



RESEARCH ARTICLE

REVISED **Development and application of a hybrid implementation research framework to understand success in reducing under-5 mortality in Rwanda [version 3; peer review: 2 approved]**

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Abstract

Background: We describe the development and testing of a hybrid implementation research (IR) framework to understand the pathways, successes, and challenges in addressing amenable under-5 mortality (U5M) – deaths preventable through health system-delivered evidence-based interventions (EBIs) – in low- and middle-income countries (LMICs).

Methods: We reviewed existing IR frameworks to develop a hybrid framework designed to better understand U5M reduction in LMICs from identification of leading causes of amenable U5M, to EBI choice, identification, and testing of strategies, work to achieve sustainability at scale, and key contextual factors. We then conducted a mixed-methods case study of Rwanda using the framework to explore its utility in understanding the steps the country took in EBI-related decision-making and implementation between 2000-2015, key contextual factors which hindered or facilitated success, and to extract actionable knowledge for other countries working to reduce U5M.

Results: While relevant frameworks were identified, none individually covered the scope needed to understand Rwanda's actions and success. Building on these frameworks, we combined and adapted relevant frameworks to capture exploration, planning, implementation, contextual factors in LMICs such as Rwanda, and outcomes beyond effectiveness and coverage. Utilizing our hybrid framework in Rwanda, we studied multiple EBIs and identified a

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common pathway and cross-cutting strategies and contextual factors that supported the country's success in reducing U5M through the health system EBIs. Using these findings, we identified transferable lessons for other countries working to accelerate reduction in U5M.

Conclusions: We found that a hybrid framework building on and adapting existing frameworks was successful in guiding data collection and interpretation of results, emerging new insights into how and why Rwanda achieved equitable introduction and implementation of health system EBIs that contributed to the decline in U5M, and generated lessons for countries working to drop U5M.

Keywords

implementation research, evidence-based interventions, under-5 mortality, Rwanda, framework, amenable mortality

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REVISED Amendments from Version 2

Thank you for taking the time to read this article. We are grateful for the comments provided by our reviewers, and have revised the article in response to their careful feedback. The main change in this revision is to expand on the detail around the rapid review for framework choice, described in the Methods.

Any further responses from the reviewers can be found at the end of the article

List of Abbreviations

CFIR	Consolidated Framework for Implementation Research
CHW	Community health worker
DHS	Demographic and Health Surveys
EBI	Evidence-based intervention
EPIAS	Exploration, Preparation, Implementation, Adaptation, Sustainment
EPIS	Exploration, Preparation, Implementation, Sustainment
ERIC	Expert Recommendations for Implementing Change
IHME	Institute for Health Metrics and Evaluation
IMCI	Integrated management of childhood illness
IR	Implementation research
KI	Key informant
LMIC	Low- and middle-income country
MDG	Millennium Development Goal
M&E	Monitoring and evaluation
MOH	Ministry of Health
PCV	Pneumococcal vaccine
U5M	Under-5 mortality

Contribution to the literature

- Implementation research frameworks are important for informing studies of successes and challenges in evidence-based intervention implementation. However, they typically reflect strategies and factors more relevant to high-income settings than low- and middle-income countries (LMICs).
- Building on existing frameworks, we developed a hybrid framework to inform the study of the strategies, context, and outcomes of LMICs implementing EBIs to reduce amenable deaths in children under 5.
- The hybrid framework was effective when applied to understand the successes and challenges of Rwanda in dropping under-5 mortality and emerged lessons including a five-step path which other countries can adapt and adopt to accelerate their work to achieve success in saving more lives.

Background

Over the past 75 years, the world has witnessed remarkable progress in the development of evidence-based interventions (EBIs) proven to reduce morbidity and mortality from the leading causes of under-5 mortality (U5M) globally. These include biomedical interventions, such as vaccinations and oral rehydration salts, as well as strategies for delivery of these interventions through the integrated management of childhood illness in facilities and through community health workers. The United Nations Millennium Development Goal (MDG) 3 called for reduction of U5M by two-thirds between 1990 and 2015. In response, low- and middle-income countries (LMICs) prioritized U5M reduction through the introduction and strengthening of relevant EBI implementation as well as by addressing other direct and contributing causes of mortality, such as female disempowerment, stunting, and poor access to reproductive healthcare services¹. While U5M rates dropped by 53% from 1990 to 2015 globally, only 70 (36%) of the 193 UN Member States achieved the U5M goal, with 98.6% of U5 deaths occurring in LMICs in 2015^{2,3}.

Many of the EBIs known to be effective in reducing U5M were either not fully implemented or implemented with variable quality (effective coverage) in many LMICs. As a result, a significant proportion of deaths among children under 5 in these countries were preventable through a stronger health system that was able to provide quality care equitably (defined as amenable death)⁴. Insights into successes and challenges in how EBIs were chosen, adapted, implemented, and sustained are often missing from available reports and publications, which often focus on coverage and effectiveness. Implementation research (IR) is defined as “the scientific study of the use of strategies to adopt and integrate evidence-based health interventions into clinical and community settings to improve individual outcomes and benefit population health”⁵. The discipline was developed in response to this gap between awareness of EBIs and their effective and equitable implementation. IR can accelerate more effective planning, implementation, scaling, and sustainment of EBIs and policies, taking into account the contextual factors that influence outcomes ranging from coverage, to acceptability, to effectiveness. IR provides a set of methods for policymakers, implementers, and researchers to design and learn how to better choose and implement EBIs through strategies devised to move evidence from research into practice^{6,7}.

Interest in and use of IR in LMICs has grown in recent years, supported by publications illustrating the value of applying these methods to understand implementation successes and challenges in high-, middle-, and low-income countries^{8–11}. However, a number of publications have identified where adaptations are needed for these frameworks which were largely developed in high income settings^{12–14}. For example, a recent review of the use of IR in LMICs found a need for its expanded use in order to understand scale-up, sustainability, and implementation in more real-world settings⁸. In addition, existing IR frameworks with adaptations are needed to understand the full path from decisions at the policy level through to sustainable

scaling. IR frameworks are also needed to understand the contextual factors specific to public sector health systems in LMICs and ensure the focus on equity, central to achieving Universal Health Coverage^{13,14}.

We describe the development and testing of an IR framework building on existing frameworks to guide the study of pathways, successes, and challenges in addressing amenable U5M – those deaths preventable through health system-delivered EBIs – in LMICs. The application of the framework was tested through a mixed methods case study of Rwanda, a country well known for its remarkable success in substantially reducing U5M from 2000 to 2015 and improving or achieving equity in many of these areas (Table 1)¹⁵. The hybrid framework was used to inform the mixed methods case study design and extraction and analysis of implementation strategies, implementation outcomes, and key

contextual factors. This facilitated understanding of the process, successes, and challenges in Rwanda from identification of the causes of death, to EBI choice, through to work on sustainability and scaling. The case study was conducted as part of the Exemplars in U5M project and is available in full at <https://www.exemplars.health/>. In this paper, we describe the framework and its value in identifying key lessons in how and why Rwanda achieved this success to create potentially transferable and actionable knowledge to inform other countries working to reduce amenable U5M.

Methods

Development of the amenable U5M implementation research framework

At the start of the research, in 2017, we reviewed existing implementation research frameworks focusing on those applied

Table 1. Changes in under-5 mortality and evidence-based intervention coverage and equity gaps in Rwanda between 2000 and 2014. (Source: Rwanda DHS 2000, 2005, 2010, and 2014–15 and DHS STATcompiler).

Mortality		2000	2005	2010	2014	Wealth equity gap in 2000	Wealth equity gap in 2014	Absolute change in wealth equity gap 2000–2014
U5M/1000 live births		207	152	76	50	73	45	-28
NMR/1000 live births		50	37	27	20	19	11	-8
U5 Cause of Death	Evidence-Based Intervention							
Lower Respiratory Infections	Care-seeking for pneumonia	15.5%	27.9%	50.2%	53.9%	20	20	0
	Vaccination: 3 doses of PCV	NA	NA	NA	94.7%	N/A	5%	N/A
	Vaccination: Hib	NA	NA	92.9%	98.2%	N/A	3%	N/A
Diarrheal Diseases	Oral rehydration therapy	20.2%	29%	36.6%	34.7%	11%	12%	1%
	Vaccination: 3 doses of rotavirus				94.7%	N/A	5%	N/A
	Care-seeking for diarrhea	15%	14.4%	41%	45%	9%	18%	9%
Malaria	Insecticide-treated nets		12.6%	69.6%	67.7%	N/A	30%	
	Care-seeking for fever	8.7%	31.3%	44.8%	50.1%	10%	24%	14%
	Treatment of children with fever by ACT*			4.0%	11.2%	N/A	-5%	N/A
	Prompt treatment of children with fever by ACT			2.6%	7.4%	NA	-1%	N/A
Measles	Vaccination: Measles	86.9%	85.6%	95.0%	95.2%	4%	6%	2
HIV	HIV counseling during antenatal care		55.8%	90.6%	93.0%	N/A	3%	
	HIV testing during antenatal care		21.5%	94.5%	97.9%		3%	
Other vaccine preventable diseases	Full vaccination coverage with 3 doses DPT, 3 doses polio, measles and BCG	76.2%	75.5%	90.3%	92.7%	6%	8%	5%

Mortality		2000	2005	2010	2014	Wealth equity gap in 2000	Wealth equity gap in 2014	Absolute change in wealth equity gap 2000–2014
Neonatal-specific interventions	Antenatal care: 1+ visits by a skilled provider	92.5%	94.4%	98.0%	99.1%	N/A	N/A	N/A
	Antenatal care: 4+ visits by a skilled provider	10.4%	13.3%	35.4%	43.9%	N/A	N/A	N/A
	Antenatal care: 1st antenatal visit in the 1st trimester	4.7%	7.9%	38.2%	56.1%	N/A	N/A	N/A
	Vaccination: 1+ doses of tetanus toxoid during pregnancy	64.8%	63.4%	76.5%	79.6%	N/A	4%	N/A
	Delivery in a health facility	26.5%	28.2%	68.9%	90.7%	43%	13%	-30
	Delivery attended by skilled provider	26.7%	28.4%	69.0%	90.7%	N/A	13%	N/A
	Delivery by Cesarean-section	2.1%	2.9%	7.1%	13.0%	N/A	13%	N/A
	Postnatal care: Postnatal visit for baby within 2 days of birth	2.9%	3.7%	4.7%	19.3%	N/A	-1%	N/A
	Postnatal care: Postnatal visit for mother within 2 days of birth			17.6%	43.0%	N/A	10%	N/A

Wealth equity gap calculated as difference between the wealthiest quintile and lowest wealth quintile. N/A: not available as equity gap not able to be calculated due to no wealth disaggregation the DHS reports for some indicators.

* ACT: artemisinin-based combination therapy.

in LMICs to study implementation strategies, identification of contextual factors, and implementation outcomes^{8,16–19}. We focused on identifying frameworks that had been used in LMICs to date which were relevant to health systems interventions, through a rapid review in PubMed with search terms “implementation science” and “LMICs.” We also reviewed publications in Implementation Science from the previous three years and conducted outreach and discussion with experts in the field at the time. We identified relevant frameworks to develop a hybrid framework, which was adapted during the case study process to reflect emerging areas where changes were needed.

EBIs to reduce amenable U5M

Reviewing existing guidelines and literature from the MDG efforts, we identified EBIs known to reduce the most common causes of U5M in LMICs for infants and children, and for neonates during the three periods of risk (antenatal, peripartum, and postpartum). This identification of EBIs guided the exploration of implementation strategies, contextual factors, and implementation outcomes (Extended data Tables 1a and 1b)^{20–22}. These EBIs also guided evidence review and key informant selection.

Extraction and analysis of implementation pathways, strategies, outcomes, and contextual factors

We used an explanatory mixed methods case study to leverage existing quantitative data on selected implementation outcomes (reach, fidelity, adoption) and equity with the qualitative sources describing strategies, contextual factors and selected outcomes (acceptability, feasibility). Reach, also defined as coverage, was calculated from the Demographic and Health Surveys (DHS)^{23–26}. The Standards for Reporting Implementation Studies (StaRI) and COnsolidated criteria for REporting Qualitative research (COREQ) Checklists were used where relevant and are included in the Extended data^{22,27,28}.

Desk review. The team conducted a rapid review of available information and published data on the rates and progress of U5M broadly and amenable causes of U5M. We further explored the uptake and implementation of specific EBIs, including policies and strategies. Initial review research was performed through MEDLINE (PubMed) and Google Scholar using the following search terms as inclusion criteria: “child mortality” or “under-5 mortality” and Rwanda, with further searches including terms for specific EBIs (ex. “pneumococcal vaccination,”

“oral rehydration salts,”), causes of death (ex. “malaria,” “measles,” “HIV”), or contextual factors (e.g. “community health workers,” “female empowerment”). Other sources included publicly available datasets and reports (Demographic and Health Survey, Countdown 2015, and existing reviews of U5M reduction work in Rwanda)^{20,23–26,29}. The review was limited to amenable causes of death from the neonatal period to early childhood, including EBIs during pregnancy and childbirth deemed critical for child survival and only English-language references were included. Important interventions that contributed to U5M reduction beyond the specific health system EBIs including health system strengthening, education, female empowerment, reproductive health, poverty reduction, improving water and sanitation, and programs designed to improve nutritional status beyond management of acute severe malnutrition were captured as potentially important contextual factors. However, references which dealt solely with implementation of these interventions were not included as beyond the scope of the research, which focused on EBIs directly led by the health sector. The desk review was an iterative process, with additional searches conducted as needed and informed by the primary research described below.

Key informant interviews. With our in-country collaborator (FS), we purposively identified 15 key informants (KIs) who had been involved throughout the process of identifying the burden of the target cause of death and selecting, implementing, and working to sustain the targeted EBIs and U5M reduction more broadly before and during the period of focus (2000–2015). These KIs included current and former Ministry of Health employees responsible for overall U5M reduction efforts, or focusing on specific diseases or intervention areas (Table 2). We also interviewed KIs from implementing non-governmental organizations, multilateral organizations, and donor organizations who had been involved in partner-supported or partner-led activities. Some KIs represented more than one viewpoint based on their experience over the 15 years and were interviewed for each of their multiple viewpoints.

The interviews were conducted by phone or face-to-face using a semi-structured guide (see Extended data for interview guide²²), based on the IR framework, designed to understand EBI selection; the implementation process, from exploration to preparation, implementation, and sustainment; and contextual factors contributing to successes and challenges in each stage.

The interviews also helped identify additional data sources important in understanding implementation and related outcomes. Follow-up interviews were conducted as gaps or additional needs were identified. All interviews except one were led by one of the project principal investigators (LRH) with one to two notetakers. Each interview’s duration was approximately one hour. The total number was not designed for saturation but instead for covering the EBIs and was also limited by time and resources. Informed consent was obtained from all interview participants, and all recordings and transcripts were de-identified and stored in password-protected folders and destroyed once the interview coding was completed. The results were disseminated to the Ministry of Health and partners.

Analysis: Following the close of the interview, notes were combined and audio recordings (if permitted) were used to clarify areas as needed. Thematic coding of interviews using inductive and deductive approaches was done by one of the researchers and reviewed by one of the principal investigators for accuracy, with discussion for differences. *A priori* codes were organized from the framework for EBIs, implementation outcomes, and context. Implementation strategies were informed by the Expert Recommendations for Implementing Change (ERIC) framework³⁰ and additional codes were added as emerging themes were identified.

Additional analyses from the International Center for Equity in Health and geospatial mapping from the Institute for Health Metrics and Evaluation (IHME) were used to understand changes in equity indices for mortality and EBI coverage.

Ethical considerations

The study was determined to be non-human subjects research by the Rwandan National Ethics Committee and Northwestern University reflecting the scope and focus.

Results

Framework

We found that no single framework covered the scope of the work from identification of EBIs to target leading causes of U5M, to selection and testing of strategies to achieve sustainability at scale, understanding the full range of potential contextual factors and exploring outcomes beyond the traditional coverage and effectiveness measures used in evaluation of

Table 2. Rwandan key informants interviewed.

Organization/Level	Number of key informants interviewed
Global/national including donors	5 (33%)
Government including Ministry of Health and Rwanda Biomedical Center	6 (40%)
Project managers and implementers	3 (20%)
Other partners	1 (7%)

health systems. We therefore combined and adapted a number of existing frameworks to synthesize a framework designed to guide our work to understand implementation of and outcomes of EBIs to reduce amenable U5M (Figure 1). The frameworks identified as appropriate for guiding our work included:

1. *Exploration, Preparation, Implementation, Sustainment (EPIS)*¹⁶: EPIS covers four key steps of the implementation process from initial decision-making through work to achieve long-term change. Within each phase, Aarons identifies potential contextual factors that may influence success.
2. *RE-AIM*³¹: The framework identifies outcomes in Reach (coverage), Effectiveness, Adoption of the EBI,

Implementation (fidelity, time, cost, and adaptations made), and Maintenance (institutionalization into routine care and policies and long-term impact).

3. *Consolidated Framework for Implementation Research (CFIR)*¹⁷: CFIR was designed to understand contextual factors that influence the success or failure of implementation of an EBI.
4. We also expanded the outcomes of RE-AIM by incorporating relevant implementation outcomes key to achieving overall effective coverage and equity¹⁸.

The framework was revised as needed as new themes emerged during the Rwanda case study. For example, we recognized

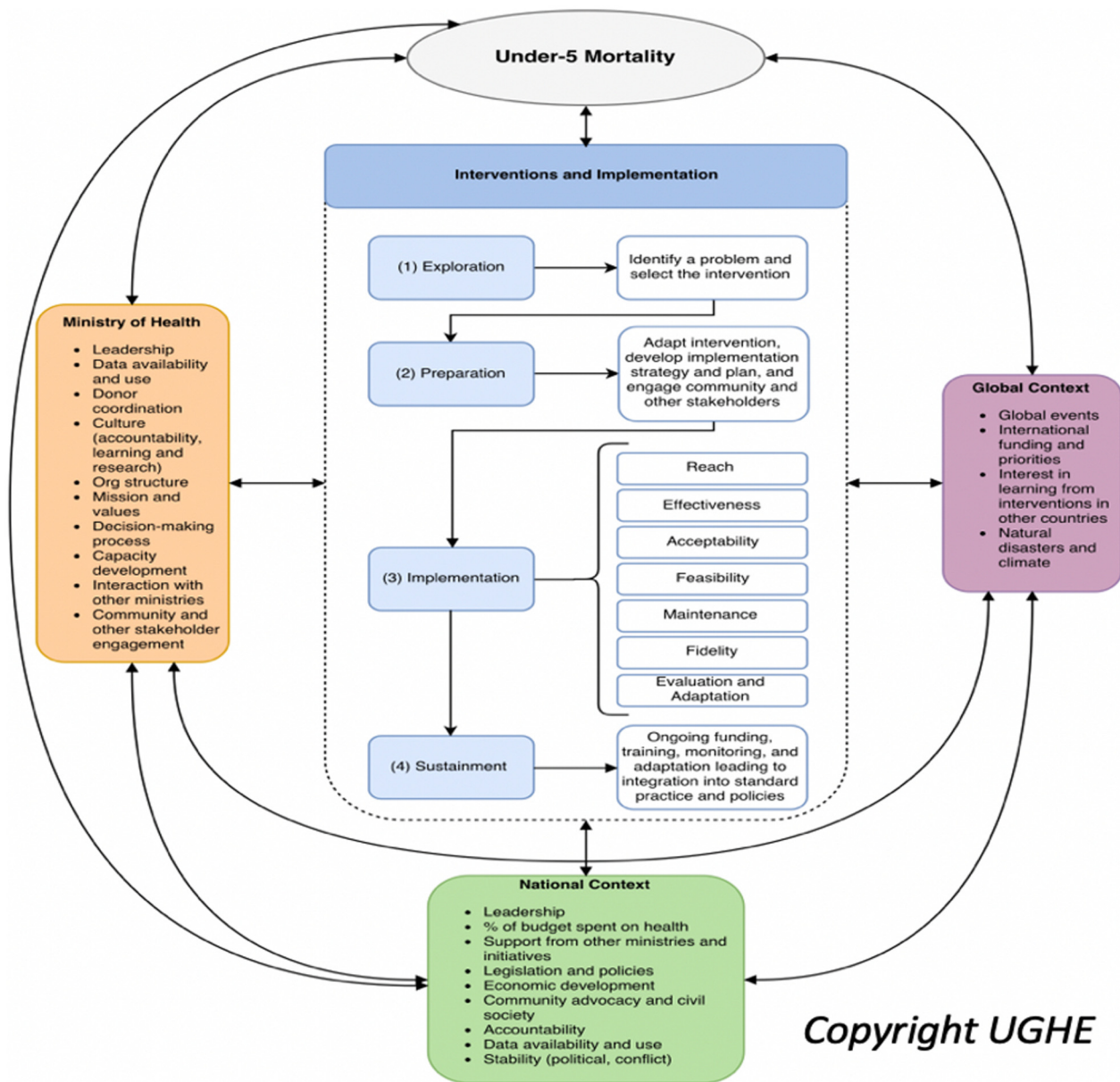


Figure 1. Hybrid Framework for Understanding Interventions to Reduce Under-5 Mortality. Reproduced with the permission of UGHE.

that adaptation was an important step during implementation and was sufficiently crucial that we included it as an explicit step rather than as an embedded implementation strategy. This led to the transformation of the four-step EPIS implementation process into the five-step EPIAS implementation process. In addition, this adapted framework expanded the levels at which we captured contextual factors, looking at global, national and subnational, ministry of health and health system, and community/family/individual levels. As the arrows indicate in Figure 1, our framework also explicitly calls out the interplay and non-siloed nature of contextual factors. This framework emphasizes the need to consider the multifaceted nature of these factors important in analyzing health sector implementation outcomes as well as broader influences at the global, national, and health system levels. These factors included those which could be leveraged to support implementation. They also represented barriers, requiring direct or indirect action to address, adaptation of implementation strategies at the local or national levels, or representing reasons for challenges in achieving targeted outcomes.

Development of a theory of change

To put the work to reduce amenable U5M within the broader work to reduce U5M, we also created a theory of change model (Figure 2). This model included the health systems EBIs which were the focus of our research (outlined) and other interventions which could directly or indirectly improve the health status of the children (resiliency), reduce the risk of falling ill or dying during an illness, or improve the ability to access care. These included interventions to improve nutrition, water and sanitation, female empowerment, and economic status. The theory of change takes into account the contextual factors at the four levels that can contribute to the reduction of amenable U5M and U5M more broadly. These factors can influence the implementation of EBIs, health resilience, prevention of disease,

and access and quality care, all of which can contribute to or hamper work to reduce amenable U5M.

Applying the framework to understand U5M reduction in Rwanda

We used the framework to develop the key informant guides and overall analysis plan. Guided by the framework, we extracted evidence of the implementation outcomes for EBIs from the available literature and quantitative data, including appropriateness, acceptability, feasibility, effectiveness, coverage or reach, and equity, where possible. We also used the framework to develop an initial set of codes for EBIs, implementation outcomes, and contextual factors. Coding was done manually using directed content analysis with additional codes added based on identification of new concepts, factors, or strategies. No software was used for this first qualitative coding. These results were analyzed using explanatory mixed methods starting with the EBI coverage data by the team and reviewed through a stakeholder meeting in Rwanda to provide feedback and validation, and to identify transferable lessons with the potential for adoption or adaptation in other countries with challenges in reducing U5M. The goals were to extract understanding of how and why Rwanda was able to successfully implement health systems EBIs known to reduce amenable U5M, and where challenges remained in implementation, sustainability, and overall U5M reduction.

Implementation steps and strategies

Implementation of all the EBIs followed the steps from the hybrid framework (EPIAS), starting with **Exploration** to determine the relative burden of an underlying cause of U5M and identify potential interventions. The **Preparation** step was carefully conducted and included a range of strategies including: stakeholder engagement; identifying contextual factors that either needed to be addressed (ex. supply chain strengthening

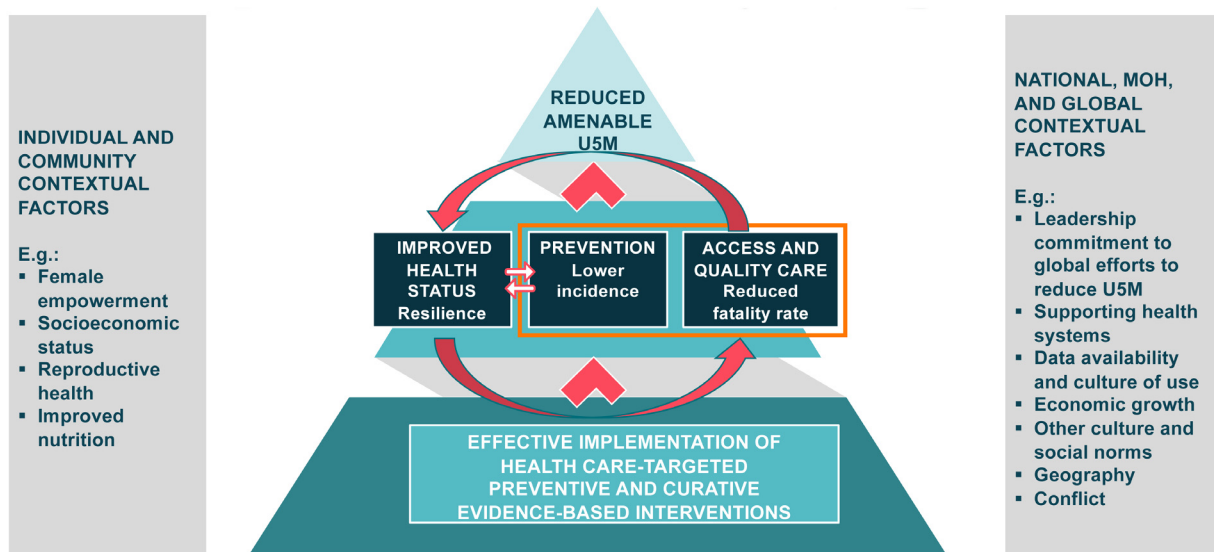


Figure 2. Theory of Change for Reduction of Amenable Under-5 Mortality.

or human resources) or that influenced the choice of implementation strategy (ex. task sharing); identifying and collecting any new evidence needed to inform strategies and adaptation; determining funding needs and sources; strengthening needed systems and developing or adapting national policies and protocols to drive systematic adoption; and integration of data needs for monitoring and evaluation (M&E) into routine information systems when possible and ensuring accountability for EBI delivery. **Implementation** then followed, with the pace of implementation based on EBI rollout needs and readiness. For example, vaccines were rapidly implemented at national scale while others, such as integrated management of childhood illness (IMCI), were rolled out as ongoing learning occurred.

The implementation of all of the EBIs included **Adaptation** starting soon after initial Implementation step. This adaptation reflected evidence emerging from ongoing monitoring and evaluation or other data sources reflecting how the strategies were put into practice, new global evidence (ex. rapid testing for malaria), or identification of areas where gains in coverage were either not reaching the most vulnerable or diseases, such as malaria, were reemerging. In Rwanda, the work for **Sustainment** was often included early in the steps through strategies including integration into national standards, ensuring access to long-term funding, fostering a culture supportive of M&E, and inclusion into training and supervision. Through these five steps, a number of implementation strategies were identified across the different EBIs (Table 3).

Table 3. Common Implementation Strategies by Exploration, Preparation, Implementation, Adaptation, and Sustainment Stages in Rwanda.

	● Strategy effectively implemented ● Strategy implemented with variable success ○ Strategy not implemented			
Implementation strategy	Exploration	Preparation	Implementation and Adaptation	Sustainment
Donor and implementing partner coordination	●	●	●	●
Focus on equity	●	●	●	●
Engagement of key national stakeholders and partners	●	●	●	●
Engagement of key international stakeholders and partners	●	●	●	●
National leadership and accountability	●	●	●	●
Building and strengthening primary healthcare systems	●	●	●	●
National prioritization of health	●	●	●	●
Rapid and early adoption of innovations	○	●	●	
Development of national policies, guidelines, and standards (including adaptation of global protocols/guidelines)	○	●	●	●
Community engagement and education	○	●	●	○
Data generation by in-country institutions and use	●	●	●	●
Data use for understanding gaps, prioritization, implementing, adapting	●	●	●	●
Multi-sector approach	●	●	●	●
Rapid scale-up	○	○	●	○
Small-scale testing	○	●	●	○
Supportive supervision and mentoring for quality	○	○	●	●
Building on community health worker program and community-based care delivery	○	●	●	●
Human resources for health expansion	○	○	●	●
Leveraging and strengthening existing systems (using to implement a strategy)	○	●	●	○
Task-shifting	○	○	●	○
Government financing	○	●	●	●

Implementation outcomes. We found that Rwanda implemented almost all of the EBIs identified as effective in reducing U5M (Extended data Table 1a²²) in LMICs with varying reach but high levels of equity (Table 1; Extended data Figure 1²²). Neonatal mortality reduction was slower and work to implement a number of the neonatal-specific EBIs (Extended data Table 1b²²) became a greater focus towards the end of the study period (Table 1). For example, PCV vaccine coverage was 94.7% in 2014 with a wealth gap of 5%. Measles vaccine coverage rose from 86.9% in 2000 to 95.2% in 2014, with the wealth equity gap hovering around 5% (4% in 2000, 6% in 2014). HIV testing and counseling during antenatal care was above 90% in 2014 with a wealth equity gap for both measures at 3%. Facility-based delivery had a higher wealth gap, but it decreased substantially from 43% in 2000 to 13% in 2014, with coverage increasing from 26.5% to 90.7% during that period.

However, extraction of many of the other implementation outcomes was limited by the available evidence from the primary and secondary resources. The most common outcomes we found from the desk review and KI interviews included feasibility, penetration/reach, and adoption. We also found sustainability outcomes for a portion of the EBIs, defined as maintaining high coverage rates from initial implementation through the end of the study period, and strategies associated with sustainability including incorporation into national policies and budgets. Fidelity and cost were infrequently found except at subnational levels from targeted studies.

Cross-cutting contextual factors. We identified cross-cutting contextual factors that were critical to successful implementation of many of the EBIs in Rwanda (Extended data Table 2²²). Equally important, a number of these also contributed to the decline in U5M by addressing causes not directly related to health. System interventions were important facilitating contextual factors throughout the five steps of EPIAS and represented the four areas from the framework (global, national, health system, and community). These included national leadership and commitment (in policy and finances) to health; a culture of data use for learning and decision-making tied to accountability at all levels; and, importantly, the existence of standards for coordination, collaboration, and communication within the health sector, across ministries, with local leaders, and between government bodies, donors, and implementing partners. Other facilitators included the availability of donor support and in-country implementing partners. The underlying health system design, with its commitment to primary care and decentralization, along with the development of a robust community health worker (CHW) program were also identified as facilitators, building on an underlying focus on equity. Resiliency of the family and child were also strengthened through national economic development, female empowerment through education and policy, development of a national health insurance free to the poorest sectors and emerging work to address nutrition and stunting.

There were also a number of contextual factors which represented challenges in Rwanda, including gaps in components

of the health system – such as ambulances and advanced equipment for the care of sick and low birthweight neonates – and cadres of human resources for health.

Example of applying the framework to understand EBI implementation: the case of pneumococcal vaccine introduction

We use the introduction of pneumococcal vaccine (PCV) to illustrate the results of employing the framework to understand the strategies, implementation outcomes, and contextual factors that explain the steps taken and overall results. We highlight examples of implementation strategies and facilitating contextual factors which emerged during the five steps outlined in our framework.

Exploration

Rwanda decided to rapidly move forward with PCV, based on the announcement by GAVI of the availability of grants for PCV; recommendations from WHO; and identification of pneumonia as the leading cause of death among children under 5 in Rwanda (*strategies*: use of external evidence and local data use for decision-making; *factors*: data availability, culture of data use)^{32–36}. This decision was led by the Rwandan Ministry of Health (MOH) and supported by the Vaccine Steering Committee, made up of MOH officials, one of whom chaired it, and national and international partners (*strategies*: national leadership, multisectoral and donor coordination; *factors*: national commitment to health, culture of coordination and intersectoral collaboration)³⁴.

Preparation

Supported by both the MOH and international partners (ex. GAVI, UNICEF, and USAID), Rwanda first performed a nationwide evaluation of the existing cold chain, which was used to address infrastructure gaps (*strategies*: integration into existing systems, leveraging global resources; *factors*: focus on primary care systems, donor funding availability). Rwanda also developed national training modules, implemented a cascading train-the-trainers model, revised vaccination guidelines and reporting forms, developed key messages for communities, and conducted a needs estimate (*strategies*: training with national protocols, integrating into existing monitoring systems, community engagement and education; *factors*: community trust in the healthcare system, existing monitoring and evaluation and health information systems)³⁵. The MOH procured the very high temperature incinerators (>1200°C) needed for destruction of prefilled glass-containing syringes³⁷. The MOH secured funding in the national budget, the counterpart fund for GAVI (*strategy*: engagement of key national stakeholders and partners) and chose to immediately roll out implementation nationwide due to confidence in their pre-implementation evaluation of the project, safety, and equity profiles of the vaccine, and a commitment to equity.

Implementation

Implementation of PCV started in 2009, with Rwanda becoming the first developing country to introduce the pneumococcal vaccine³⁸. It rolled out province-by-province as planned and was completed within five months of the start date. The

implementation strategy ensured equity by using motorcycles and cold boxes to deliver vaccines and leveraging CHW data to determine which areas needed additional vaccination days. A number of implementation outcomes were achieved, facilitated in part by the strategies chosen (Table 4).

Adaptation

In 2011, in response to high cold storage and incineration temperature requirement for PCV-7, Rwanda switched from using the PCV-7 to the PCV-13 vaccine which also provided protection against six more bacterial strains. These changes allowed for adoption of new vaccines, which had similar storage and disposal needs, with little increase in infrastructure and informed the strategy for introduction of other new vaccines in Rwanda in the future^{34,35}.

Sustainment

Full vaccination rates with PCV remained consistently high from introduction through the end of the study period and beyond, with coverage at 97–98% since 2010. Strategies that were identified as supporting this sustainment included integration by the MOH into its standard pediatric vaccine schedule; regular data use through monthly monitoring data, which are analyzed at the central level with feedback to address coverage gaps³⁴, and continuation of national funding for PCV, which has been included in the annual national budget since its introduction in 2009.

Rwanda has been highlighted as a country that leads in work to drop U5M. We were able to surface a number of lessons transferable to other countries that wish to accelerate their work to reduce U5M. These emerged from the successful strategies directly related to implementation, as well as from contextual factors, which can be modified to facilitate successful implementation outcomes (Table 5).

Discussion

We found that by building on and combining established IR frameworks and adapting based on themes that emerged during our case study, we were able to develop a hybrid framework. This framework was successfully used to guide how we prioritized research areas and analysis to extract knowledge of how Rwanda chose, implemented, and sustained EBIs to contribute to their remarkable drop in U5M, contributing or hindering actors and the implementation outcomes achieved, including a focus on equity as an explicit outcome. Adaptations included adding in an additional step of adaptation after implementation because of its prominence as an explicit stage in the pathway to successful implementation, and expansion of the levels at which we captured contextual factors. This successful use of IR builds on existing work in other countries in Africa, which have also found the value in understanding how and why interventions were successfully implemented and if outcomes including and beyond effectiveness were achieved^{10,11,39}. Our finding of a need for adaptations of existing IR frameworks reflects findings from other researchers working to increase IR use and effectiveness in LMIC. For example, a recent review of uses of the CFIR framework found modifications needed to be more applicable for use in these settings with similar results from work using RE-AIM, highlighting emerging use of IR and where additional work is needed^{12,13}.

Applying this framework also supported the extraction of implementation strategies that were used in the work to introduce and expand access across most or all of the EBIs. These often went beyond the categories outlined in guidelines for categorizing strategies, such as ERIC³¹, potentially reflecting the use of IR in a different context than the ones for which ERIC was designed. Identifying these strategies was important as they represent opportunities for learning and adoption in other countries, although differences in contextual factors would

Table 4. Pneumococcal Vaccine Implementation Strategies and Selected Implementation Outcomes.

	Implementation Strategy	Implementation Outcomes
Acceptability	Sensitization of local leaders, teachers, and traditional healers; outreach by CHWs on risk and benefits of vaccinations and through newspapers, radio, and television based on messages created by MOH ^{34,35} .	High acceptability because Rwanda's "population trusts very much their government and what they are doing and that [the MOH's] main interest is our beneficiaries." (KI)
Feasibility	The supply chain and M&E were successfully adapted with data use to identify gaps in coverage.	No stockouts occurred during the vaccine rollout and vaccinations were able to be implemented ³⁵ .
Fidelity	MOH officials performed regular supervisory visits at every health center and provided feedback ³⁵ . UNICEF, the Centers for Disease Control and Prevention (CDC), the American Red Cross, and USAID/MCHIP joined local evaluators to organize the post introduction evaluation.	The rollout was completed as planned within five months.
Effectiveness and Reach	Infrastructure assessment and investment; cascade training for vaccinators; needs estimation by CHWs; nationwide, province-by-province, rolled out over five months.	PCV coverage quickly increased to 97% by 2010. There was a 53% reduction in child hospitalization due to pneumonia after introduction of PCV ^{40,41} .

Table 5. Transferable Lessons for Countries Looking to Accelerate Decline in Under-5 Mortality Through More Effective Evidence-Based Intervention Implementation.

• Ensure accountability at all levels and engage community to support
• Build capacity of implementers and policymakers in the ministry and locally
• Change the culture of data use to include training, increased data use and quality, and linkages to accountability systems
• Coordinate donor and implementing partner funds and activities to follow the national vision and strategy, leveraging these important resources
• Provide support to strengthen leadership at all levels through delegation of responsibility accompanied by the accountability
• Create laws, policies, and regulations needed for effective quality implementation, and enforce them to ensure quality and delivery
• Engage the community and civil society at all levels and in meaningful ways, including through bylaws and national regulation
• Invest in health systems and inputs, including physical accessibility and quality broadly and leverage them for specific EBIs
• Ensure financial accessibility and protection through systems designed to ensure equity
• Engage the private sector, nongovernmental, and faith-based organizations as key partners in care delivery
• Plan for equity from the beginning

need to be addressed. For example, one cross-cutting strategy was coordination of donors and partners but led by a national plan and vision and stakeholder engagement throughout the five steps of EPIAS. These strategies were identified as critical for the feasibility, fidelity, and reach of the EBIs, as well as an ability to continue focusing on equity. These strategies built on contextual factors in a number of the four domains including strong national and ministry leadership and a culture of accountability, factors which may need to be strengthened in other settings. Another key strategy was integrating new EBIs into existing systems, including primary healthcare. The success of these strategies was facilitated by the national commitment to primary healthcare, including expanding health facilities and a robust community health worker program. This strategy, combined with rapid data use for decision-making and planning, was also used to rapidly roll out new vaccines during the study period and beyond^{34,42}.

The focus on contextual factors and the theory of change also allowed for exploration of interventions and other factors beyond the health system-delivered EBIs that contributed to their effectiveness and overall decline in U5M. These included female empowerment, access to family planning to improve birth spacing, economic improvement, reduction in stunting (albeit less impressive than the reduction in U5M), and other efforts. The contribution of these factors is consistent with modeling work done by IHME in Rwanda, as well as results from the Countdown 2015 studies in other countries^{43,44}.

There are a number of limitations to our work. We relied on available quantitative data and published reports for the measurement of many of the outcomes. As noted, reports and data on key factors such as quality, cost, and reasons for variability

in implementation outcomes were often missing. The key informant interviews relied on recall, so bias cannot be excluded. We also ensured confidentiality, but as in all interviews, there may have been social desirability bias, a factor we tried to limit by having the interviews conducted by investigators other than the coauthors involved in the work done in Rwanda during the study period (AB and FS). As is the case with many retrospective IR studies, there were no validated measures for outcomes such as adoption, acceptability, and reported appropriateness. Finally, we explicitly designed the study to focus on the implementation of known EBIs in a real world setting and so the attribution of the degree of contribution to the overall reduction in U5M could not be directly measured, although modeling results are available at www.exemplars.health.

Conclusion

In conclusion, we found that using the developed U5M IR framework facilitated the identification of the implementation pathway, priority implementation outcomes, and contextual factors important in healthcare in LMICs. The case study was able to increase insights into how and why Rwanda achieved the equitable introduction and expansion of EBIs contributing to the decline in U5M. The framework has now been successfully used in five other countries (Peru, Senegal, Ethiopia, Nepal, and Bangladesh) with results available at <http://www.exemplars.health>. The goal of the case study and project is to create generalizable and actionable knowledge needed by other countries working to accelerate and ensure equity in their reduction of U5M. This work is also part of an ongoing movement to expand the use of IR as a powerful tool for understanding and evaluating performance, identifying contextual factors that require strategy adaptation or direct action, and revealing global promising

practices, which countries can use to achieve the goal of eliminating deaths in children everywhere.

Data availability

Source data

The Demographic and Health Surveys data used in the current study are available from the DHS website.

Rwanda DHS 2015: <https://dhsprogram.com/pubs/pdf/FR316/FR316.pdf>

Rwanda DHS 2000: <https://dhsprogram.com/pubs/pdf/FR125/FR125.pdf>

The Institute for Health Metrics and Evaluation (IHME) Low- and Middle-Income Country Neonatal, Infant, and Under-5 Mortality Geospatial Estimates 2000–2017 Local Burden of Disease data used in the current study are available for download from IHME: <http://ghdx.healthdata.org/record/ihme-data/lmic-under5-mortality-rate-geospatial-estimates-2000-2017>.

Underlying data

Data access is restricted to users with appropriate ethics approval from the committees listed in the Ethical Considerations section. A reader or reviewer may apply to the authors for access by providing a written description of background, reasons, and intended use. If the methodology does not violate the condition of informed consent under which the interview was conducted, and the proposal approved by UGHE and other relevant ethics boards, the user can obtain the data from the corresponding author, and include one of the authors in the project and analysis.

Extended data

DRYAD: Development and application of a hybrid implementation research framework to understand success in reducing under-5 mortality in Rwanda. <https://doi.org/10.5061/dryad.kh189324x22>

This project contains the following extended data:

- Interview guide, accessible here: https://ughe.org/wp-content/uploads/2021/02/1.-Interview-Guide_Exemplars-U5M.pdf.

- Tables and figures, accessible here: <https://ughe.org/wp-content/uploads/2021/02/2.-Extended-Data-Tables-1a-and-1b-Table-2-Figure-1.pdf>.

Reporting guidelines

DRYAD: StaRI checklist for ‘Development and application of a hybrid implementation research framework to understand success in reducing under-5 mortality in Rwanda’ <https://doi.org/10.5061/dryad.kh189324x22>. Accessible here: <https://ughe.org/wp-content/uploads/2021/02/3.-StaRI-checklist-IS-Exemplar-framework-methods.pdf>.

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Ethics approval and consent to participate: The study was determined to be non-human subjects research by the Rwandan National Ethics Committee and Northwestern University reflecting the scope and focus.

Interviewees were informed about the goals and structure of the project, and verbal informed consent for participation and for audio recording was obtained separately from the interview.

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No further comments

Competing Interests: No competing interests were disclosed.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Version 2

Reviewer Report 08 December 2021

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I appreciate the authors' revisions and clarifications following my earlier comments.

I still do have some reservations.

Whereas the authors provide explanations/clarifications to some of my earlier concerns raised, some of these were changes not effected in the manuscript. It should be noted that the response to reviewer comments only addresses the reviewers, but without translating this clarification to the main manuscript, there is no clarification for the readers. For example, the manuscript still does not detail how and when the authors searched the literature for IS frameworks. The authors provide some explanations to the reviewer's comments, but the manuscript still does not detail this process.

Competing Interests: No competing interests were disclosed.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Author Response 10 Dec 2021

Amelia VanderZanden, University of Global Health Equity, Kigali, Rwanda

Comment: *I appreciate the authors' revisions and clarifications following my earlier comments. I still do have some reservations.*

Whereas the authors provide explanations/clarifications to some of my earlier concerns raised, some of these were changes not effected in the manuscript. It should be noted that the response to reviewer comments only addresses the reviewers, but without translating this clarification to the main manuscript, there is no clarification for the readers. For example, the manuscript still does not detail how and when the authors searched the literature for IS frameworks. The authors provide some explanations to the reviewer's comments, but the manuscript still does not detail this process.

Response: Thank you for your careful consideration. While the open peer review and response process means that all readers are able to see both the reviewer comments and the authors' responses in addition to the article, we agree that in our previous revision we did not include changes to the article beyond our response to this reviewer's comment about the rapid review for framework choice. For all other previous comments from this reviewer we have reviewed and added as needed to other previously documented responses.

The work on framework development was done in 2017. The authors focused on identifying implementation research frameworks which had been used in LMICs at that time and were relevant to health systems interventions. We conducted a search for "implementation science" and "LMICs" in PubMed as a rapid review. We also reviewed publications in Implementation Science in the last three years, and through outreach and discussion with experts in the field at the time. No single framework captured the contextual factors and stages of implementation as well as implementation outcomes, so a hybrid framework which could be used across the scope of the work was developed.

We have now expanded the Methods section text under the header, "Development of the amenable U5M implementation research framework," to include the following italicized

text: "At the start of the research, in 2017, we reviewed existing implementation research frameworks focusing on those applied in LMICs to study implementation strategies, identification of contextual factors, and implementation outcomes 8, 16– 19 . We focused on identifying frameworks that had been used in LMICs to date which were relevant to health systems interventions, through a rapid review in PubMed with search terms "implementation science" and "LMICs." We also reviewed publications in Implementation Science from the previous three years and conducted outreach and discussion with experts in the field at the time. We identified relevant frameworks to develop a hybrid framework, which was adapted during the case study process to reflect emerging areas where changes were needed."

Competing Interests: No competing interests were disclosed.

Version 1

Reviewer Report 12 October 2021

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This is a really interesting contribution to the body of knowledge on the application of implementation science methods, theories, models and frameworks in global health.

The authors have very well highlighted a gap which is increasingly being pointed out by many researchers and actors in global health:

Most implementation science frameworks were designed for western contexts. Adaptations for use in global health are necessary.

I do have a few comments which will make this article stronger and more replicable.

Methods:

Mixed-methods vs multi-methods

The authors state that they used "mixed methods case study to leverage existing quantitative data on selected implementation outcomes (reach, fidelity, adoption) and equity with the qualitative sources describing strategies, contextual factors and selected outcomes (acceptability, feasibility). The Standards for Reporting Implementation Studies (StaRI) were used where relevant and is included in the Extended data"

1. I know this varies across schools of thought but I wonder whether this was not rather a

multi-methods study. I see that at least two systematic reviews were conducted, qualitative interviews were also conducted, and the authors make reference to analysing quantitative data

2. It is not clear how quantitative methods were used in this study. The methods and results sections do not reflect this adequately
3. Given the multi-methods approach of this study, I believe that the StaRI is not sufficient as a checklist for this study. Could the authors also consider the COREQ and PRISMA checklists as well to ensure that the components of the qualitative and systematic review processes are covered?

Development of the amenable U5M implementation research framework

The authors state that they "*reviewed existing implementation research frameworks focusing on those applied in LMICs to study implementation strategies, identification of contextual factors, and implementation outcomes*"

However, there is no information on how this was carried out. Was there a systematic search strategy? This is important because several publications have emerged recently in an attempt to bridge this same gap. Were these emerging frameworks part of the review or was this a selective review process. This is not clear.

Documentation of this process is very important for replication. Particularly as the authors posit in the results section that "*We found that no single framework covered the scope of the work from identification of EBIs to target leading causes of U5M, to selection and testing of strategies to achieve sustainability at scale, understanding the full range of potential contextual factors and exploring outcomes beyond the traditional coverage and effectiveness measures used in evaluation of health systems.*"

Such inference can only be made if all available frameworks were reviewed systematically. Thus, it would be very helpful for the authors to detail this search process.

The only search strategy detailed seems to be around the EBI.

Key informant interviews

It would be helpful to provide further details on who was interviewed. Also, it is not very clear in the results section what the outcomes of these interviews were.

Is the work clearly and accurately presented and does it cite the current literature?

Partly

Is the study design appropriate and is the work technically sound?

Partly

Are sufficient details of methods and analysis provided to allow replication by others?

No

If applicable, is the statistical analysis and its interpretation appropriate?

Not applicable

Are all the source data underlying the results available to ensure full reproducibility?

Partly

Are the conclusions drawn adequately supported by the results?

Partly

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Implementation Science, Global health

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Author Response 16 Nov 2021

Amelia VanderZanden, University of Global Health Equity, Kigali, Rwanda

We are grateful for your close review and comments on this article and have responded to each comment below as well as in the manuscript.

Methods

The authors state that they used "mixed methods case study to leverage existing quantitative data on selected implementation outcomes (reach, fidelity, adoption) and equity with the qualitative sources describing strategies, contextual factors and selected outcomes (acceptability, feasibility). The Standards for Reporting Implementation Studies (StaRI) were used where relevant and is included in the Extended data"

I know this varies across schools of thought but I wonder whether this was not rather a multi-methods study. I see that at least two systematic reviews were conducted, qualitative interviews were also conducted, and the authors make reference to analysing quantitative data.

Response: Thank you for your comments and identifying areas which were less clear.

We understand that this could be a multi-methods, but because we used the qualitative methods to explain the quantitative findings (explanatory mixed methods), we have opted to keep the mixed methods terminology.

It is not clear how quantitative methods were used in this study. The methods and results sections do not reflect this adequately

Response: We used quantitative methods to look at the implementation outcomes of reach (coverage) and where possible, although limited, fidelity and equity. Because this coverage was our main metric of success, we used this to drive our qualitative work to help explain the quantitative results, implementation strategies, and contextual factors. We have added the following sentence to the Extraction and Analysis section of the Methods: "Reach, also defined as coverage, was calculated from the Demographic and Health Surveys (DHS)." We have also expanded on the quantitative results we report under implementation outcomes, excerpted below:

"For example, PCV vaccine coverage was 94.7% in 2014 with a wealth gap of 5%. Measles

vaccine coverage rose from 86.9% in 2000 to 95.2% in 2014, with the wealth equity gap hovering around 5% (4% in 2000, 6% in 2014). HIV testing and counseling during ANC was above 90% in 2014 with a wealth equity gap for both measures at 3%. Facility-based delivery had a higher wealth gap, but it decreased substantially from 43% in 2000 to 13% in 2014, with coverage increasing from 26.5% to 90.7% during that period."

Given the multi-methods approach of this study, I believe that the StaRI is not sufficient as a checklist for this study. Could the authors also consider the COREQ and PRISMA checklists as well to ensure that the components of the qualitative and systematic review processes are covered?

Response: Thank you for the suggestions. We did not use PRISMA as this was a rapid review and not a systematic review. We agree that the COREQ checklist was a reasonable one to include and have added it here, in the extended data.

The authors state that they "reviewed existing implementation research frameworks focusing on those applied in LMICs to study implementation strategies, identification of contextual factors, and implementation outcomes." However, there is no information on how this was carried out. Was there a systematic search strategy? This is important because several publications have emerged recently in an attempt to bridge this same gap. Were these emerging frameworks part of the review or was this a selective review process. This is not clear.

Documentation of this process is very important for replication. Particularly as the authors posit in the results section that "We found that no single framework covered the scope of the work from identification of EBIs to target leading causes of U5M, to selection and testing of strategies to achieve sustainability at scale, understanding the full range of potential contextual factors and exploring outcomes beyond the traditional coverage and effectiveness measures used in evaluation of health systems." Such inference can only be made if all available frameworks were reviewed systematically. Thus, it would be very helpful for the authors to detail this search process. The only search strategy detailed seems to be around the EBI.

Response: Thank you for your question. The work on framework development was done in 2017. The authors were focused on implementation research frameworks which had been used in LMICs at that time. We conducted a search for implementation science in LMICs as a rapid review. We reviewed implementation science journals, as well as searching for IS frameworks in LMICs, and through outreach and discussion with experts in the field at the time.

In terms of the newly emerging frameworks, we are excited by this growing interest. At the time that this framework was initially developed there were much fewer publications. We do refer to emerging work for example the Means et al article focused on expanding CFIR for LMICs, in the discussion, and have added the below (new text underlined here for emphasis): "For example, a recent review of uses of the CFIR framework found modifications needed to be more applicable for use in these settings with similar results from work using RE-AIM, highlighting emerging use of IR and where additional work is needed."

Methods/Results

It would be helpful to provide further details on who was interviewed.

Response: Thank you for this comment. We have put together a table of type/role of KI for Rwanda to provide further detail. This is now Table 2 in the paper and is included here at

bottom for reference.

Also, it is not very clear in the results section what the outcomes of these interviews were.

Response Thank you for your comment. We have worked to make this more clear. We extracted information from the interviews to explain the coverage and understand the implementation strategies and qualitatively other implementation outcomes. The interviews were also important in identifying contextual factors which served as facilitators (such as culture of data use) or barriers, and specific strategies (such as donor coordination and accountability). The data from these interviews was also combined with results from the literature and reports on EBI implementation to capture strategies, contextual factors, and implementation outcomes. We have added the below expanded detail on the outcomes of interviews in analysis to the results (in the section titled, Applying the Framework to Understand U5M Reduction in Rwanda): “Guided by the framework, we extracted evidence of the implementation outcomes for EBIs from the available literature and quantitative data, including appropriateness, acceptability, feasibility, effectiveness, coverage or reach, and equity, where possible. We also used the framework to develop an initial set of codes for EBIs, implementation outcomes, and contextual factors. Coding was done manually using directed content analysis with additional codes added based on identification of new concepts, factors, or strategies. These results were analyzed using an explanatory mixed methods starting with the EBI coverage data by the team and reviewed through a stakeholder meeting in Rwanda to provide feedback and validation, and identify transferable lessons with the potential for adoption or adaptation in other countries with challenges in reducing U5M.”

Table 2. Rwandan key informants interviewed

Organization/Level

Number of key informants interviewed

Global/national including donors
5 (33%)

Government including Ministry of Health and Rwanda Biomedical Center
6 (40%)

Project managers and implementers
3 (20%)

Other partners
1 (7%)

Competing Interests: No competing interests.

Reviewer Report 06 July 2021

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Betregiorgis Zegeye 

HaSET Maternal and Child Health Research Program, Shewarobit Field Office, Shewarobit, Ethiopia

The article entitled “Development and application of a hybrid implementation research framework to understand success in reducing under-5 mortality in Rwanda” [version1; peer review: awaiting peer review] is methodologically innovative and appreciable works. It is a well prepared draft. Few minor comments are given below.

General comment

I think authors used very long sentences even up to six or more lines throughout the text, may lead readers to not easily understand the meanings. Therefore, I recommend shortening the sentences without changing the concept.

Abstract

First line, please check the grammar as describe or should it read as described.

Background

Last paragraph: line 1-4, do you believe the sentence after “amenable U5M” or “Deaths preventable through health system delivered evidence-based intervention (EBIs) defined amenable U5M? What about under-five death preventable through other than health system EBIs? Last paragraph: line 1st and 4th as mentioned in above comment; please check the grammar as describe or should it read as described.

Methods

Desk review: line 3 from the bottom, authors captured many contextual factors during desk review, but mentioned some of those factors were beyond the study's scope. Can you mention those factors that are beyond the study's scope?

Desk review: What was the inclusion and exclusion criteria during desk review?

Desk review: line 12-17 have repeated paragraph, please remove one without citation.

Key informant interview (line 7), in the sentence “.....MOH employees responsible for overall U5M efforts, or specific disease or intervention areas” is a little confusing. It seems they had been working to facilitate U5M. So, please revise it.

Key informant interview (Second paragraph, line 11), please specifically mention which type of consent authors were obtained; verbal or written?

Key informant interview (Second paragraph, line 12), authors mentioned about recordings, but not clearly stated whether audio or video recordings are used.

Key informant interview (Second paragraph, line 19), revise the typo error (principle in to principal).

On Figure 2, to keep the logical flow the phrase “curative and preventive” better to be changed in to “preventive and curative”.

Results

Cross cutting contextual factors; line 5 needs revision.

Authors used women empowerment and female empowerment interchangeably (e.g., figure 2, desk review line 9 from the bottom, discussion 3rd paragraph: line 4), but they are not same and need to be select one and use throughout the texts.

Discussion

Second paragraph (line 2), the first sentence ended with “...across many if not all of the EBIs”, need revision.

Is the work clearly and accurately presented and does it cite the current literature?

Yes

Is the study design appropriate and is the work technically sound?

Yes

Are sufficient details of methods and analysis provided to allow replication by others?

Yes

If applicable, is the statistical analysis and its interpretation appropriate?

Yes

Are all the source data underlying the results available to ensure full reproducibility?

Yes

Are the conclusions drawn adequately supported by the results?

Yes

Competing Interests: No competing interests were disclosed.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Author Response 16 Nov 2021

Amelia VanderZanden, University of Global Health Equity, Kigali, Rwanda

We are grateful for your close review and comments on this article and have responded to each comment below as well as in the manuscript.

General comment

I think authors used very long sentences even up to six or more lines throughout the text, may lead readers to not easily understand the meanings. Therefore, I recommend shortening the sentences without changing the concept.

Response: Thank you for your feedback, we agree the long sentences are challenging and have worked to shorten throughout the article.

Abstract

First line, please check the grammar as describe or should it read as described.

Response: Thank you for your comment. We believe it should remain “describe” as we are explaining what we will do in the article

Background

Last paragraph: line 1-4, do you believe the sentence after “amenable U5M” or “Deaths preventable through health system delivered evidence-based intervention (EBIs) defined amenable U5M?”

Response: The sentence describes the focus of our study, which was specifically deaths preventable through health system-delivered EBIs.

What about under-five death preventable through other than health system EBIs?

Response: U5 death preventable through other than health system EBIs are important as well but were not the focus of the work described in this paper.

Background

Last paragraph: line 1st and 4th as mentioned in above comment; please check the grammar as describe or should it read as described.

Response: Thank you for your comment. Again, we believe it should remain “describe” as it pertains to what is covered in the article and is not discussing the research work done (which is in the past tense).

Methods

Desk review: line 3 from the bottom, authors captured many contextual factors during desk review, but mentioned some of those factors were beyond the study's scope. Can you mention those factors that are beyond the study's scope?

Response: Thank you for your question. The authors stated that in-depth reviews of the *implementation* of these interventions not directly led by the health sector were beyond the scope of the research – specifically of interventions including health system strengthening, education, female empowerment, reproductive health, poverty reduction, improving water and sanitation, and programs designed to improve nutritional status beyond management of acute severe malnutrition. We treated them as contextual factors which may have facilitated or hindered implementation of the targeted EBIs (health system delivered targeted U5M directly) but not as a focus of the implementation research into how they were implemented.

Desk review: What was the inclusion and exclusion criteria during desk review?

Response: We conducted a rapid review with no consort diagram. Inclusion criteria included anything that included one of the EBIs from the list (Extended Data Tables 1a and 1b), included qualitative or quantitative information on contextual factors, implementation

strategy, or implementation outcomes, and was specific to the country of focus. We have edited the text in the desk review section to make this more explicit.

Desk review: line 12-17 have repeated paragraph, please remove one without citation.

Response: Thank you for pointing this out as it appears to have been added during the typesetting. We have made this correction.

Key informant interview (line 7), in the sentence “.....MOH employees responsible for overall U5M efforts, or specific disease or intervention areas” is a little confusing. It seems they had been working to facilitate U5M. So, please revise it.

Response: We have revised to include the work “reduction”, as below (underlined here for ease of viewing): “current and former Ministry of Health employees responsible for overall U5M reduction efforts, or focusing on specific diseases or intervention areas.”

Key informant interview (Second paragraph, line 11), please specifically mention which type of consent authors were obtained; verbal or written?

Response: Thank you for your comment. A statement about consent was included in the ethical approval and consent to participate section. We have revised the text to clarify that it was verbal consent.

Key informant interview (Second paragraph, line 12), authors mentioned about recordings, but not clearly stated whether audio or video recordings are used.

Response: We have revised to specify that they were audio recordings.

Key informant interview (Second paragraph, line 19), revise the typo error (principle in to principal).

Response: This typo has been corrected.

On Figure 2, to keep the logical flow the phrase “curative and preventive” better to be changed in to “preventive and curative”.

Response: We agree with this edit and have made the change in the figure.

Results

Cross cutting contextual factors; line 5 needs revision.

Response: We have reviewed the text and made the correction to include the missing close parenthesis on line 3.

Authors used women empowerment and female empowerment interchangeably (e.g., figure 2, desk review line 9 from the bottom, discussion 3rd paragraph: line 4), but they are not same and need to be select one and use throughout the texts.

Response: Thank you for flagging this, you are correct that these are not interchangeable. We have revised to “female empowerment” in Figure 2 for consistency.

Discussion

Second paragraph (line 2), the first sentence ended with “...across many if not all of the EBIs”, need revision.

Response: Thank you for your comment. We have changed the sentence from “Applying this

framework also supported the extraction of implementation strategies that were common across many if not all of the EBIs.” to now read (underlined here for ease of reading the changed text): “Applying this framework also supported the extraction of implementation strategies that were used in the work to introduce and expand access across most or all of the EBIs.”

Competing Interests: No competing interests.
