



Unitaid Executive Board Meeting
44th Session
18-19 June 2024
Geneva, Switzerland

Agenda item 9

Area for Intervention:

Improving access to care for moderate and severe anaemia in vulnerable groups in LMICs

Programmatic Priorities: Women's and Children's Health: *Improve access to better tools for safe pregnancy and birth for women and newborns*; Malaria: *Improve access to quality case management and Introduce and optimize prevention tools*

For Information For Review and Advice For Decision

Contents

1. Purpose and context of this document	3
2. Introduction	3
3. Public health challenge and key access issues.....	3
4. Innovations to improve access to anaemia care	6
5. Partner engagement.....	7
6. Opportunities for Unitaid investment	9
7. Assessment of the opportunity	11

1. Purpose and context of this document

This Area for Intervention (Afi), submitted for Executive Board endorsement, outlines opportunities for accelerating access to prevention, diagnosis and management to address moderate and severe anaemia in vulnerable populations in low- and middle-income countries (LMICs). The purpose of this document is to provide an overview of anaemia with relevance to Unitaid's strategy, potential opportunities considering the current landscape, and prioritization analysis.

2. Introduction

Anaemia is a condition where haemoglobin – a protein contained in red blood cells that is necessary to move oxygen around the body – is low. The most common cause of anaemia is iron deficiency, which is estimated to contribute to about half of all cases. Anaemia is also caused by other nutritional deficiencies (such as vitamin A, folate, vitamin B12 and riboflavin); infections - particularly malaria - as well as TB, HIV, and other neglected tropical diseases; inherited blood disorders; and causes linked to nutrient loss - such as blood loss from childbirth or menstruation.

People with anaemia have haemoglobin concentration that is too low for the body to operate optimally, resulting in symptoms such as fatigue, weakness, dizziness and shortness of breath – and potentially severe outcomes in more serious cases. Pregnant and postpartum women, and infants and young children are particularly vulnerable to anaemia and the resulting burden.

During pregnancy, anaemic women have an increased risk of developing perinatal infection, pre-eclampsia, and haemorrhage, and an increased risk of adverse perinatal outcomes such as intrauterine growth retardation, prematurity, and low birth weight. Childhood anaemia can negatively affect mental, motor, and cognitive development, and in severe cases, can be fatal. Maternal anaemia is considered a strong determinant of childhood anaemia.

This document will first describe the global burden of anaemia, then the current WHO recommendations for anaemia care, and barriers to their implementation in LMICs. The document will then highlight promising tools and interventions that could address the most pertinent barriers, and potential opportunities that Unitaid could consider to catalyse their uptake. Lastly, the document will present an assessment of prioritized opportunities based on fit with Unitaid's comparative advantage and potential impact.

3. Public health challenge and key access issues

Public health burden and progress against global goals

Anaemia is a major, persistent public health concern globally. WHO estimates that anaemia affects 1.8 billion people worldwide – 40% of all children aged 6–59 months and 30% of women aged 15–49 years – increasing to 37% in pregnancy. In 2021, the global prevalence of severe and moderate anaemia – responsible for most anaemia related Disability-Adjusted Life Years – were estimated to be 0.9% and 9.3% respectively.¹

In pregnant women alone, anaemia caused 50 million Disability-Adjusted Life Years in 2019,² with the greatest prevalence in sub-Saharan Africa and South Asia. Recent studies demonstrate that women with severe anaemia had nearly double the risk of postpartum haemorrhage (PPH) – the leading cause of maternal mortality – than women with moderate anaemia, who are already at elevated risk compared to those without anaemia.³ Studies also find that pregnant women with severe anaemia have an 8 times higher risk of low birthweight compared to women without anaemia, and a 6 times higher risk of preterm delivery.⁴

Children and infants also represent a vulnerable group in terms of anaemia burden – with malaria a significant cause. There is a strong correlation between malaria infection and rates of anaemia as a result of damage to red blood cells caused by the malaria parasite. Household survey data suggests that of children with a positive malaria test, 9% have severe anaemia and 54% have moderate anaemia. WHO estimates that of the 24

¹ [Prevalence, years lived with disability, and trends in anaemia burden by severity and cause, 1990–2021: findings from the Global Burden of Disease Study 2021 - The Lancet Haematology](#)

² [Measuring the global burden of anaemia - The Lancet Haematology](#)

³ [Maternal anaemia and the risk of postpartum haemorrhage: a cohort analysis of data from the WOMAN-2 trial - The Lancet Global Health](#)

⁴ [Severe anaemia is associated with a higher risk for preeclampsia and poor perinatal outcomes in Kassala hospital, eastern Sudan - PMC \(nih.gov\)](#)

million children were infected with malaria in sub-Saharan Africa in 2018, approximately 1.8 million were likely to have severe anaemia.⁵ Recurrent severe malarial anaemia constitutes 19% of all episodes in moderate-to-high transmission settings.⁶

Of particular note, vulnerability to anaemia is further increased by the effects of climate change, particularly in these high-risk groups. For example, studies have shown that children in sub-Saharan Africa are at an increased risk of childhood anaemia linked to higher temperatures and extreme weather events – particularly droughts – leading to reduced nutritional intake.

Progress toward the global anaemia targets is slow. The 65th World Health Assembly committed to halving the prevalence of anaemia in women of reproductive age by 2025. The Sustainable Development Goals also reflect this ambitious target – to end all forms of malnutrition by 2030. The world is not on track to reach these goals. Progress has stagnated since 2012, and prevalence in pregnant women has increased over this time. Only three LMICs are likely to achieve the target at a national scale by 2030.

Barriers to anaemia care

WHO has a number of recommendations to guide approaches to diagnosis, prevention and management of anaemia. This Area for Intervention will focus on WHO guidelines related to key commodities (health tools) and delivery innovations, barriers to access, and potential opportunities that can increase access to health tools, in line with Unitaids strategy and comparative advantage. With anaemia a particularly broad area, this Area for Intervention will focus on opportunities that are closest to Unitaids comparative advantage, and already highlighted in the Strategy 2023-2027 under the *Improving access to quality case management for malaria*, and *Improving access to better tools for safe pregnancy and birth for women and newborns* Programmatic Priorities.

This section provides an overview of pertinent access barriers related to these Programmatic Priorities, and is followed by analysis of key innovations and opportunities to respond to them.

Prevention

WHO recommends oral iron and folic acid supplements for all women and girls of reproductive age in areas where anaemia prevalence is high, and in particular during or prior to pregnancy, as iron requirements are particularly difficult to meet during pregnancy without additional supplements. In many LMICs, particularly across sub-Saharan Africa, very few pregnant women receive the recommended course of antenatal iron and folate, increasing the risk of anaemia and adverse outcomes. Only 8% of pregnant women in 22 countries surveyed under a recent Demographic and Health Surveys analysis received the recommended iron and folate supplements daily for 6 months. Access is limited due to a number of factors, such as gastrointestinal side effects and nausea, pill burden, fear of increased blood pressure, and low awareness of the importance of the supplements, but access to recommended antenatal care is considered the most important predictor of adherence.

PPH is also a key cause of anaemia due to significant blood loss. To prevent PPH, and thus anaemia, WHO recommends the use of uterotonics and umbilical cord clamping directly after delivery. There are numerous barriers that prevent access to quality uterotonics, some of which Unitaids is addressing through its portfolio of PPH grants. Studies firmly establish anaemia as a risk factor for PPH, further demonstrating the significant clinical link between the two conditions.

For children, WHO recommends daily iron supplementation to prevent anaemia in ages 6 months –12 years in geographic areas where anaemia is a public health problem. This comes in the form of daily drops or syrup for younger children, and in tablets or micronutrient powders for children above 5 years old. Similar to the maternal use case, access to this preventive treatment remains limited in low-resource settings. Vulnerability to malaria infection also represents a significant risk factor for anaemia in this age group.

⁵ World malaria report 2019 (who.int)

⁶ Projected health impact of post-discharge malaria chemoprevention among children with severe malarial anaemia in Africa | Nature Communications

WHO's malaria prevention recommendations are important for anaemia prevention, so activities to address barriers to uptake of malaria prevention – including Unitaid's portfolio of existing investments – likewise aid the anaemia response. Of particular note, children who have contracted severe anaemia remain at high risk even after management. The risk of mortality during the first six months after hospital discharge from a severe anaemia case is 72% higher than during hospitalisation.⁷

Considering this high risk of readmission, WHO (in addition to other malaria prevention guidelines) recommends Post Discharge Malaria Chemoprevention (PDMC) for children under-5 in areas where malaria parasite prevalence is above 10%. PDMC is a 3-month course of antimalarial drugs at discharge after being admitted to hospital for severe anaemia. Studies that informed the WHO recommendation showed a 70% reduction in risk of deaths or readmissions in children who received the intervention. However, this recommendation has been in effect only since mid-2022, and uptake to date has been limited. Countries are showing some interest in implementation, but many questions on optimal delivery exist – and act as a significant barrier to uptake. Guidance is needed on a range of questions, including optimal duration of the intervention in different geographical and transmission settings, methods for optimizing adherence at scale, costs of and coverage under different approaches, and feasibility of implementing PDMC in parallel with other malaria chemoprevention interventions.

Diagnosis

To effectively manage anaemia (and avoid the wrong treatment), appropriate diagnosis is required. This is dependent on two key pieces of information: 1) haemoglobin concentration to identify presence and severity of anaemia, and 2) cause of the anaemia. The current WHO recommended 'gold-standard' for anaemia detection is an automated haematology analyser, but this requires lab infrastructure and specialised training not available in all low-resource settings.

At lower levels of the health system, hand-held haemoglobinometers can be used for initial anaemia screening. There are many of these products on the market, but most are not suited to LMICs. Looking at tools that are minimally invasive (small prick of capillary blood) and non-invasive (alternative methods such as light), research by PATH indicates haemoglobinometers are generally not available in basic primary health care in LMICs, or even at advanced primary care centres in some countries surveyed. Access barriers that prevent uptake in LMICs include challenging data collection methods, complex data analysis and feature extraction processes, low affordability, portability, and accuracy. There is a Target Product Profile available to guide research and development – but no available products market fully meet the profile characteristics.

Haemoglobin diagnostic accuracy is a priority for WHO. To ensure an accurate reading, WHO recently released a technical brief on best practices for haemoglobin measurement (in the context of population-level anaemia surveys). This document encourages the use of venous blood draw for haemoglobinometers – noting the potential of error and low accuracy from tests using less invasive blood methods like capillary blood, which is more accessible in low-resource, primary care settings. This technical update reflects a priority within the anaemia community to answer important questions on the epidemiology and etiology of the condition, but does not address barriers to enable access at the patient and clinical level. To this point there is some disagreement in the anaemia community around the level of variability that is acceptable for point-of-care anaemia testing vs. screening. WHO has developed a colour scale to identify anaemia using a prick of blood that can be used in low-resource settings where haemoglobinometers are not accessible, but this tool, and others using similar clinical signs (e.g., pallor), have very low accuracy.

Biomarkers are important to the second step of point-of-care diagnosis – identifying the specific causes of anaemia. Ideally, a point-of-care diagnostic using a biomarker would be administered following identification of anaemia – such as a test for ferritin levels, the primary biomarker used to identify iron deficiency. However, point-of-care tests for anaemia cause are limited, and developing tests for these biomarkers is challenging. Where available, they are often unaffordable for use in LMICs. Furthermore, these biomarkers are often not reliable in the clinical setting as anaemia can be due to multiple causes, and can be further complicated by other biological factors such as inflammation. Some newer tests are in the pipeline, but still relatively upstream.

⁷ [Projected health impact of post-discharge malaria chemoprevention among children with severe malarial anaemia in Africa | Nature Communications](#)

There is no Target Product Profile available to guide research and development priorities for these tools – even for the most common causes. As a result, people will need to be referred to care at higher levels of the health system to complete their diagnosis, or receive presumptive treatment based on common causes and clinical signs (e.g., iron deficiency).

Management

Following correct diagnosis of anaemia, prompt treatment is required to manage the condition. In that sense, diagnostics can be seen as key to addressing the complexity of the anaemia space, by ensuring that interventions are appropriately tailored, resourceful, impactful, and do no harm.

With iron deficiency the most common cause of anaemia, treatment is often focussed on managing the nutritional deficiency. WHO recommends that people who have iron deficiency anaemia receive a higher dose of iron (and folate in pregnancy) until haemoglobin level returns to normal. Oral dosing is most common in LMICs, but uptake is low (like for prevention). IV iron provides a promising option that can enable rapid replenishment, but this requires delivery at higher levels of the health system, requires time and multiple infusions (often at different visits) and is often unaffordable in low-resource settings.

There are significant gaps in the evidence on what works best in practice to address anaemia. Given the complexity of the condition – with high prevalence, diverse and at times multiple causes that make diagnosis difficult, and the need for specific and targeted care to manage it – multisectoral interventions that cover the continuum of care from pre-conception to infancy are needed. Despite this, most of the evidence that is currently available on successful anaemia interventions are from specific single interventions (e.g., oral iron and folate vs. IV iron), with limited data on the potential benefits and risks of more comprehensive programmes considering the complexity of the anaemia algorithm. There is limited evidence on the potential impact, operational feasibility or cost-effectiveness of coordinated packages of contextually appropriate anaemia prevention and control interventions – particularly utilising new tools, and especially in LMICs.

Summary of barriers affecting access to anaemia care

- **Quality:** Low accuracy of diagnostics in low-resource settings; IV iron and MMS products of uncertain quality
- **Affordability:** Unaffordability of key commodities – particularly diagnostics and IV iron
- **Demand and Adoption:** Limited uptake of WHO PDMC recommendation at country level; low levels of access to comprehensive antenatal care in LMICs; scant evidence for new anaemia tools (MMS and IV iron); questions on key needs for to drive anaemia diagnostics uptake
- **Innovation and Availability:** Lack of point-of-care diagnostics to determine anaemia cause; available products do not meet Target Product Profile; lack of evidence on comprehensive approaches to anaemia prevention and management in LMICs.

4. Innovations to improve access to anaemia care

New, underutilised, and impactful tools are showing promise to help address barriers to anaemia care. This section will highlight some of the most promising tools in the pipeline, and how they could be positioned to address the burden of anaemia. Potential opportunities for Unitaid to support access to these tools will be described further in Section 5.

Multiple Micronutrient Supplementation (MMS) for pregnant women is gaining momentum as an alternative to oral iron and folic acid to prevent anaemia. MMS is a single daily tablet that contains 15 essential vitamins and minerals, including iron and folate. It is more palatable than oral iron and folate, and studies have found similar reductions in anaemia in pregnant women who take MMS compared to those who take iron and folate supplements alone.⁸ However, the MMS formulation may be superior as the inclusion of additional vitamins and minerals can deliver extra benefits such as prevention of non-iron deficiency anaemia, preterm labour,

⁸ [Multiple micronutrient supplements versus iron-folic acid supplements and maternal anemia outcomes: an iron dose analysis - Gomes - 2022 - Annals of the New York Academy of Sciences - Wiley Online Library](#)

and low birth weight and stunting in children. Cost-benefit analyses on MMS use across different settings consistently show a high return on investment compared to iron and folate supplements alone.

MMS is included in the WHO Essential Medicines List, but, given outstanding questions around levels of iron in the formulation and feasibility for delivery, is recommended by WHO only when implemented in the context of rigorous research. Due to research gaps, WHO does not currently recommend switching from iron and folate supplements to MMS as part of routine antenatal care. Despite this, countries are already starting to scale MMS as a replacement for oral iron folate. Additional operational guidance on MMS use as part of a comprehensive approach to anaemia is needed in these earlier adopter countries.

On the market side, four companies currently manufacture an MMS product that matches the globally recommended formulation of the United Nations Multiple Micronutrient Preparation (UNIMMAP). Most of the global supply for countries undertaking operational research or transitioning to scale come through donations from a philanthropic funder that purchases from a single US-based supplier and provides it to country implementers. There is growing interest and potential for regional manufacturing of MMS, which could potentially expand the MMS market, enhance affordability, enable programme ownership and local economies, eliminate regulatory issues associated with importation, and ultimately ensure that commodities are closer to where they are needed most.

For treatment, **intravenous (IV) iron** can enable greater haemoglobin replenishment compared to oral iron supplements in pregnancy. **Ferric carboxymaltose (FCM)** and other modern IV iron products provide an opportunity to give large doses of iron in a single short infusion, do not require prolonged or multiple infusions, and have lower risk of reactions. FCM is more effective at reducing anaemia in second trimester pregnant women with iron deficiency anaemia,⁹ and ongoing study results are looking promising on the ability of FCM to reduce anaemia in all women in third trimester of pregnancy. Early modelling by the Bill & Melinda Gates Foundation suggests that a targeted approach to address moderate and severe anemia with IV iron can significantly reduce anaemia-associated Disability-Adjusted Life Years. IV iron products like FCM are not yet part of routine anaemia treatment, but with additional evidence expected this year, WHO may recommend the product for use in pregnancy and postpartum by early 2025. At that point **there will be a need for large scale operational evidence on deployment of modern IV iron as part of a comprehensive package of care with other innovative tools.**

FCM is a complex product, currently manufactured by the originator in Switzerland and targeted at high-income countries at a price that is unaffordable for most LMICs. The product is under patent in the US, but no longer in Europe. Production complexity may deter additional quality manufacturers from entering the market in the near-term without targeted efforts to support market entry. Anecdotal evidence suggests numerous generic manufacturers have entered the Indian market, but as yet none is quality assured.

Innovative delivery models for antenatal care access are gaining prominence in low-resource settings and are supported by robust evidence to demonstrate capacity to improve uptake of quality care. Approaches like group antenatal care (Group ANC), whereby small groups of women of similar gestational age attend formalised antenatal care visits together, have shown increased number of ANC visits, timely access to ANC, and importantly increases in quality of care compared to one-on-one visits. Midwife-led models similarly represent a positive evidence-based divergence from traditional models of care led by doctors only – and are now endorsed by WHO and professional organizations as a key approach in delivery of maternal health care. These care delivery methods, along with others such as community care, could be utilized in the context of new innovative tools for anaemia if deployed simultaneously to increase levels of access to quality care with more effective and accessible tools.

5. Partner engagement

Global efforts to address anaemia globally are set to gain momentum following WHO's recent publication *Accelerating anaemia reduction: a comprehensive framework for action*. Launched at the 2023 International Maternal Newborn Health Conference in Cape Town, South Africa, the Framework highlights anaemia as a

⁹ [An implementation research programme to support an intravenous iron intervention for pregnant women with moderate and severe anaemia in Malawi: study protocol - PMC \(nih.gov\)](#)

complex condition that requires multisectoral approaches to accelerate progress. This cross-department commitment highlights key areas of action, including areas relevant to Unitaid's mandate: prioritizing key preventive and therapeutic interventions, optimizing service delivery across platforms and sectors, and expanding research, learning and innovation. Additionally, WHO has prioritized access to antenatal care in alignment with the Every Newborn Action Plan/Ending Preventable Maternal Mortality targets – with plans to launch a Global Midwifery Acceleration Roadmap this year. This would in turn serve to accelerate the maternal anaemia response. WHO's Global Malaria Programme remains committed to addressing anaemia through malaria prevention activities, with particular attention on protection for the most vulnerable in highest burden settings – including a strong interest in the potential of PDMC as part of the suite of chemoprevention tools. WHO's Human Reproduction Programme has indicated its intention to update guidelines for IV iron during pregnancy and post-partum in early-2025, with MMS evidence likewise being monitored.

Despite the prioritization by WHO, funders in this space are limited. **The Bill & Melinda Gates Foundation** (BMGF) is a leading stakeholder and has positioned anaemia as a key area of work whilst supporting a number of investments to advance potentially high-impact health tools. BMGF specifically highlighted IV iron as a priority tool in the Goalkeepers Report. For FCM, BMGF is exploring opportunities to bring down the price of the FCM originator product, whilst actively scoping capacity expansion. In parallel they are funding additional ongoing studies into the effectiveness of FCM vs. oral iron, as well as implementation studies across Africa and Bangladesh. BMGF is also undertaking work on product assessments and validation for non-invasive haemoglobin and point-of-care iron status diagnostics, focussing specifically on the Indian market. BMGF is also supporting MMS scale-up efforts in high-priority countries.

Regarding malarial anaemia, and PDMC specifically, work has been conducted at a moderate scale with funding from **EDCTP3** and the **Government of Norway** to establish the important evidence that led to the WHO guideline update, and is ongoing to add to the evidence on delivery approach in earlier adopter countries.

Like other areas of maternal and child health, scale-up funding outside of HIV, TB, and malaria remains a challenge. Beyond domestic funding sources, **USAID** represents one of the key funders of delivery, with significant programmatic funding to maternal and child health efforts, including commodities. World Bank's maternal and child health financing arm **Global Financing Facility** (GFF) also represents a key partner as it has the capacity to leverage additional funding from diverse sources to support country scale-up. UN agencies also represent a potential scale-up financing partner; for example, the **UNFPA** Supplies Match Fund can support countries to increase domestic resources for quality-assured commodities by matching government contributions in this area on a 2:1 basis up to \$2m per year.

Looking specifically at malaria scale-up funders, the **President's Malaria Initiative** recognizes anaemia as a priority – highlighting the ongoing need for prevention efforts, including chemoprevention in vulnerable groups in high-transmission settings, and expressing specific interest in ways to increase the impact of PDMC. Given funding constraints, **The Global Fund** has reiterated its ongoing focus on case management and insecticide treated bed nets at the core of its malaria strategy – but recognizes the need for efficient and cost-effective ways of delivering care for the most vulnerable, such as PDMC.

Stakeholder convenings have enabled country stakeholders to share experiences and plans, and to express needs for adoption and implementation of PDMC – and can serve as a starting point to guide planning. There is emerging consensus on preferred drug use, the need to expand the target group, and the need for implementation research more generally.

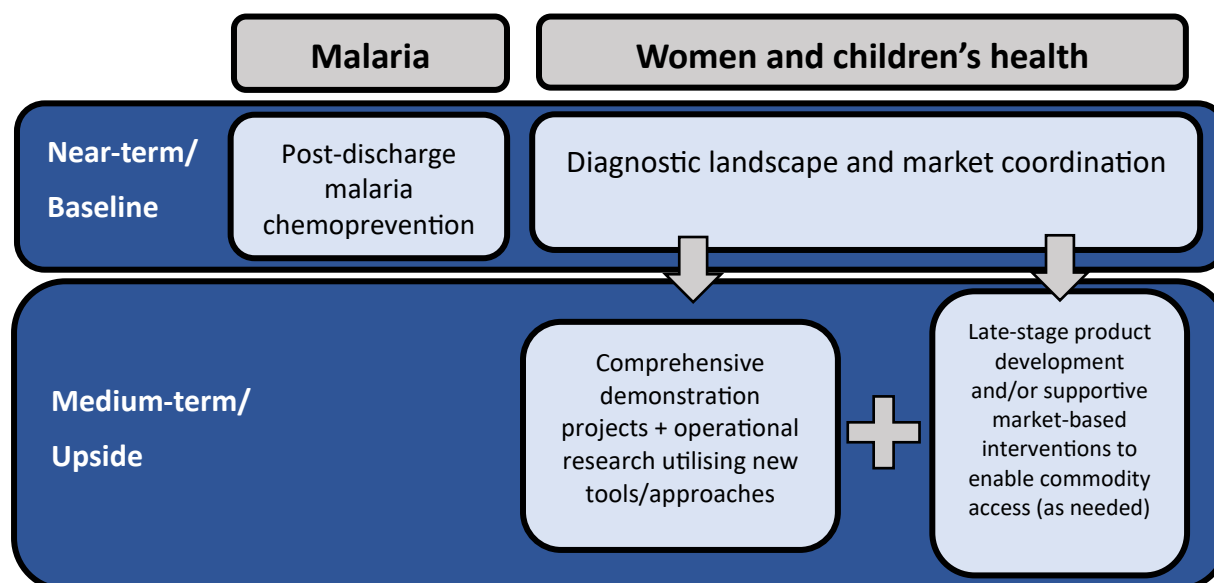
Although there are few early adopter countries utilising new tools and approaches, momentum is promising. Country, community and civil society actors have reiterated the importance of addressing anaemia in LMICs generally – particularly considering the links between anaemia and PPH. The need for comprehensive, end-to-end approaches to care that focus on local needs and specifics has been emphasised. There is also growing interest in a broad maternal health summit – similar to the 2023 PPH Summit that informed the PPH Roadmap – that will pull together global partners, including community and civil society groups, to guide priority agenda setting to address anaemia in pregnancy.

6. Opportunities for Unitaid investment

Sections 3 and 4 of this Area for Intervention described barriers to care for anaemia that are in scope of Unitaid's Programmatic Priorities, and promising tools and approaches that can help address them. Building on this, the Secretariat has identified near-term opportunities positioned for funding in the 2025 baseline investment pipeline (Figure 1).

Opportunities that could have higher potential following outputs from the proposed near-term activities, ongoing evidence generation, and WHO guideline updates have been included in the 2025 upside investment pipeline, to be pursued in the event of additional funding.

Figure 1. Baseline and Upside opportunities for 2025-2026 anaemia funding



Near-term/baseline opportunities

Malaria

Accelerate PDMC uptake through at-scale demonstration projects and operational research

WHO currently recommends PDMC for children admitted to hospital with severe anaemia to reduce risk of reinfection and readmission. Impact modelling in high- and moderate-transmission malaria settings suggests that over 38,000 malaria-associated readmissions could be prevented annually if all children admitted to hospital received PDMC. Economic analysis has demonstrated that PDMC is not only cost-effective, but cost-saving in the context of avoiding readmission, blood transfusion and other severe events. However, WHO has identified that significant gaps exist in terms of evidence on feasibility, operational guidance and cost-effectiveness, as well as guidance on best approaches in the context of other malaria interventions for maximum effectiveness.

Unitaid could respond to key demand and adoption barriers, and catalyse uptake of the intervention by supporting a large-scale demonstration project with embedded operational research to answer operational questions that prevent PDMC uptake – such as most effective delivery and retention strategies, the most appropriate drug in specific settings, length of dosing, target age group (which could in turn increase target population and enable market access), approaches to administration in coordination with other malaria and anaemia interventions, strategies for patient retention, effectiveness of PDMC on severe anaemia of non-malaria causes – which could also include the opportunistic addition of azithromycin, and minimum service requirements for at-scale implementation.

Ultimately this intervention could serve to generate important evidence to help guide operationalisation of this intervention at the country level for early adopters. At the global level, this could inform WHO operational guidance, or potentially help strengthen the current malaria prevention guideline recommendation.

Importantly, this would represent a timely intervention if deployed in line with WHO's forthcoming subnational tailoring strategy, expected in late 2024, particularly in the context of other malaria tools (also supported by Unitaid).

Women & children's health

Establish anaemia diagnostic landscape and direction through market coordination

Given the current challenges and lack of coordination in the anaemia diagnostic space, Unitaid could play an important role to catalyse the anaemia community to address the significant gap for anaemia testing in vulnerable populations. An efficient, time-limited, and modest investment could support anaemia diagnostics market work to facilitate a shared vision on activities and deliverables needed to address key access barriers in the anaemia diagnostics space.

This could include a comprehensive landscaping of the anaemia diagnostics market (both for haemoglobin and anaemia cause biomarkers), and generating evidence for anaemia screening and biomarkers tool manufactures. Activities may include validation of pipeline tools against Target Product Profiles and field assessments to identify the most promising candidates, and identification of future areas of work required to accelerate progress – such as late-stage development or product adaptation for low-resource settings.

This proposed piece of work would represent an important step in enabling access to effective anaemia diagnosis, which could inform work in the medium-term, for larger, more comprehensive interventions to address the challenges in the anaemia care continuum more broadly.

Medium-term/upside opportunities

Women & children's health

Introduce new anaemia tools across the care continuum, including through innovative delivery approaches

The anaemia pipeline is robust with tools that have the potential to positively impact the response to the global burden of anaemia – particularly for pregnant women – including MMS, modern IV iron such as FCM, and next-generation tests to enable point-of-care screening and diagnosis. These tools are at varying stages of readiness for deployment with validation, safety and efficacy studies ongoing, and key results expected throughout 2024-2025. Outcomes of these ongoing studies, in addition to forthcoming WHO guidance and the diagnostics coordination efforts described above, will inform Unitaid work to address access barriers in anaemia care on a larger scale in the medium-term.

Unitaid's role could include supporting a **comprehensive anaemia prevention and management program, including early introduction (or validation as needed) of point-of-care screening and diagnosis, and integration of promising new tools like MMS (in alignment with WHO recommendations) and modern IV iron treatment. This could include large-scale implementation pilots that cover the whole anaemia care pathway – from screening and prevention at pre-conception, through to relevant care and management post-partum – along the care algorithm.** These activities would support policy transition, in alignment with normative guidance, as well as generate data on impact, cost-effectiveness, and feasibility through rigorous operational research. This would be completed with targeted demand creation activities at national level, including policy and advocacy to support translation and uptake.

Similar to past Unitaid investments to enable access to new innovations, **alternative delivery platforms that demonstrate potential to increase ANC uptake – such as Group-ANC, midwife-led models of care, and community health worker delivery – could help compound potential gains in access if deployed through large-scale demonstration projects along with new tools.** Deployment of these interventions with operational research, including impact, cost-effectiveness, and feasibility could help strengthen delivery platforms for specific groups in different settings to improve the quality, coverage, and acceptability of antenatal care in the context of new tools for anaemia.

Market-shaping activities to strengthen the market for priority anaemia products

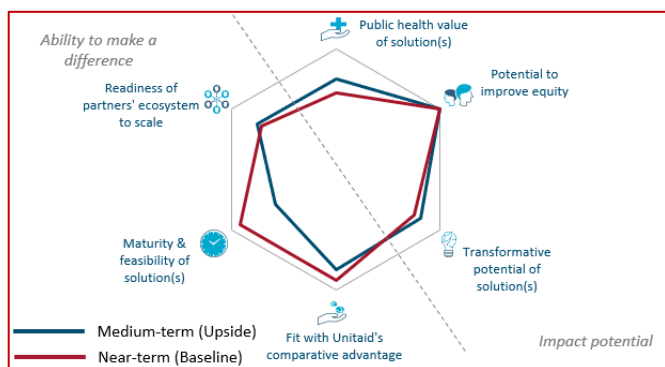
New tools that are primed for scale to address the burden of anaemia in LMICs may require targeted market-shaping activities to ensure broad access and reliable supply. This will partially be informed by the diagnostics landscape activities described above, but may also be considered for modern IV iron products such as FCM, and MMS as appropriate.

The near-term diagnostics work proposed in the baseline investment pipeline has the potential to make the case for better access to fit-for-purpose anaemia diagnostics as a key driver of impact in the anaemia response. Outputs from that piece of work will give strong indications on outstanding access barriers that prevent uptake of diagnostics as part of a comprehensive model of care. This could potentially lead to high priority work for market support to increase access to key diagnostic candidates, or late-stage development as needed.

Market shifts suggest that following FCM originator patent expiration in 2023, generic manufacturers offering products of uncertain quality may begin to dominate supply. Efforts will need to ensure a competitive market of quality suppliers to ensure supply security and enable affordability. This could include work to bring down the price of the originator product and/or to support generic manufacture of quality assured product.

Although there are several quality-assured MMS manufacturers on the market, the space is mostly dominated by a single provider. Additional manufacturers are developing variations of the formulation but are of varying quality standards. In addition, some reports suggest that although cost-effective, these alternatives may not be affordable in many contexts. There could be an opportunity for Unitaid to support manufacturing capacity in LMICs, in line with its regional manufacturing Strategic Initiative.

7. Assessment of the opportunity



Impact potential, including the public health value of the solution, the potential to improve equity and the transformative potential of the solution

Given the complexity of anaemia and its etiology, modelling and data on potential impact linked to specific interventions is lacking – making estimates on public health value difficult. However, considering the scale of anaemia as a global health problem, and emerging evidence on new tools and models of care, there appears to be significant potential to deliver public health benefit through the proposed opportunities –

particularly if delivering a comprehensive model of care (prevention, screening, diagnosis, management) at the most severe end of the anaemia spectrum. The impact would be most significant in the maternal health cases given the links to severe adverse outcomes, and infant and child health. The impact from a malaria-focused intervention would be somewhat more modest as the target group is a smaller, vulnerable and high-risk population – but could be expanded strategically with effective operational research. For both areas, integration of effective diagnostics could help drive impact by preventing progression of more common anaemia cases to moderate and severe stages, where adverse outcomes are most likely.

Given both interventions focus on highly vulnerable groups who have already been affected by anaemia, the equity potential of these interventions should be considered very high. An additional consideration for the equity of the intervention is the potential to address drivers of the poverty cycle – such as through lost productivity and learning outcomes as an effect of anaemia.

The transformative potential of the opportunities can be seen most prominently in improvement of care outcomes. For the most part, the tools proposed in these opportunities represent significant improvements on current standards of care – such as through improved accuracy of the diagnostics and the broader health benefits they can enable, and additional health benefits through MMS and modern IV iron. Modern IV iron formulations could also transform the patient experience by enabling delivery in a single short infusion. Quality of care will likewise be improved by enabling better diagnosis that will result in more appropriate triage to effective care, which will furthermore deliver health system efficiencies. The strongest benefit in terms of

quality of care is through the accelerated uptake of PDMC, which will help the most vulnerable groups avoid readmission and poor health outcomes. In terms of positive externalities, activities in anaemia care for pregnant women can unlock improvements in PPH outcomes, given the significant link between anaemia and PPH.

Ability to make a difference, including fit Unitaids comparative advantage, maturity and feasibility of the solution and readiness of partner ecosystem

The opportunities show a close fit with Unitaids comparative advantage in a number of areas. The opportunities propose activities that will enable Unitaids in its influencer role through coordination of the anaemia diagnostics market, potentially leading into activities well within organizational strength in late-stage research and development, or addressing specific product barriers for LMIC uptake. Unitaids also has a strong background supporting deployment of large-scale, multi-country implementation projects to generate operational evidence that will accelerate demand through providing guidance at the country and global levels.

The proposed investments would strategically complement current investments in PPH and malaria – as well as potential future opportunities in monoclonal antibodies, given possible use cases in long-acting prevention of malaria (PDMC). There is a clear role for Unitaids in this space to build on investments from other funders whilst further demonstrating its important role in women and childrens health and malaria.

The maturity of the proposed solutions varies; this is the main differentiator between the proposed baseline and upside opportunities. The proposed malaria intervention in PDMC can be deployed in the near-term, as there is already momentum in this space with a WHO recommendation, some early country interest, and very clearly articulated questions that need to be addressed to catalyse uptake.

For the maternal health intervention, there are outstanding questions to be answered to inform a larger intervention. Notably, although there are a number of haemoglobinometers currently available on the market with differing levels of accessibility and registration, activity in the biomarker space is further behind – and could hold great potential for unlocking impact across the whole algorithm of care. There is also a lack of coordination amongst global stakeholders on how to best address gaps in anaemia diagnostics. This is in addition to the ongoing studies that will help inform the most promising opportunities for new tools in maternal anaemia.

There is strong momentum in the anaemia partner landscape. WHO has prioritized anaemia through its cross-departmental Framework for Action, and there are strong implementers who will be able to support catalytic efforts at the country level – building on a small level of early country activity. The manufacturing base for diagnostics will need to be coordinated to enable appropriate positioning of potential future opportunities – representing one of the challenges in the ecosystem. Additional challenges include the need for different approaches to scale-up funding in the women and childrens health space, and constraints in dedicated financing for malaria.

7.1 Risk

This Area for Intervention offers strong strategic alignment with the global landscape, and with Unitaids portfolio and role within the global health space – supported by significant stakeholder engagement. In terms of operationalization, the opportunities are structured and sequenced to minimize implementation risk, which will ensure availability of products and evidence for deployment in the longer term. Scalability, as with other maternal health focussed interventions, poses a challenge due to the absence of a clear scale-up funder. The Secretariat will need to build on learnings from other activities in maternal health, such as PPH, to identify approaches to scale-up funding with partners such as USAID, Global Financing Facility, and other UN Agencies, prioritizing country-level business cases to encourage domestic funding of effective strategies to address anaemia.