023b). The **renewed global action aims to produce and use evidence**, especially in the analysis of causes and risks, the effectiveness of interventions, and the overall expansion of research, learning, and innovation.

As part of this renewed global action, WHO and UNICEF created the Anaemia Action Alliance, uniting government, non-government, and international multilateral stakeholders committed to collaborative initiatives for anaemia reduction. The Alliance's aim is to implement the comprehensive framework, support the overarching goal of

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<sup>8</sup> Multi-sectoral governmental actors, non-governmental organizations, UN agencies, and the private sector all contributed to the development of this framework.

collectively achieving anaemia reduction and improve health and well-being. It works to achieve its goal by supporting the implementation of timely and effective measures to prevent and manage anaemia.

**Evidence on the impacts of interventions addressing the direct causes, intermediate risk factors, and underlying risk factors of anaemia can play a pivotal role in helping decisionmakers effectively utilize their limited resources.** Although a large body of evidence exists on physiology, epidemiology, and interventions on tackling the direct causes of anaemia (e.g., nutritional, anti-malaria and deworming programs), there is a perceived lack of evidence on mitigating the effects of risk factors and fundamental drivers. The multidimensionality of anaemia poses a challenge to researchers, practitioners, and donors, who often restrict their focus to a limited number of issues within the broad field of anaemia. Stakeholders generally prioritize direct causes of anaemia, such as iron and nutrient deficiency and infectious diseases.

This evidence gap map (EGM) on anaemia interventions aims to make the evidence that is available on anaemia reduction more accessible and support the prioritization of new research. Despite the large body of evidence, no comprehensive map covers the diverse range of interventions addressing the multidimensional causes of anaemia. The Living Food Systems and Nutrition Evidence and Gap Map (3ie), which 3ie updates regularly, maps food systems interventions measuring food security and nutrition outcomes, but it excludes populations with diagnosed medical conditions, such as anaemia.

This new map is comprehensive in its scope, including interventions and outcomes reflecting the broader concept of anaemia (direct causes, intermediate and underlying risk factors) and to covers populations of all ages, sexes, and reproductive statuses.

**This map is uniquely valuable as it presents the evidence in an organized and interactive way that can be tailored to the interests of key stakeholders** through the use of the map's filtering options. It directly reflects the research agendas of the four working groups of the Anaemia Action Alliance<sup>9</sup> and collates the available information needed to achieve the research agenda outlined by Loech and colleagues (2023).

## 1.4 What is an EGM?

EGMs organize rigorous evidence of effectiveness thematically, aiding policymakers, practitioners, and researchers in making informed decisions within a specific thematic area. The map organizes the body of evidence over a framework of interventions and outcomes that represents a theoretical linkage to the concepts of the theme. EGMs improve accessibility to existing evidence, aiding in prioritizing future research by mapping studies in a field based on interventions and outcomes. Along with the volume of evidence, EGMs also report the types of evidence (completed or ongoing, impact evaluations (IEs), or systematic reviews (SRs)), research gaps, and SR confidence ratings reflecting the degree to which SRs followed gold-standard methodology. The results are displayed on 3ie's platform, offering a graphical and interactive representation of the evidence in a matrix form. The interactive map allows users to filter evidence in the EGM by region, disease of interest, gender, reproductive status, and evaluation

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<sup>9</sup> These working groups focus on national integrated anaemia action, programmatic implementation, investment for anaemia, and integrated research.

methods, among other options. EGMs do not provide information on interventions' effectiveness and cost-benefit analysis (beyond identifying which studies include cost data). In addition, quality appraisals of impact evaluations are typically beyond the scope of an EGM. Appendix A provides more information on how to use and interpret EGMs.

## 1.5 Objectives of the EGM

The specific objectives of this EGM are:

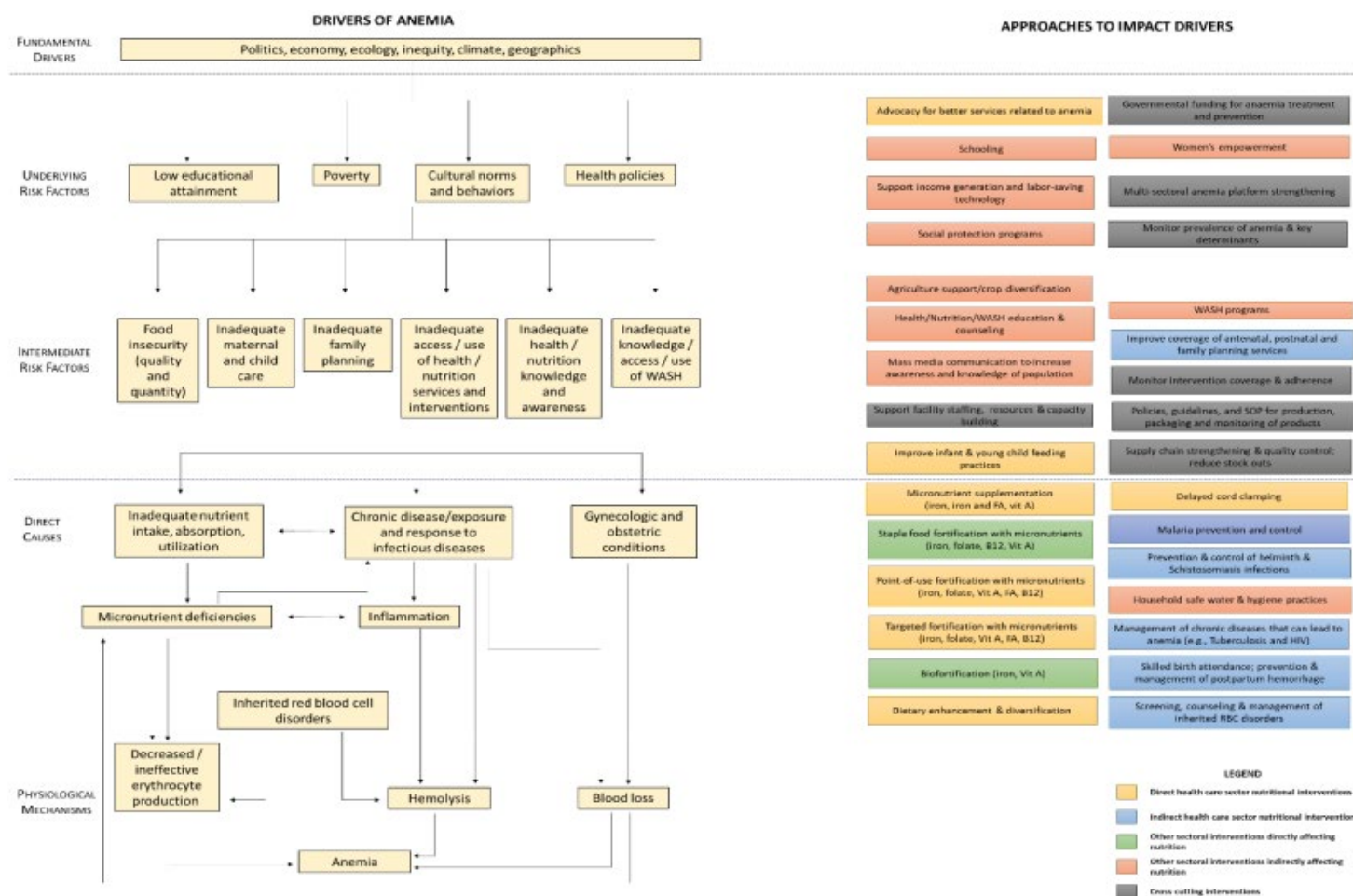
1. Identify and describe the characteristics of impact evaluations and systematic reviews which evaluate the effects of interventions to reduce anaemia directly or that address the determinants of anaemia (direct, intermediate, and underlying risk factors) in L&MICs.
2. Summarize findings from high- and medium-confidence systematic reviews on the effects of interventions to reduce anaemia directly or address the intermediate and underlying risk factors for anaemia in L&MICs.
3. Identify primary evidence gaps and synthesis gaps.

## 2. The theoretical framework guiding our conceptualization of intervening to address anaemia

Our theoretical framework is grounded in the well-established literature on anaemia aetiology (Hess et al. 2023; Chaparro and Suchdev 2019; Namaste et al. 2017; Stoltzfus and Klemm 2017). We approached anaemia as an interdisciplinary issue caused by biological, socio-economic and ecological risk factors, reflecting the multidimensional aetiology of anaemia (Hess et al. 2023; Chaparro and Suchdev 2019). **The framework was developed through a collaborative process with partners from Nutrition International and members of our Advisory Group** (see our protocol, Lane et al. 2023 for a list of advisors).

Politics, economy, ecology, inequity, climate, and geography are **fundamental drivers** of anaemia (Figure 1). These drivers influence the **underlying risk factors**: low education, poverty, cultural norms, and inequitable health policies, which, in turn, affect **intermediate risk** factors related to food insecurity, maternal and childcare, family planning, health knowledge, and access to services. These fundamental drivers, underlying risk factors, and intermediate risk factors collectively influence the **direct causes** of anaemia. Iron deficiency is the direct cause most commonly associated with anaemia. Other direct causes include insufficient nutrient intake or absorption, chronic diseases, infectious diseases, gynaecological and obstetric conditions, and inherited blood disorders. These act at the **physiological level** to induce low red blood cell count, commonly termed as anaemia. **Our EGM focuses on the three middle domains: underlying risk factors, intermediate risk factors, and direct causes** (Figure 1).

**Figure 1: A theoretical framework for anaemia interventions**



Note: Based on Chaparro and Suchdev (2019); Hess and colleagues (2023) and Keats and colleagues (2021). Approaches to impact drivers are meant to be illustrative and not exhaustive. They draw heavily on the new framework proposed by Keats and colleagues (2021) which proposes that nutrition interventions can be conceptualized as a two-by-two matrix consisting of direct and indirect approaches which function within and outside of the health care system.

## 2.1 What interventions and outcomes did we include?

A list of relevant interventions and outcomes was developed based on the three middle domains in the theoretical framework, defining the scope of the EGM (Table 1 and Table 2). This decision balances proximity to our outcome of interest with the practicality of implementing the interventions through development assistance. We do not include fundamental drivers in our intervention-outcome framework as these interventions might be too difficult to measure with our outcome of interest to warrant significant evaluation. We also focus on public health interventions as opposed to intervening at the physiological mechanisms level, which would likely require medical intervention rather than general development assistance.

**Table 1: Types of interventions included in the EGM**

Intervention domain and sub-domain	Description
<b>Direct causes</b>	
Chronic disease/exposure and response to infectious diseases	Population-level treatment and prevention programs for malaria, helminths & other parasites, HIV & tuberculosis
Gynaecological and obstetric conditions	Delayed cord clamping, management of heavy menses & postpartum haemorrhage
Inadequate nutrient intake, absorption, and utilization	Micronutrient supplementation, food fortification, and dietary enhancement and diversification interventions.
<b>Intermediate risk factors</b>	
Food insecurity	Nutrition-sensitive agriculture e.g., including homestead food production systems, livestock transfer programs, value chains for nutritious foods, and irrigation programs.
Access/use of health/nutrition services and interventions	Efforts to encourage antenatal and postnatal visits to healthcare facilities; provisioning resources and staff for these facilities.
Inadequate family planning	All family planning and birth spacing counseling, provision of information, contraceptives.
Inadequate health/nutrition knowledge and awareness	Interventions that focus on breastfeeding and IYCF education and support, anaemia and other nutrition education and counseling and habit support; provision of care for anaemia due to genetic blood disorders.
Inadequate access/use of WASH	The provision of water access, sanitation, and hygiene resources; education on hygiene
<b>Underlying risk factors</b>	
Low educational attainment	Interventions related to general education or schooling
Health policies	Country-driven efforts to strengthen multi-sectoral anaemia platforms, policy/advocacy for better services related to anaemia, registration and standardization of anaemia products and governmental funding for anaemia treatment and prevention services.
Cultural norms and behaviors	Initiatives to empower women for decision-making, including education, gender equality in marriages, equitable access to food and health services, and shifts in cultural norms away from early pregnancies and short birth spacing.

Intervention domain and sub-domain	Description
Poverty	Social assistance, social insurance, social care services provided by the state or non-state actors, and labor market policies and interventions to the most vulnerable.

Note: For further details, see Table 2 of the protocol (Lane et al. 2023).

**Table 2: Types of outcomes included in the EGM**

Outcome group	Indicator
Primary outcomes	Measures of anaemia and haemoglobin <sup>10</sup>
Inadequate nutrient absorption and utilization	Biomarkers and plasma/serum concentration of iron, folate, vitamins A, B12, B6, C, D, E, copper, zinc, selenium and riboflavin
Chronic disease/exposure and response to infectious disease	Measures of the frequency or severity of malaria, schistosomiasis, gastro-intestinal disease, kidney disease, and diseases cause by soil-transmitted helminths
Gynaecologic and obstetric conditions	Measures of postpartum blood loss, including mortality due to postpartum haemorrhage; measures of the frequency of delayed cord clamping or the time period between birth and cord clamping.

Note: For further details, see Table 3 of the protocol (Lane et al. 2023).

### 3. Our methods for developing the anaemia EGM

To develop this EGM, we followed standards and methods developed by 3ie (Snijlsteit et al. 2017; 2016; White et al. 2020). The process is summarized briefly below, and the comprehensive details, including on the comprehensive literature search, methods for searching, screening, critical appraisal of systematic reviews and data coding, are available in the protocol (Lane et al. 2023).

#### 3.1 Inclusion criteria for studies in the EGM

In Table 3, we summarize the inclusion criteria for the EGM, including the populations, interventions, comparators, outcomes, and study designs (PICOS), as well as the language and status of eligible studies.

<sup>10</sup> Measures using the WHO definition of anaemia were separated from those using other measures. The WHO (2011) considers the cutoffs for haemoglobin levels as follows: for children aged 6-59 months, the level should be less than 110 g/L; for children aged 5-11 years, less than 115 g/L; for children aged 12-14 years and non-pregnant women above 15 years, less than 120 g/L; for pregnant women, less than 110 g/L, and for men older than 15 years, less than 130 g/L. The WHO classifies the public health significance of anaemia in populations based on the prevalence of estimated levels of haemoglobin. This classification includes severe anaemia (40% or higher), moderate anaemia (20.0-39.9%), mild anaemia (5.0-19.9%), and normal (4.9% or lower). However, the WHO is currently in the process of updating these guidelines (Garcia-Casal et al. 2023).



**Table 3: Summary of criteria for studies included in the EGM**

Criteria	Description
Population	Low- and middle-income countries.
Interventions	Interventions addressing <b>direct causes</b> , <b>intermediate risk factors</b> and <b>underlying risk factors</b> , reflecting the three domains of the aetiology framework. For further details, see Table 2 of the protocol (Lane et al. 2023).
Comparison	Must have a comparison group (of any type).
Outcomes	<b>Primary outcomes</b> (anaemia and haemoglobin), <b>inadequate nutrient absorption and utilization</b> related outcomes, <b>chronic disease/exposure and response to infectious disease</b> related outcomes and <b>gynaecologic and obstetric conditions</b> related outcomes. For further details, see Table 3 of the protocol (Lane et al. 2023).
Study designs	<b>Quantitative impact evaluations (IEs):</b> <ul style="list-style-type: none"> <li><i>RCTs and natural experiments</i></li> <li><i>Quasi-experimental designs</i> (fixed effects including difference-in-difference, instrumental variable estimations, interrupted time series analysis, regression discontinuity design, statistical matching)</li> </ul> <b>Systematic reviews:</b> Narrative/thematic synthesis with or without meta-analysis. Detailed descriptions of included study designs are available in Appendix C of the protocol (Lane et al. 2023).
Language	English and Spanish. And Portuguese, although search terms were in English.
Publication date	2012 or later.
Status of studies	<ul style="list-style-type: none"> <li>Published and unpublished studies (grey literature)</li> <li>Ongoing studies (prospective study records and protocols).</li> </ul>

Note: For further details on the PICOS, see the published protocol (Lane et al. 2023). During the implementation of the EGM, we had to make some adaptations to the original protocol to keep the EGM within practical limits. See section 3.3 and Appendix B for further details.

## 3.2 How we searched for evidence

We collaborated with an information specialist to search for relevant literature across 12 academic databases (in May 2023) and eight grey literature sources (in June 2023). A complete list of literature sources is presented in Appendix C, and search terms are available upon request.

The electronic database searches were complimented by screening the studies included in the systematic reviews identified in this EGM. Furthermore, we consulted with our advisory board members to suggest any relevant literature and published an open invitation through a blog (Nabi et al. 2023).

## 3.3 How we screened and extracted study characteristics

We used EPPI Reviewer to organize and screen the imported search results (Thomas et al. 2023). We combined screening by trained reviewers<sup>11</sup> with the Classifier – a machine-

<sup>11</sup> Reviewers were trained extensively on eligibility criteria and screening processes. They were tasked to screen titles and abstracts and full text records only when their screening reliability scores with the core team were above 85 percent. Further, at least one core team was present during the reconciliation sessions until they were confident with the reviewers' performance.

learning tool by the EPPI Reviewer<sup>12</sup> – to screen these records based on the titles and abstracts. Eligible records were independently double-screened at full text. Disagreements between reviewers were reconciled, with the input of a third reviewer when necessary.

Trained reviewers extracted data on various study characteristics from the included studies, including the year of publication, country of intervention, and study design. The data extraction template can be found in Appendix D of our protocol (Lane et al. 2023). Senior team members checked ten percent of the records to ensure the quality of screening and data extraction. To ensure comprehensive information and minimize overlap, we created a unified entry that combined linked publications associated to one research study (see section 4.4.6 of the protocol for details).

We critically appraised and rated the identified SRs with confidence ratings of low, medium, or high using an adapted version of the SURE checklist (Specialist Unit for Review Evidence\_(SURE) 2018), which offers objective judgments on the confidence one can place in the findings of a review, based on whether biases are introduced at various stages of the review process. The appraisal assesses the rigor of methods applied in each SR, including search, screening, data extraction, and synthesis methodologies, against gold standard practices. The systematic review critical appraisal criteria are available in Appendix E of our protocol (Lane et al. 2023).

## **4. What we found**

### **4.1 Search results**

Following the PRISMA guideline for reporting reviews (Page et al. 2021), Figure 2. presents the number of records identified, screened, and included in the map. We identified 41,817 records from 12 academic databases in May 2023 and 3,374 records from 8 grey literature sources in June 2023. We identified a further 1,369 records through citation tracking and 53 records from other sources, including suggestions from advisors and experts and via a blog post. After removing duplicate records, 43,316 records remained. We excluded 13,914 records through EPPI reviewer's machine learning classifier tool<sup>13</sup>, and independent reviewers double-screened the remaining titles and abstracts. We identified 9,219 records for screening at full text, of which 7,515 records were retrieved.<sup>14</sup>

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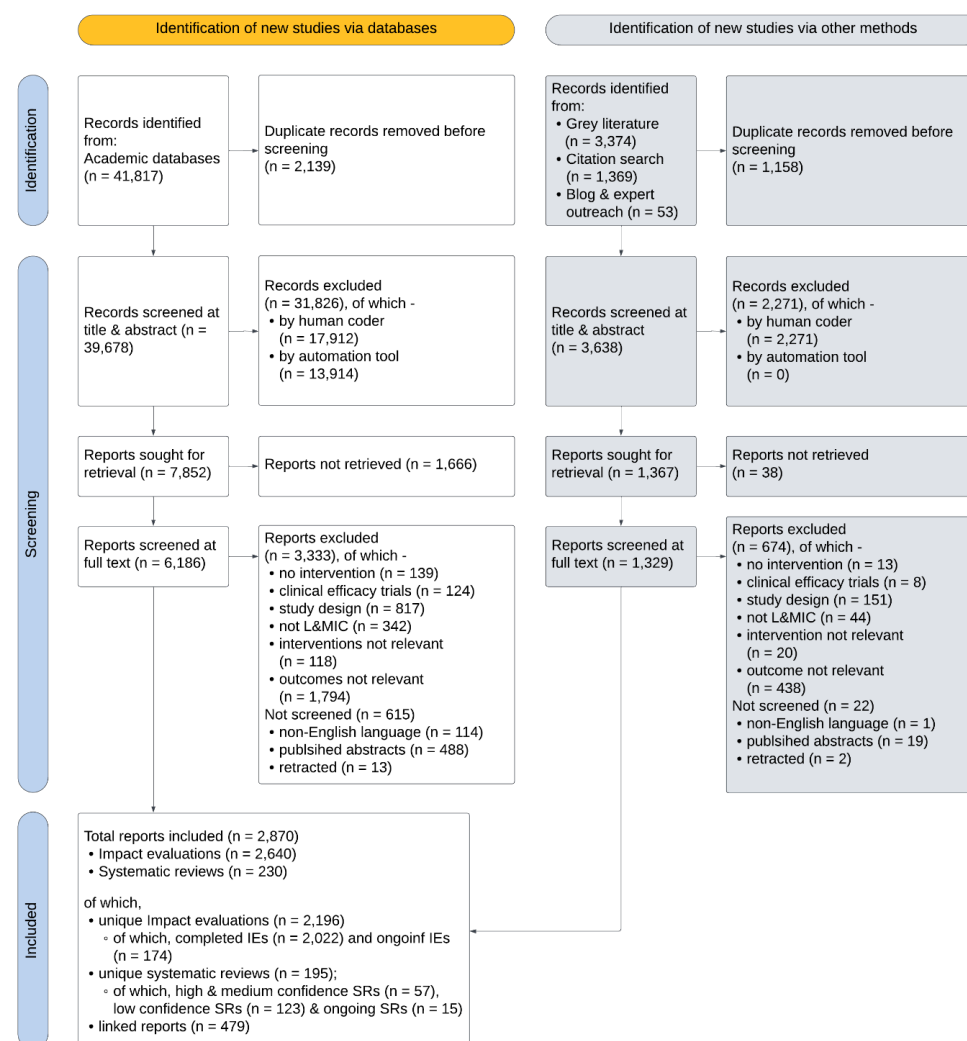
<sup>12</sup> We employed a machine learning tool integrated into EPPI reviewer (Thomas et al. 2023). Utilizing multiple sets of items that have already been screened and coded with include or exclude labels (by 3ie's past database of screened records and manually screened records from this EGM), the classifier tool categorizes references, arranging them based on the likelihood of relevance. We auto-excluded any records with an inclusion probability of less than 30 percent.

<sup>13</sup> See section 3.3 for further information on the classifier tool (Thomas et al. 2023).

<sup>14</sup> We were unable to locate the full text for 1,145 records, mostly due to missing bibliographic information such as publication sources and web-links. There were 548 records behind paywall which we could not access with 3ie's institutional library access. In addition, we could not screen 507 records that were published as conference abstracts, posters and presentations, and 15 records were not retrieved as they were retracted or under review for retraction. Due to limited time and resources, we were unable to make further attempts to retrieve the unlocated or paywall restricted records. Appendix D provides a list of the unretrieved records mentioned above.

Ultimately, 2,870 reports satisfied our inclusion criteria, including 2,196 unique IEs (including 174 ongoing), 195 unique SRs (including 15 ongoing), and 479 linked reports.<sup>15</sup> Examples of studies excluded at full text can be found in Appendix D2. Out of the 195 SRs identified, our analysis of the SR appraisals and findings (section 4.7) and the online map represent 57 high- and medium-confidence SRs and 15 ongoing SRs. A complete list of included studies is available in Appendix D3, D4 and D5.

**Figure 2: PRISMA Diagram of systematic search and screening**



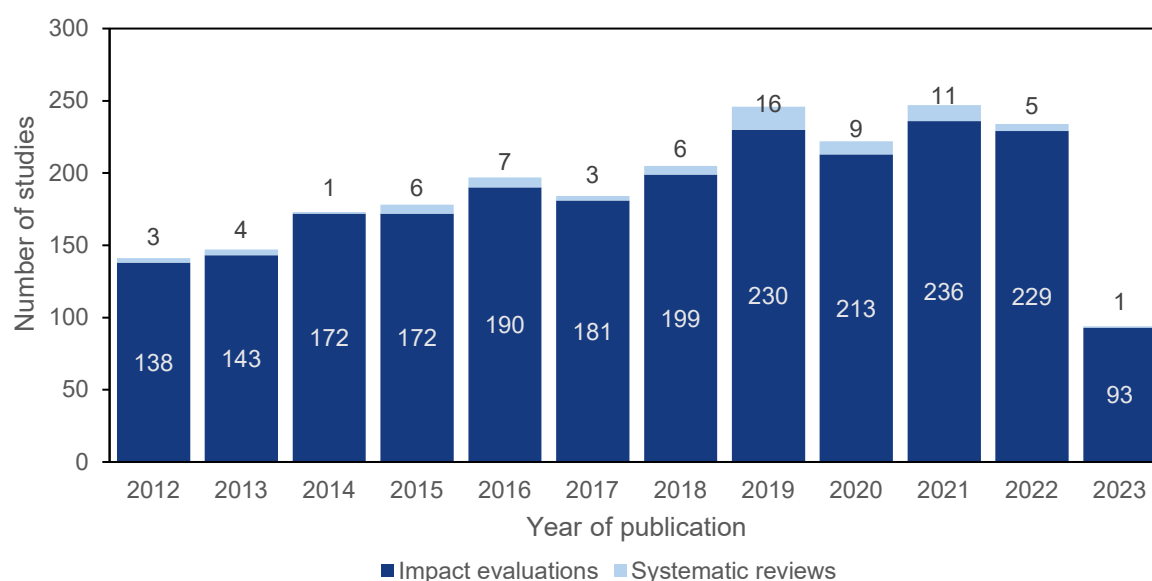
Note: The online map shows 2,268 studies which includes 2,196 unique IEs (2022 completed and 174 ongoing IEs) and 72 SRs (57 high and medium confidence SRs and 15 ongoing SRs).

<sup>15</sup> We deemed papers to be linked when they shared common authors and studied the same or partially overlapping research questions. These papers assessed either the identical intervention(s) or a subset of them and often they shared the same trial or protocol registration numbers. These linked papers frequently featured identical or a subset of the samples from the same population and analyses but differed in publication status, such as trial registry records or protocol documents, or one being a working paper and another a journal article. Alternatively, certain papers utilized a subset of the dataset from the main paper(s), included additional analyses and concentrated on extra outcome measures. In the analysis for this EGM, we only considered the “master” version from a set of linked papers. For more insights into our process of identifying the master and the linked papers, please refer to section 4.4.6 of the protocol (Lane et al. 2023).

## 4.2 Evidence on the effectiveness of anaemia interventions has been growing steadily over the last decade

Our systematic search showed an increase in the production of evidence on interventions addressing the direct causes, underlying risk factors, and intermediate risk factors for anaemia over the last decade (Figure 3) with 2019 (n = 246) and 2021 (n = 247) having the highest numbers. There was a slight dip in 2020, possibly due to research and publication interruptions related to the COVID-19 pandemic, but an uptick again in 2021 and 2022. Since the numbers for 2023 reflected mid-year figures, it was too early at the time of this analysis to confirm that the trend continues in 2023.

**Figure 3: Number of impact evaluations and systematic reviews identified by year**

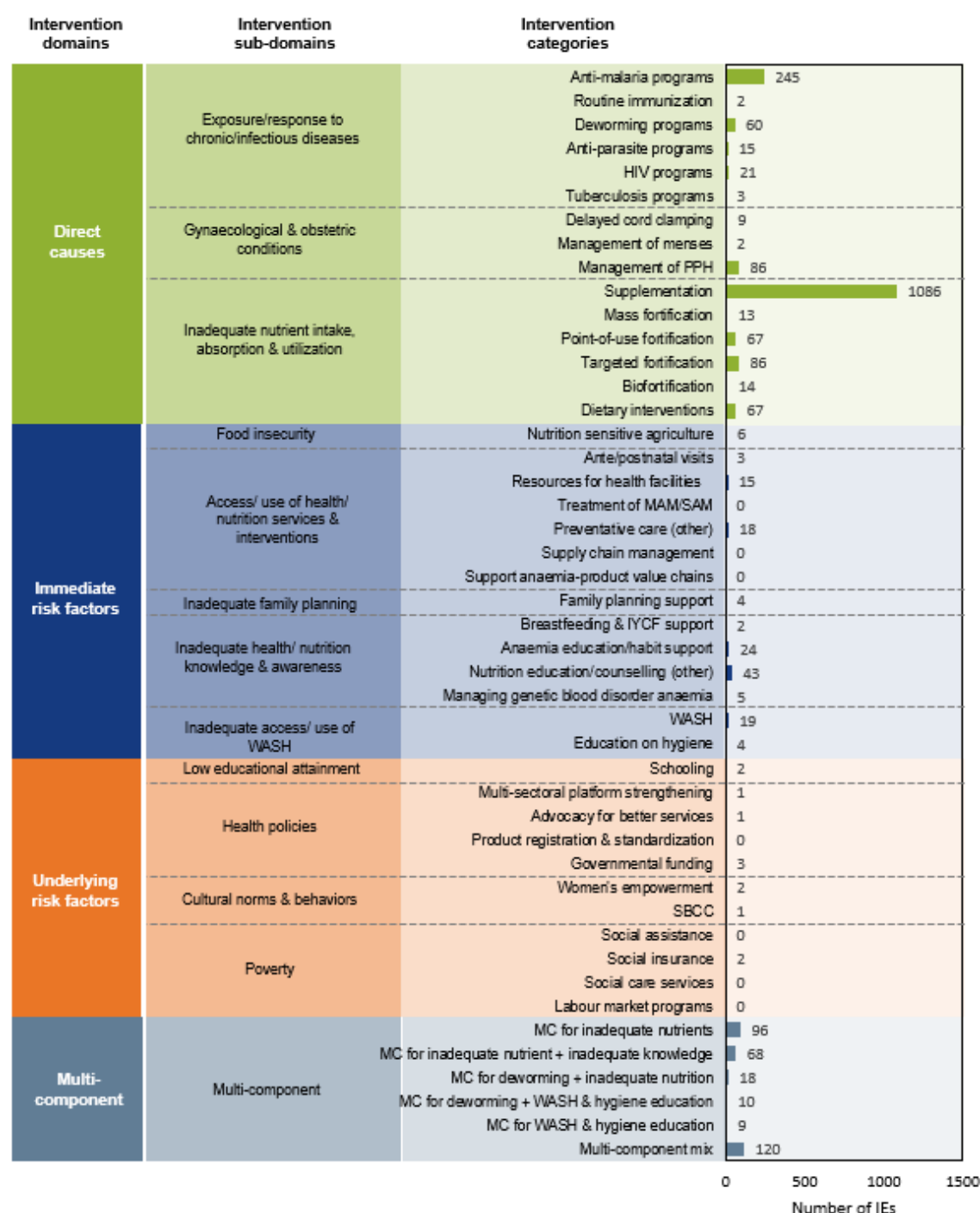


Note: The figure for 2023 is based on mid-year data. SRs include high and medium confidence as well as ongoing SRs.

## 4.3 Over 70% of IEs evaluate direct causes of anaemia

Our analysis showed that **45.5% (n = 998) of all the included IEs reported direct measures of haemoglobin**. The majority of included IEs evaluated a single intervention category, while 321 evaluated interventions across multiple categories and were designated as multi-component. Figure 4 presents the breakdown of IEs by intervention domains, sub-domains, and categories.

**Figure 4: Number of impact evaluations by intervention categories included in the map**



Note: To improve readability we truncated some of the intervention labels as: management of PPH (management of postpartum haemorrhage), dietary interventions (dietary enhancement and diversification), treatment of MAM/SAM (treatment of moderate or severe acute malnutrition), Preventative care, other (Provision of other preventative care), Supply chain management (Education and direct support for supply chain management), Support anaemia-product value chains (Mobilization of public and private sector actors to support anaemia-product value chains), Family planning support (Family planning and birth spacing counselling), Breastfeeding & IYCF support (Breastfeeding and IYCF education and support), Management of genetic blood disorder anaemia (Counselling and management of anaemia due to genetic blood disorders), WASH (Water access, sanitation, and hygiene resources), Governmental funding (Governmental funding for anaemia treatment and prevention), SBCC (Social and behaviour change communication on gender norms), MC for inadequate nutrients (Multi-component interventions for inadequate nutrient), MC for inadequate nutrient + inadequate knowledge (Interventions for inadequate nutrient + inadequate knowledge), MC for deworming + inadequate nutrition (Deworming + interventions for inadequate nutrition), MC for deworming + WASH & hygiene education (Deworming + WASH & hygiene education), MC for WASH & hygiene education (Multi-component interventions on WASH & hygiene education).

As expected, of the three broad intervention domains, **the highest number of IEs was identified for interventions addressing the direct causes of anaemia** (n = 1,776; 81%). Within this domain, the sub-domain of ***inadequate nutrient intake, absorption, and utilization*** had the largest evidence cluster (n = 1,333), with ***supplementation of preventative and therapeutic micronutrients*** being the most studied intervention category (n = 1,086). The identified IEs in this sub-domain covered all outcome categories except for the *frequency of delayed cord clamping*, for which there is no theoretical reason to expect an effect, so IEs here were not anticipated.

The second largest evidence cluster within the *direct causes* domain was the sub-domain of interventions focused on ***chronic disease/exposure and response to infectious diseases*** (n = 346). The effects of *anti-malaria programs* were evaluated by 245 IEs. This sub-domain's second most evaluated intervention category (although much lower than the most evaluated) focused on *deworming programs* (n = 60). The studies categorized under the *chronic/infectious disease* interventions reported on all primary and relevant *disease-related* outcomes, most of the *nutrient absorption/utilization-related* outcomes, but not on *gynaecologic and obstetric conditions* outcomes.

We identified 96 studies that evaluated interventions addressing ***gynaecological and obstetric conditions*** leading to anaemia, including *management of postpartum haemorrhage* (n = 86), *delayed cord clamping* (n = 9) and *management of menses* (n = 2). These studies reported *primary outcomes* and *gynaecological and obstetric conditions* related outcomes, but rarely reported on *nutrient absorption/utilization* (n = 4), and one study reported an outcome related to *chronic/infectious disease*.

**Studies of intermediate risk factors comprised 6.5% of the identified IEs.** Within this domain, we found the largest number of IEs for the sub-domain of interventions focusing on *inadequate health/nutrition knowledge and awareness* (n = 74) followed by *access/use of health/nutrition services and interventions* (n = 36) and *inadequate access to/use of WASH* (n = 23). Most evidence was clustered around nutrition education-related activities (n = 67) categorized under *anaemia education and habit support* (n = 24) and *other nutrition education and counselling* activities (n = 43). While *primary outcomes* and *chronic disease / exposure and response to infectious disease related* outcomes were frequently measured by studies of anaemia interventions, evidence was thinly spread across *inadequate nutrient absorption and utilization* related outcomes. We also found **no interventions in this domain measuring the frequency of delayed cord clamping**, despite improved health care being a major component of this intervention domain.

We found the least evidence evaluating the interventions addressing *underlying risk factors* of anaemia (n = 23). Within this group, 111 IEs evaluated interventions addressing *poverty*, such as *social assistance* (n = 9). Majority of the studies in this domain (n = 18) reported on *primary outcomes*. We found very little evidence in the *underlying risk factor* domain that measured *gynaecological and obstetric conditions outcomes* (n = 2) or *inadequate nutrient absorption and utilization outcomes* (n = 1).

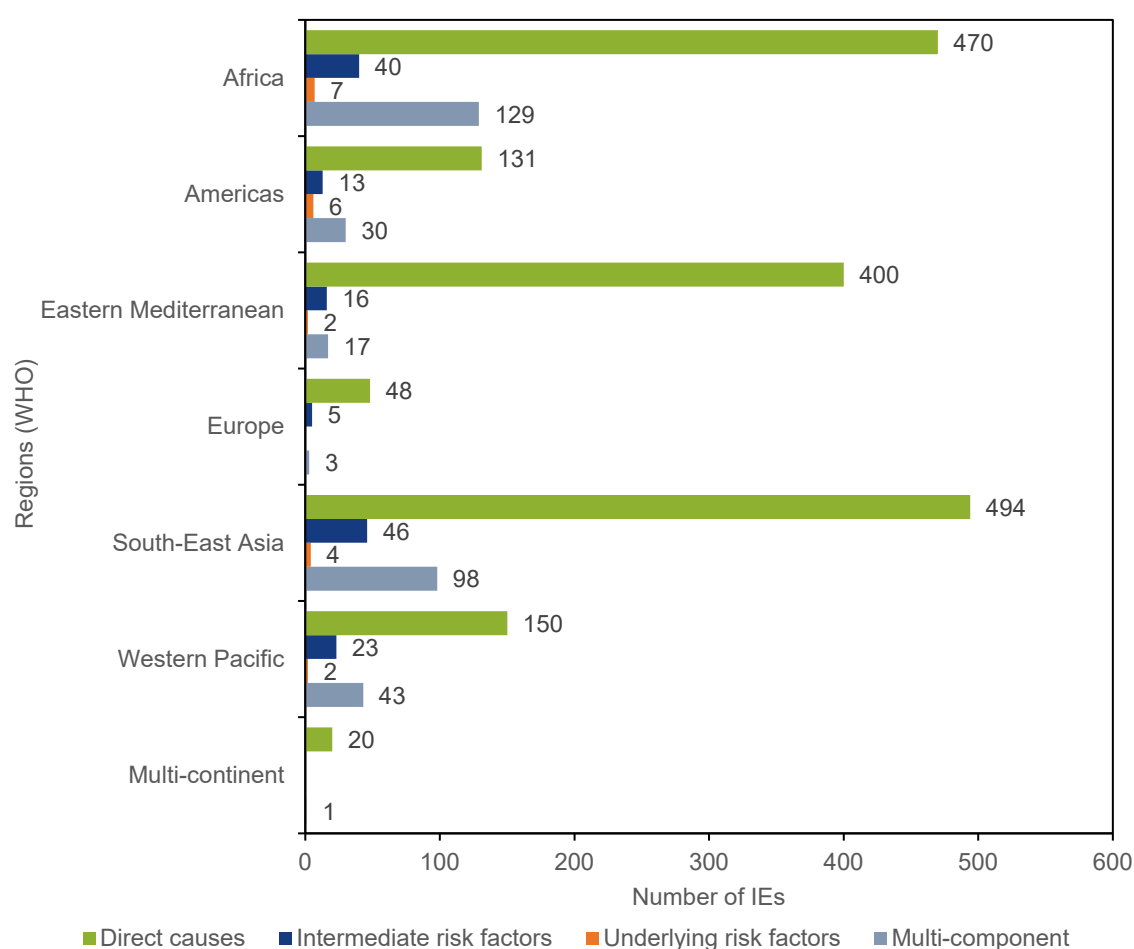
Overall, we found no absolute gaps in the evidence base for any of the intervention-outcome domains or sub-domains. However, the effects of interventions to address *gynaecological and obstetric conditions* on *inadequate nutrient absorption and utilization*

were relatively understudied with *iron* being the only nutrient considered. These interventions tended to be studied for their effects on *anaemia*, *haemoglobin*, *postpartum haemorrhage*, and *delayed cord clamping*. Similarly, the effects of *nutrition sensitive agriculture* on *gynaecological and obstetric conditions* were rarely considered. Instead, evaluations of these interventions focused on outcomes such as *anaemia* (n = 5), *haemoglobin* (n = 4) and *iron* (n = 3). In both cases, the relative dearth of information on these specific sub-domain combinations is likely because there is little theoretical reason to expect a relationship.

#### 4.4 Evidence is clustered in Africa (n = 661) and South-East Asia (n = 659) but is absent in several countries with high anaemia prevalence

These regions also have the highest anaemia prevalence (Global Burden of Disease Collaborative Network 2023). In all regions, *direct causes* was the domain with the most evaluations, followed by multicomponent interventions and *intermediate risk factors*. As shown in Figure 5, **at least 70 percent of the interventions evaluated in each region targeted the *direct causes* of anaemia** (Global Burden of Disease Collaborative Network 2023). The prevalence of IEs for *intermediate risk factor* interventions varied more across regions, with few in the Eastern Mediterranean (n = 16; 4%) compared with the Western Pacific (n = 23; 11%) and Africa (n = 40; 6%).

**Figure 5: Distribution of broad intervention levels by regions**



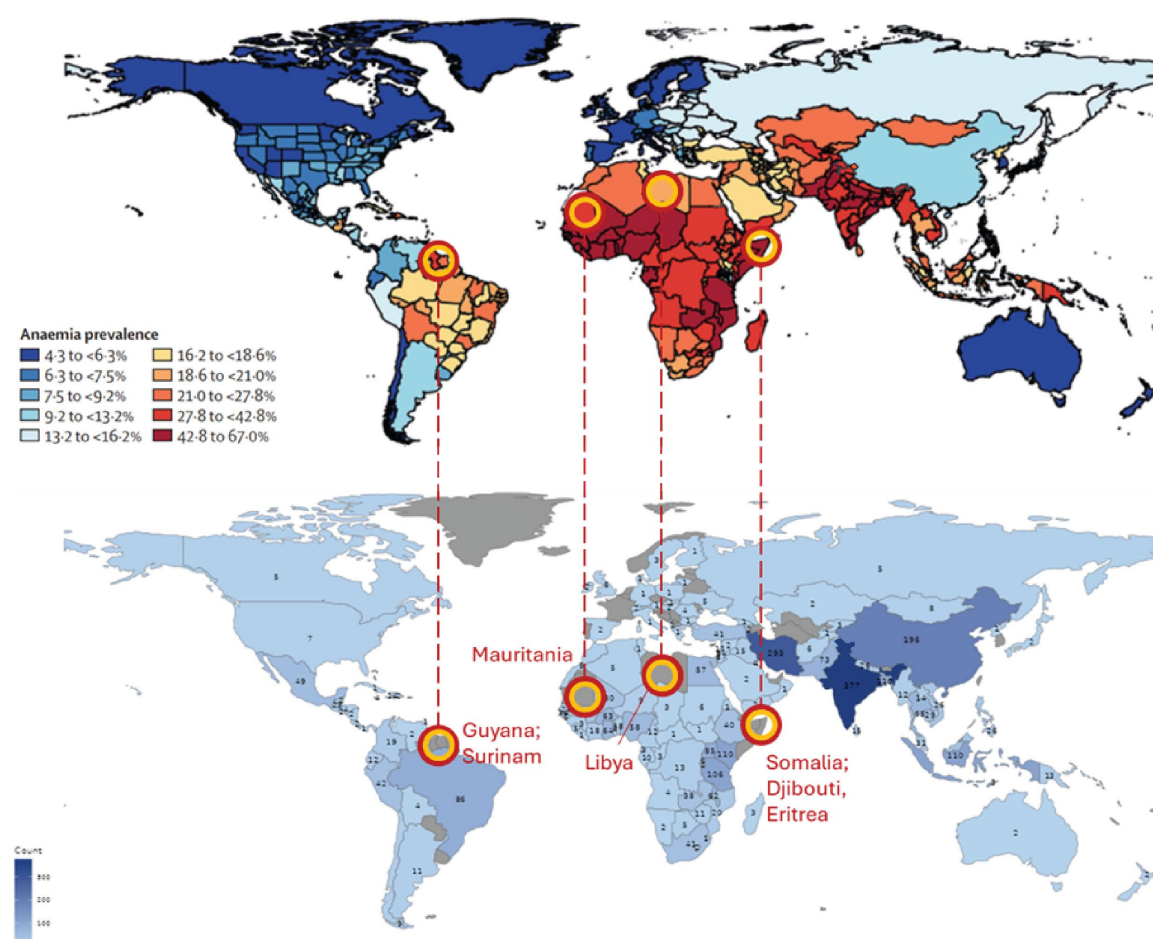
**India (n = 348), Iran (n = 286), China (n = 171), Indonesia (n = 85), and Tanzania (n = 83) are the countries with the most IEs.** India and Tanzania have high prevalence of anaemia (between 28 and 67%), while the prevalence in the other three countries is lower (between 9 and 21%; (Global Burden of Disease Collaborative Network 2023).

**We also identified several countries with high anaemia prevalence where no studies have been conducted** (Figure 6). These include Guyana, Mauritania, Suriname, Libya, Somalia, Djibouti, and Eritrea. The countries with the highest prevalence of anaemia (>50%) in 2021 were Mali, Zambia and Togo have anaemia (Global Burden of Disease Collaborative Network 2023), yet few studies took place in Mali (n = 17), Zambia (n = 21), or Togo (n = 1).

**When disaggregating different population groups, the countries with the highest prevalence differ slightly.** According to WHO data from 2019, nearly 80% of children aged 6-59 months in Yemen, Mali and Burkina Faso have anaemia (World Health Organization 2023b). We found one study in Yemen, eight in Mali and 24 in Burkina Faso evaluating outcomes for children in this age group. Anaemia prevalence for women of reproductive age was highest in Yemen (over 60%), Mali (60%) and Benin (55%), yet we found five studies from Benin and none from Yemen or Mali targeting women of reproductive age. When addressing geographical gaps, researcher should consider the context-specific aetiology in order to decide which interventions are appropriate. In addition, while interventions on direct causes may work similarly across contexts given their biological mechanisms, the mechanisms of interventions on intermediate and underlying risk factors are more sociological in nature, and thus may need to be evaluated across contexts.



**Figure 6: Comparison of anaemia prevalence vis-à-vis number of studies identified.**

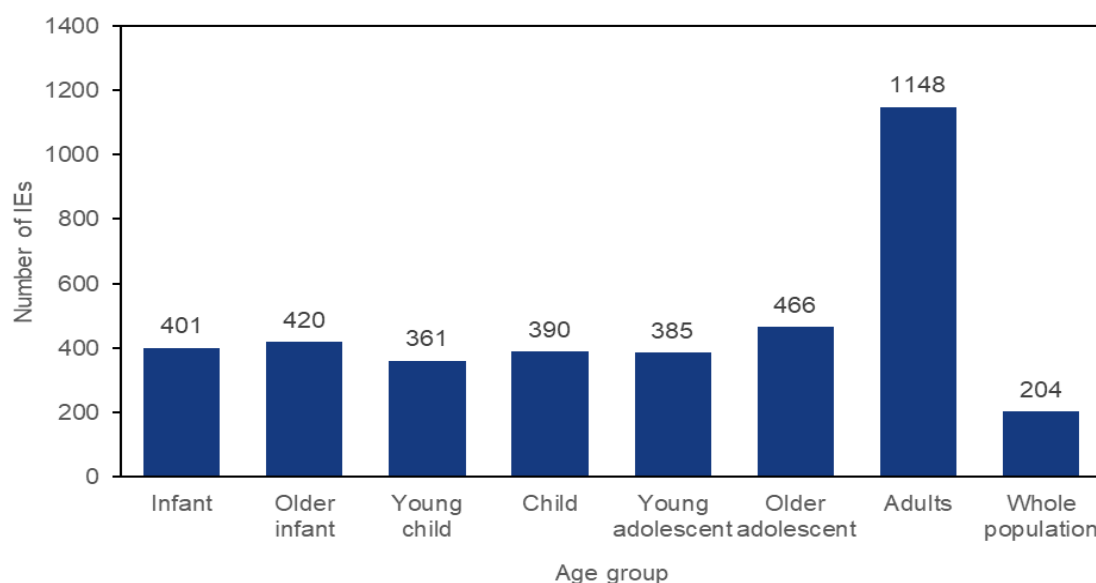


Note: Top map - Anaemia prevalence by country. Bottom map - Number of impact evaluations by country. Countries marked in circles have relatively high anaemia prevalence but no identified evidence.

#### 4.5 More than half of the IEs evaluated impacts on an adult population

Adults were the most commonly studied age group ( $n = 1,148$ ), likely because this age group spans the most years. Infants and children under five were studied almost as frequently as adults ( $n = 1,181$ ). We broke down the age groups of individuals and found between 15 and 19% of the IEs evaluated each group (Figure 7). Nearly half of the included IEs evaluated programs across more than one age group ( $n = 1012$ ; 46%).

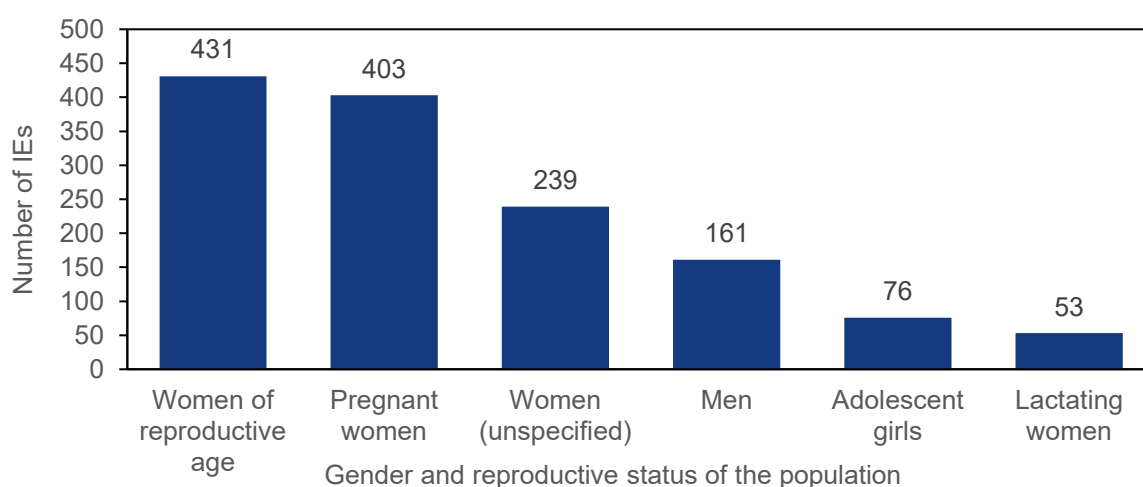
**Figure 7: The age distribution of the population analyzed in the 2,197 included impact evaluations**



Note: Where studies reported more than one age group, multiple coding was permitted; thus, the total number of evaluated populations may exceed the total number of included IEs. Age classification: Infants (0-6 months), older infants (7-23 months), young child (24-59 months), child (5-9 years), young adolescent (10-14 years), older adolescent (15-19 years), adults (>19 years) and whole population (covered the entire population, or no age specification reported).

**Women of reproductive age were the most commonly evaluated group by reproductive status.** While 60.4 percent of the studies did not focus on specific groups regarding the participant's gender and reproductive status, women (combining pregnant women, lactating mothers, women of reproductive age, and adolescent girls) were much more frequently targeted than men (Figure 8).

**Figure 8: Distribution of studies by gender and reproductive status of the population**



Note: Multiple coding was permitted where studies reported more than one group. Thus, the total number of evaluations reflected in the figure may exceed the number of included IEs. Women of reproductive age included any women between 15 and 49 years of age.

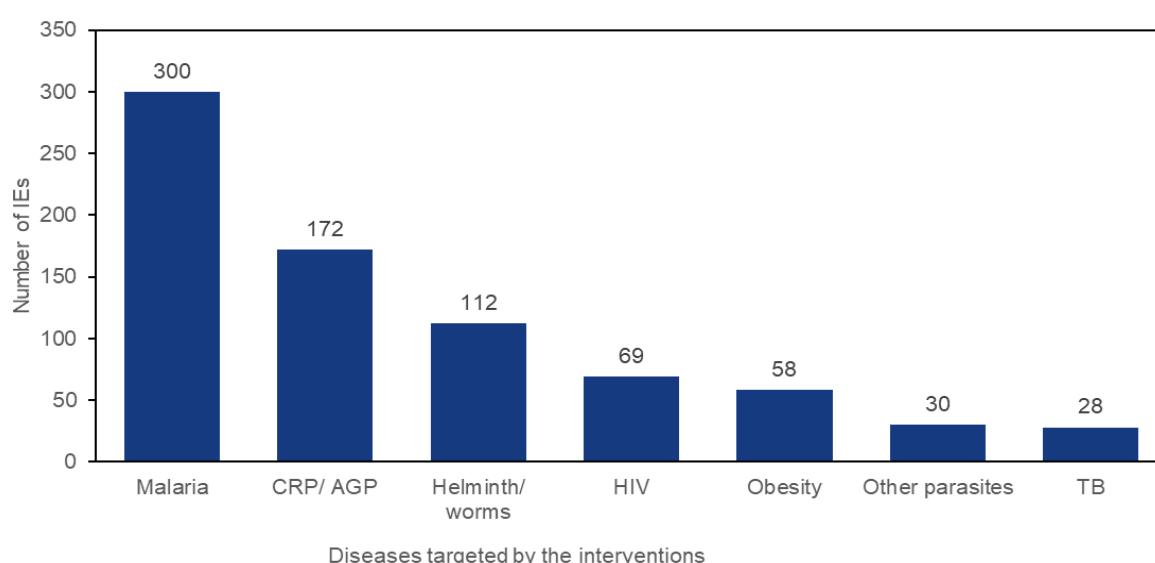
**Rural settings hosted most of the IEs that reported on evaluation locations.**

Although most studies (n = 1,487) did not specify any location, about a quarter of the studies (n = 540) reported that the IE was conducted in a rural area.

**Overall, 31% of the IEs reported having targeted or evaluated a specific disease.**

Malaria was the disease most commonly reported, with 300 IEs (13.7%) evaluating malaria programs or measuring malaria outcomes (Figure 9). About 8 percent of the IEs reported measures of inflammation (i.e., C-reactive protein, CRP and  $\alpha$ -1-acid glycoprotein, AGP). Less than 1% of studies (n = 38) reported that their interventions targeted a population with genetic blood disorders such as  $\beta$ -thalassemia, sickle cell disorder, glucose-6-phosphate dehydrogenase (G6PD), and  $\alpha$ -thalassemia.

**Figure 9: Distribution of IEs reported to have targeted a disease**



Note: Multiple coding was permitted where studies reported more than one group. Thus, the total number of evaluations reflected in the figure may exceed the total number of included IEs. The 66% of the IEs that did not report to have focus on any disease were not presented in this figure. Acronyms: C-reactive protein (CRP),  $\alpha$ -1-acid glycoprotein (AGP), Human Immunodeficiency Virus (HIV), Tuberculosis (TB).

#### **4.6 The majority of the IEs were RCTs**

The vast majority of IEs in this body of evidence were evaluated using RCTs (92%; Table 4). Although we excluded purely qualitative studies, we identified 55 mixed-methods IEs among our included studies.

Fixed-effect methods (including difference-in-difference) was the most commonly used quasi-experimental methods. These studies evaluated *supplementation* (n = 57), *anti-malaria programs* (n = 37), *nutrition education and counselling* (n = 22), *dietary enhancement and diversification* (n = 20) and *deworming and helminth programs* (n = 19) among other interventions.

**Table 4: Frequency of included IEs by study design**

<b>Evaluation Design</b>	<b>No. of studies</b>
<b><i>Experimental impact evaluations</i></b>	<b>1941</b>
Randomized controlled trial	1941
<b><i>Quasi-experimental impact evaluations</i></b>	<b>255</b>
Fixed effects (including difference in difference)	188
Statistical matching	31
Interrupted time series analysis	12
Regression discontinuity design	10
Instrumental variable estimation	7
Synthetic control	7

Note: These figures represent a study's dominant estimator. For example, if statistical matching was used to select a sample and then authors used a difference-in-differences or fixed effects regression, the difference-in-differences or fixed effects was coded as the dominant estimator. Hence, statistical matching refers to cross-sectional studies only and is characterized by the strong ignorability assumption. The group of difference-in-difference and fixed-effect studies are primarily characterized by the parallel slopes assumption.

About 59% of the IEs (n = 1,293) reported that the study or the protocol was pre-registered, and 87% reported having obtained ethical approval (n = 1,903). Of the IEs, 64% (n = 1,238) of the RCTs reported to have pre-registered and 88% (n = 1,808) reported obtaining ethical approval. Among the SRs, 19 of the 57 high and medium confidence reviews reported pre-registration (33%). However, our analysis was based on information reported in the publications and as such, does not necessarily indicate that the studies did not pre-register or obtain ethical clearance.

Approximately 6% of included IEs (n = 131) reported some cost data. However, many of these (n = 94) reported minimal cost-related information, such as the cost of one or more components of the intervention or program, the delivery cost of a particular component, outreach costs, etc. Other reported cost-related information included cost-benefit analysis (n = 19) or the program's total budget (n = 11).

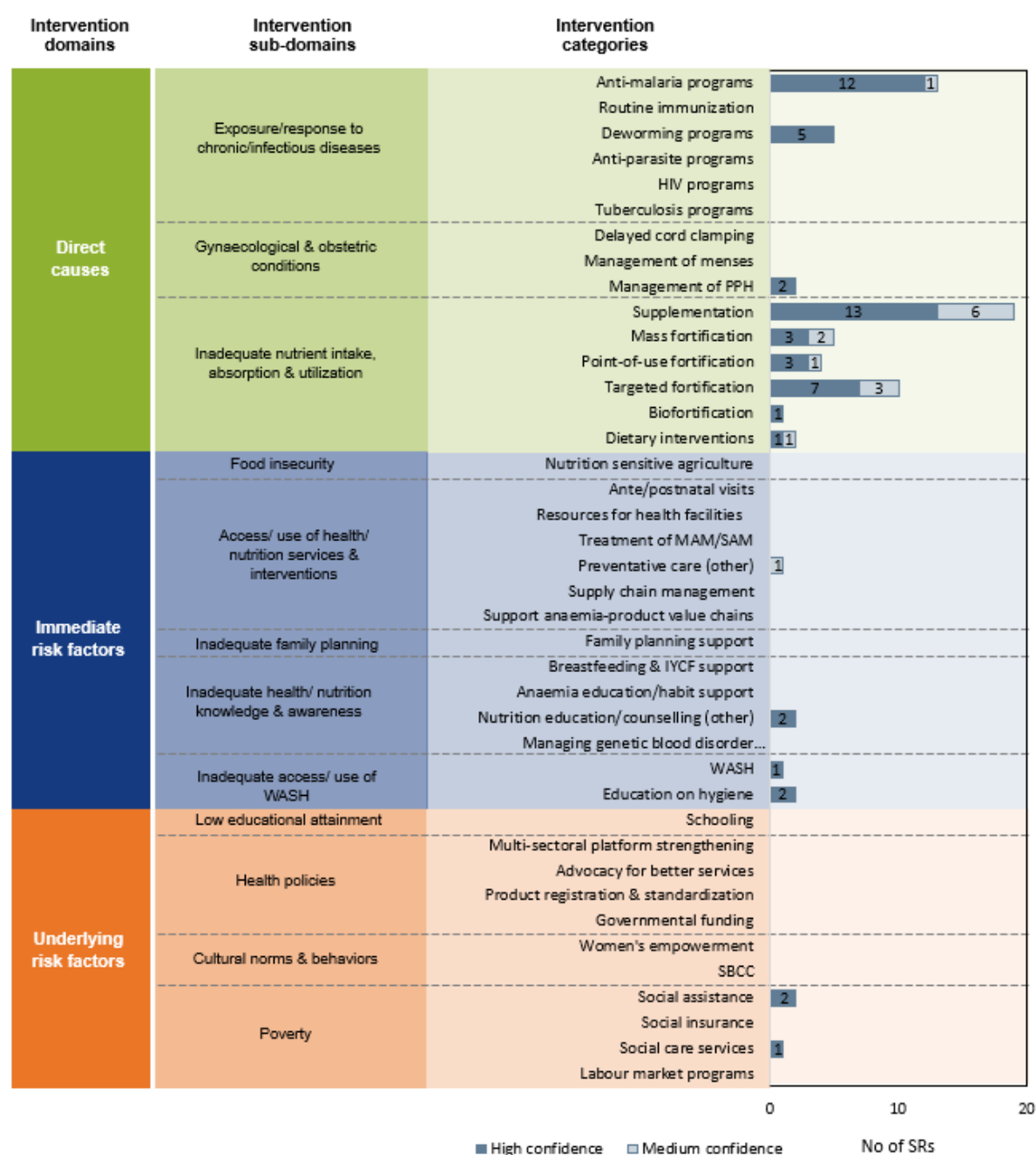
## **4.7 Systematic review appraisal and findings**

### **4.7.1 Most SRs considered interventions that address the direct causes of anaemia (n = 53)**

Within this domain, SRs focused on intervention sub-domains of *inadequate nutrient intake, absorption, and utilization* (Figure 10, n = 34) and *chronic disease/exposure and response to infectious diseases* (n = 18). Three SRs synthesized interventions under the sub-domain of *gynaecological and obstetric conditions*. Within the domain of interventions addressing *intermediate risk factors, inadequate health/nutrition knowledge and awareness* (n = 2), *access/use of health/nutrition services and interventions* (n = 3) and *inadequate access to/use of WASH* (n = 3). No SRs were found for the sub-domains of *food insecurity* and *inadequate family planning*. As with included IEs, *underlying risk factors* was most underrepresented domain, with two SRs evaluating the impacts of interventions under the *poverty sub-domain*.

We also identified 15 ongoing SRs protocols covering interventions sub-domains of *chronic disease/exposure and response to infectious diseases, gynaecological and obstetric conditions, inadequate nutrient intake, absorption and utilization, access/use of health/nutrition services and interventions* and *inadequate access to/use of WASH*.

**Figure 10: Distribution of high and medium confidence SRs by interventions**



Note: To improve readability we truncated some of the intervention labels as: management of PPH (management of postpartum haemorrhage), dietary interventions (dietary enhancement and diversification), treatment of MAM/SAM (treatment of moderate or severe acute malnutrition), Preventative care, other (Provision of other preventative care), Supply chain management (Education and direct support for supply chain management), Support anaemia-product value chains (Mobilization of public and private sector actors to support anaemia-product value chains), Family planning support (Family planning and birth spacing counselling), Breastfeeding & IYCF support (Breastfeeding and IYCF education and support), Management of genetic blood disorder anaemia (Counselling and management of anaemia due to genetic blood disorders), WASH (Water access, sanitation, and hygiene resources), Governmental funding (Governmental funding for anaemia treatment and prevention), SBCC (Social and behaviour change communication on gender norms).

#### **4.7.2 Existing systematic reviews are typically of low confidence**

We identified 230 reports representing 195 unique SRs (180 completed and 15 ongoing SRs). We critically appraised 180 completed SRs and assessed 123 as low confidence, 14 as medium confidence, and 43 as high confidence.

SRs were rated as low confidence when they did not use gold standard synthesis methodology, such as duplicate independent screening for eligibility or data extraction and risk of bias assessments were not completed by two independent reviewers. In some SRs, the risk of bias was not assessed at all. In other cases, the study quality was not incorporated into the analysis (e.g., through a sensitivity analysis), which made it difficult to determine which conclusions were based on high-quality evidence. Another common issue resulting in a low confidence rating was that the SRs did not conduct comprehensive searches of the literature. The authors either did not search relevant or grey literature databases or did not search the reference lists of the included studies. In some cases, the searches were limited to studies published only in English.

#### **4.7.3 Main findings of high/medium confidence SRs**

Although there is a large body of high and medium confidence systematic reviews on interventions to reduce anaemia, they show that **there is no silver bullet**. For most interventions, results were inconclusive, inconsistent, or directly contradictory. For example, systematic reviews reported that providing children with iron-fortified food both reduced anaemia prevalence (De-Regil, Jefferds, and Peña-Rosas 2017) and had little or no effect on anaemia prevalence (Das et al. 2013). Although Das and colleagues (2013) find no effect on anaemia, they report an effect on haemoglobin, which is simply the continuous version of the binary anaemia measure. Their finding may be related to the severity of anaemia, and corresponding changes in haemoglobin levels, as opposed actually reflecting a true null effect. Iron fortified wheat reduced anaemia but had little to no effect on iron deficiency (Field, Mithra, and Peña-Rosas 2021). However, iron and micronutrient fortified wheat had the reverse effects: it reduced iron deficiency but had little to no effect on anaemia (Field, Mithra, and Peña-Rosas 2021). When given to children and youth, micronutrient fortified food reduced iron deficiency and iron deficiency anaemia but had no effect on haemoglobin levels. This finding likely reflects low prevalence of iron deficiency anaemia within the populations, which resulted in a decrease in that specific cause of anaemia without a population level improvement in the underlying measure of haemoglobin. Such variation in the underlying causes of anaemia may explain many of the inconsistent findings. Another explanation is that the underlying distribution of haemoglobin levels and whose haemoglobin improves could result in variation in whose haemoglobin levels improve sufficiently to get over the anaemia threshold.

Based on findings reported by SR authors, some **interventions may show promise** as evaluations reported positive effects. SRs found that iron **supplementation and fortification interventions** has inconsistent but often positive effects on anaemia outcomes across various populations. Iron fortification improves haemoglobin outcomes in children. Iron supplementation, sometimes combined with folic acid, during pregnancy improves measures of maternal anaemia. **Multiple micronutrient fortified foods** as well as the provision of **specialized whole foods**, such as lipid-based nutrient supplements, also generally improve primary anaemia outcomes for children. The effectiveness of fortification and supplementation with other micronutrients was not

examined enough in high and medium confidence systematic reviews to reach strong conclusions. Many **malaria treatment programs** were also effective at improving primary anaemia outcomes; although, there was some variation based on population and the approach adopted. The effectiveness of **deworming interventions** in improving anaemia outcomes is less clear and may vary by population and frequency of helminths in the population.

We provide more detailed summaries for each of the 57 high and medium confidence SRs [here](#). In Appendix E (Tables 4-9), we present high-level summary tables of the results, while the policy and research implications are presented in Section 5.

#### **4.7.4 Large synthesis gaps are concentrated in the direct causes domain**

Although there are many SRs within the **direct causes** domain, there are several categories where these reviews are now outdated (Table 5). We found one high or medium-confidence SR evaluating the interventions under the sub-domain of *gynaecological and obstetric conditions* (evaluated by 97 IEs) with no such SRs for interventions of *delayed cord clamping* and *management of menses*. Meanwhile, no high or medium-confidence SRs published after 2021 were identified for the intervention categories *point-of-use fortification*, *targeted fortification* and *dietary enhancement*. However, since 2021, 10 IEs evaluating *point-of-use fortification*, 20 evaluating *targeted fortification* IEs, and 17 IEs evaluating *dietary enhancement* have been published, meaning an updated synthesis may be warranted.

There are also opportunities for synthesis for interventions in the intermediate risk factors domain, including interventions which provide *resources and staff for health facilities*, and interventions providing *anaemia education and habit support*. In both cases, there are no existing high or medium confidence SRs.

**Table 5: Opportunities for additional SRs**

Intervention categories	No. of IEs	No. of high/medium confidence SRs	No. of high/medium confidence SRs in last 5 years (since 2018)
<b>Direct causes</b>			
HIV programs	21	0	0
Management of postpartum haemorrhage	85	3	0
Point-of-use fortification	67	2	0
Biofortification	14	1	0
<b>Intermediate risk factors</b>			
Resources and staff for health facilities	15	0	0
Anaemia education and habit support	24	0	0

Note: Opportunities for additional SRs are defined as intervention categories for which there are at least 10 IEs and no high or medium confidence SRs completed in the last 5 years.

Because no intervention categories in the **underlying risk factors** domain were evaluated by more than seven IEs, these categories are considered primary evidence gaps and not opportunities for evidence synthesis.



## 4.8 Most studies do not report program implementation or funding agencies

When reported in the identified studies, we extracted data on the program implementers, program funders, and research funders. As presented in Table 6, about 85.9 and 81.6% of studies did not report program implementation or funding agencies, respectively. This is unsurprising, given that many IEs were conducted within or around the catchments of health facilities. Government agencies were the most common implementers ( $n = 112$ ) and funders ( $n = 137$ ) of interventions and were also the most common research funders for IEs ( $n = 518$ ) and SRs ( $n = 24$ ).

**Table 6: Number of studies by reported implementation and funding agency types**

Agency types	Program Implementation		Research Funding	
	Implementing Agency	Funding Agency	Impact Evaluation	Systematic Review
Academic institution	109 (5.0%)	52 (2.3%)	426 (16.3%)	17 (17.4%)
Charity/private foundation	8 (0.4%)	72 (3.2%)	307 (11.7%)	16 (16.3%)
For-profit firm	7 (0.3%)	61 (2.7%)	88 (3.4%)	2 (2.0%)
Government agency	112 (5.1%)	137 (6.1%)	518 (19.8%)	24 (24.5%)
International aid agency	17 (0.8%)	57 (2.6%)	136 (5.2%)	28 (28.6%)
International financial inst.	2 (0.1%)	0 (0.0%)	19 (0.7%)	1 (1.0%)
Non-profit organization	54 (2.5%)	32 (1.4%)	136 (5.2%)	6 (6.1%)
Not specified	1876 (85.9%)	1821 (81.6%)	987 (36.7%)	3 (3.1%)

Note: Multiple coding was permitted where studies reported more than one agency.

The Bill and Melinda Gates Foundation was the most common funder of program implementation and research (Table 7). The World Food Programme, UNICEF, and the government of India were tied as the most commonly reported program implementation agencies.

**Table 7: Top 5 most commonly reported implementing and funding agencies**

	Program Implementation		Research Funding
	Implementing Agency	Funding Agency	
1.	ICDDR,B (7)	Bill & Melinda Gates Foundation (46)	Bill & Melinda Gates Foundation (142)
2.	UNICEF (6)	USAID (13)	Wellcome Trust (45)
3.	Gov. of India (6)	UNICEF (8)	NIH (42)
4.	WFP (5)	Wellcome Trust (7)	WHO (34)
5.	HKI (4)	WFP (7)	FCDO/DFID (30)

Note: Multiple coding was permitted where studies reported more than one agency. Acronyms: International Centre for Diarrhoeal Disease Research, Bangladesh (ICDDR,B), Helen Keller International (HKI) International Food Policy Research Institute (IFPRI), National Institutes of Health (NIH), United Nation's Children Fund (UNICEF), Foreign, Commonwealth & Development Office of the UK, former DFID (FCDO/DFID), World Food Programme (WFP), World Health Organization (WHO)



## 5. Conclusions

**This EGM offers a large well-organized body of 2,196 IEs and 57 high- and medium-confidence SRs** that decision-makers can customize to their areas of interest and use when designing and funding anaemia policies, interventions, and program evaluations. There has been steady growth of this body of evidence over the last decade, with a peak in 2019. Evidence is concentrated in South-East Asia and Africa, but we identified several substantive and geographical gaps, highlighting areas that require urgent research regarding anaemia interventions, outcomes, and the methods. Similar gaps have already been identified by the Anaemia Action Alliance and Loech and colleagues (2023). **We recommend that policymakers, funders, researchers, and other stakeholders collaborate and prioritize strategically addressing the most critical evidence gaps.**

We found **clusters of evidence for intervention sub-domains of *inadequate nutrient intake, absorption and utilization, chronic disease/exposure and response to infectious diseases, inadequate health/nutrition knowledge and awareness and inadequate access to/use of WASH*** across all outcome domains. We did not find any absolute gaps in primary or synthesis evidence for any of the three intervention domains. However, we found a relatively lower volume of evidence for the intervention sub-domains on *gynaecological and obstetric conditions* (under the domain of interventions addressing the *direct causes* of anaemia) and *inadequate family planning* (under the domain of interventions addressing *intermediate risk factors*). **We found the least evidence for the interventions categorized under the domain of *underlying risk factors*.**

**Across all intervention domains, we identified studies reporting *primary outcomes*, more frequently than other outcome domains.** Not all interventions should be evaluated against all of the outcomes. Because of the broad nature of the map, there is not a theoretical justification to expect that all included interventions would affect all included outcomes. For instance, interventions addressing *chronic diseases and exposure and response to infectious diseases* may not need to be evaluated for their effect on *delayed cord clamping*. Nonetheless, there were some instances where there are strong theoretical reasons to expect a relationship and evidence was not found. **Few evaluations focusing on the effects of interventions addressing *underlying and intermediate risk factors* of anaemia measured outcomes in the domains of *inadequate nutrient absorption and utilization and gynaecologic and obstetric conditions*** despite these domains focusing on food security and healthcare.

We found little cost evidence presented in the included studies. While the development sector more broadly reports cost data for about 1 in 5 studies (Brown and Tanner 2019), we found **only about 1 in 20 studies include any cost information.** Although studies may be prioritizing establishing efficacy or effectiveness, cost-evidence can be an important aspect of evidence informed decision making, particularly in resource constrained contexts.

## 5.1 Limitations: deviations from the published protocol

We modified the original protocol in several ways due to practical considerations of time and resource constraints resulting from the very high number of records deemed eligible for the EGM:

- We restricted search timeframe to the last decade (between 2012 and 2023). The cut-off year 2012 was selected to match the World Health Assembly Resolution 65.6, which set a global target for anaemia reduction (World Health Organization 2012).
- We focused our grey literature search on eight sources and five keywords directly related to anaemia. These were prioritized through a deliberative process with our Nutrition International colleagues.
- We limited the scope of citation tracking to all included systematic reviews, regardless of their level of confidence.

The full details of these changes are provided in Appendix C.

We also identified many non-English publications. Due to limited resources and limited capacity of the team to translate many of the non-English languages, we could not screen or extract data from 115 studies. A full list of these publications is presented in Appendix D1.

## 5.2 Implications for policymakers

**We encourage decision-makers to prioritize the evidence from included SRs that have been evaluated as high or medium confidence.** Decision-makers can also consult the list of low confidence SRs identified (provided in Appendix D6). However, we urge decision-makers to approach these SRs cautiously, as the evidence is more likely to be biased.

The main policy implications derived from these SRs were summarised in section 4.7.2 and in more detail here. We did not find relevant high or medium confidence systematic reviews for most of the interventions recommended in the WHO Framework. This does not mean that there is evidence against these interventions, nor does it mean that there are no other types of evidence supporting these activities. Instead, additional synthesis efforts related to these topics may support evidence informed decision making. We suggest referring to the original reports for more details. In summary, we found:

- Several high and medium confidence SRs reported on the effectiveness of various forms of **supplementation and fortification** interventions on primary anaemia outcomes.
  - Results were inconsistent, supporting the WHO's conclusion that these interventions are likely to be effective in certain contexts and for certain populations.
  - Iron fortification improves child anaemia outcomes.
  - Antenatal iron supplementation, sometimes combined with folic acid, reduces maternal anaemia.
- Several high and medium confidence SRs reported on the effectiveness of various **malaria treatment and prevention programs**.

- They found inconsistent, but generally positive effects on anaemia outcomes. This aligns with the WHO recommendation for such interventions for at risk populations and in endemic zones.
- Several high and medium confidence SRs reported on the effectiveness of various **deworming programs**.
  - These found highly variable effects, largely driven by population and frequency of helminths within the population. This aligns with the WHO recommendation of targeted use of these interventions.
  - A few high and medium confidence SRs reported on the effectiveness of other **WASH interventions** on various intermediate outcomes, but they did not measure primary anaemia outcomes.
- Three high or medium confidence SRs reported on **gynaecological and obstetric interventions**.
  - They did not find evidence of an effect. However, the specific interventions recommended by the WHO were not considered in these SRs.
- One SR focused on the effectiveness of **social protection** (food vouchers or subsidies) on micronutrient levels and related outcomes; however, the evidence was insufficient to reach strong conclusions.

### 5.3 Implications for future research

#### 5.3.1 Primary research

Our EGM has identified a large body of rigorous evidence to be consulted when designing programs to support anaemia reduction. Based on our findings, we suggest that in commissioning and designing new IEs, decision-makers consider:

- Prioritizing primary research gaps in intervention categories and sub-categories where evidence related to anaemia outcomes is scant (such as *management of menses* under the intervention sub-domain of *gynaecological and obstetric conditions*, *treatment of malnutrition* under *access/use of health/nutrition services* sub-domain, and all interventions under the *underlying risk factor domains*).
- Prioritizing geographical gaps with a relatively high prevalence of anaemia, but where little or no evidence was found (i.e., Guyana, Mauritania, Surinam, Central African Republic, South Sudan, Somalia, Djibouti and Eritrea), particularly in cases where interventions are unlikely to work in the same way across contexts. Geographical priorities may also be adjusted to the population of interest. For example, there is a gap for studies of children in Yemen and for women of reproductive age in Yemen and Mali. However, when addressing geographical gaps, researcher should consider the context-specific aetiology in order to decide which interventions are appropriate.
- Conducting theory-based mixed-methods evaluations when planning new programs to determine the interventions' effectiveness and understand the underlying reasons. Besides physiological factors, several socio-cultural factors may have implications for anaemia (coined as the intermediate and underlying risk factors). Evaluating different versions of the interventions in various contexts and using comparable measures for socio-cultural and human welfare outcomes can help elucidate meaningful evidence on these non-physiological risk factors.
- Standardizing data collection tools and making them widely available in order to improve our ability to compare results across studies.

- Employing credible counterfactual designs to generate more reliable evidence when conducting impact evaluations. This does not have to be exclusively RCTs but can include quasi-experimental designs capable of determining causal attribution.
- Filling gaps on research in urban settings given the rapid migration to urban slums where food and nutrition security may be even more precarious than in rural settings.
- Evaluating trade-offs of multicomponent intervention strategies. They may better-address multifaceted issues such as anaemia, but it is often difficult to disentangle the contributions of the various intervention activities when they are provided as a package.
- Ensuring that partners make their datasets accessible to other researchers to improve future research efforts and avoid duplication.
- Increasing the quality of future primary studies by:
  - Blinding outcome assessors
  - Reporting the causes and rates of attrition (particularly differential attrition)
  - Ensuring that studies are adequately powered
  - Controlling for confounding
  - Establishing control groups are at a sufficient distance from intervention groups to avoid contamination
  - Collecting baseline and endline assessments of both control and intervention participants.
- Conducting cost-effectiveness or cost-benefit analyses. This information can be valuable for decision-makers, particularly in resource-constrained settings.
- Ensuring studies are sensitive to the needs of vulnerable groups by obtaining and reporting ethical clearance and pre-registration of evaluations. Journals and other publication avenues should require such reporting to ensure primary studies have complied with the highest standards of research ethics.

### **5.3.2 Implications from high/medium confidence SRs**

The implications discussed below reflect general conclusions drawn by multiple of the high- or medium-confidence reviews included in this EGM. Some implications apply more generally to development studies, and we indicate where the implications are specific to a certain intervention types.

#### **Methodological implications**

- There is a general call for higher-quality rigorous research. SRs cite multiple methodological weaknesses of included primary studies and suggest that particular attention be paid to the randomization method, allocation concealment, blinding outcome assessors, and causes of attrition. They also indicate the need for studies to be adequately powered, and appropriately control for confounding. Control groups should be at a sufficient distance from intervention groups to avoid contamination, and studies should include baseline and endline assessments of both control and intervention participants.
- While cluster RCTs may be the ideal, they are often outside of the fiscal or logistical capacity of an organization. In this case, quasi-experimental studies can offer a robust alternative when correctly applied. Authors also called for process evaluations and mixed methods approaches to be considered.

- Standardizing data collection tools and making them widely available will improve our ability to compare results across studies.
- Relatedly, definitions and quantifications should be consistent across studies (e.g., how animal source foods are defined and quantified).
- Where possible, populations with different biological requirements should be differentiated within analysis. This is particularly important in relation to nutrient consumption during different developmental periods. There is some evidence that younger children may benefit more than older children.
- Researchers and practitioners in L&MICs could improve future research efforts by making their datasets accessible to researchers.
- Teams should monitor and evaluate programs on a continuous basis.
- Authors should provide sufficient detail on how gender is integrated into project design.
- Authors call for more research in urban settings given the rapid migration to urban slums where food and nutrition security may be even more precarious than in rural settings.
- More high-quality research is needed on the evaluation of large-scale feeding programs.

### Programming implications

- Multicomponent intervention strategies may better-address multifaceted issues such as anaemia, but it is often difficult to disentangle the contributions of the various intervention activities when they are provided as a package.
- Acceptability of interventions should be assessed in new contexts.
- Feeding interventions for children may be more effective when delivered in an institutional setting, such as a supervised feeding center, day-care, or preschool.
- For feeding supplementation interventions, provide extra rations to reduce the risk of redistribution of the target participant's ration.
- Supplementation interventions should continue for at least 18-24 months to allow sufficient time for affects to manifest.

### 5.3.3 Synthesis research

Researchers should ensure that future synthesis projects are conducted using international gold standards for synthesis (e.g., Page et al. 2021; Higgins et al. 2019; The Methods Group of the Campbell Collaboration 2019a; 2019b) so that decision-makers can have more confidence in the conclusions. When researchers and funders are planning new synthesis efforts, we suggest they consider:

- Prioritizing synthesis gaps identified where there are no up to date high or medium confidence reviews, by commissioning new synthesis projects. Examples include gaps in evidence on:
  - **Direct causes of anaemia**, specifically *biofortification, HIV programs, and anti-parasite programs other than malaria and helminths*
  - **Intermediate risk factors**, specifically *the provision of other preventative care, such as annual check-ups and adult immunization, the provision of resources for health facilities, anaemia education and habit support, and other nutrition education activities*
  - All interventions under the **underlying risk factors** domain.

- Updating existing medium- and high-confidence reviews in areas where new evidence is available. For example, updating SRs on *point-of-use fortification*, *targeted fortification* and *dietary enhancement* given the plethora of new evidence.
- Commissioning a 'living' synthesis project to ensure decision-makers can access the most up-to-date evidence. Much of the work on the horizon would be relevant, but continuous evidence surveillance will be needed to ensure the map stays up to date.

## **Online appendixes**

### **Online appendix A: Interpreting and using EGMs**

<https://3ieimpact.org/sites/default/files/2024-04/EGM-Anaemia-Online-appendix-A.pdf>

### **Online appendix B: Deviations from protocol**

<https://3ieimpact.org/sites/default/files/2024-04/EGM-Anaemia-Online-appendix-B.pdf>

### **Online appendix C: Search methods**

<https://3ieimpact.org/sites/default/files/2024-04/EGM-Anaemia-Online-appendix-C.pdf>

### **Online appendix D: Lists of records**

<https://3ieimpact.org/sites/default/files/2024-04/EGM-Anaemia-Online-appendix-D.pdf>

### **Online appendix E: High-level summary of high/medium confidence SRs**

<https://3ieimpact.org/sites/default/files/2024-04/EGM-Anaemia-Online-appendix-E.pdf>

### **Online appendix E: References**

<https://3ieimpact.org/sites/default/files/2024-04/EGM-Anaemia-Online-appendix-F.pdf>

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