BOLSTERING THE CASE FOR ENHANCED SAMPLE REGISTRATION SYSTEMS IN RESOURCE LIMITED COUNTRIES

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INTRODUCTION

Comprehensive civil registration and vital statistics systems (CRVS) are the gold-standard source for population data, capturing all vital events, including births and age-and-sex-specific deaths.(1) Yet fully functioning CRVS are often incomplete or non-existent in many resource-limited countries.(1, 2, 3, 4, 5) In 2021, the WHO reported that 44% of countries have either poor or no capacity to fully register births, deaths, and cause of deaths.(6) In Africa, fewer than half of all births and only 10% of deaths were registered.(6) Specific causes of death were reported for only 8% of deaths registered in resource-limited countries.(6) These findings are consistent with research published in the *Lancet* that lament the prolonged neglect of civil registration in resource-limited countries and the corresponding inability to generate useful vital statistics for those countries.(3, 7, 8, 9, 10)

Lack of population data limits countries' ability to establish infrastructure, prioritize and plan for their health and education needs, and measure and mitigate mortality and morbidity.(4, 6, 11, 12) In some resource-limited countries, alternative systems are used to measure the size, attributes, and health of the population; notable examples of such systems include the Demographic and Health Surveys (DHS) and Health and Demographic Surveillance Systems (HDSSs). Yet these alternative systems are often limited by infrequent data collection, data collection methods, or lack of national coverage. Given these limitations, and noting that enumerating the dead is one of the world's best investments for improving global health,(4) an appeal has gone out to improve the availability of timely, nationally representative population data in resource-limited countries.(1, 2, 3, 4, 6, 7, 8, 9)

As an interim step towards complete civil registration, some have proposed the establishment of *Sample Registration Systems* (SRS) that combine sample based vital registration with Verbal Autopsy (VA), a post-mortem interview tool used to determine likely cause of death when a clinical autopsy is not possible.(4, 13) We concur that SRS represents an interim step towards complete civil registration, but argue that augmenting such systems with a more precise method for determining etiology-specific causes of death would strengthen the ability of these systems to generate precise population health data. With this goal in mind, we propose *Enhanced Sample Registration Systems* (E-SRS) that combine SRS and VA of with the Minimally Invasive Tissue Sampling (MITS) procedure, which generates pathogen-specific cause of death data.(14)

Herein we present E-SRS as a platform for generating national and sub-national population and health statistics. We further discuss how adding precise causes of death to mortality statistics from these systems would facilitate detection of under-recognized causes of death, such as latent infections, anti-microbial resistant pathogens, and emerging and re-emerging diseases. We then highlight how the establishment of an E-SRS network could advance the establishment of CRVS systems, as the expansion of infrastructure, expertise, and capabilities required to establish E-SRS could be leveraged to enhance national population and health registries. Finally, we present estimates of the number of lives that could be saved through the establishment of E-SRS in three countries as an interim step towards complete civil registration.

Estimating the possible impact of improved intervention targeting via E-SRS

Establishing E-SRSs is expected to save lives by enhancing knowledge of the spatial distribution of subnational disease burdens and cause specific mortality. This enhanced knowledge will inform equitable implementation of effective health interventions through providing more precise information on specific causes of death, thereby denoting any needs for revised treatment strategies, and by improving effective coverage through identifying geographic areas with the highest disease burden where limited resources should be allocated.

Interventions anticipated to have higher impact when informed by MITs include Pneumococcal vaccine, Oral antibiotics for pneumonia, Rotavirus vaccine and Insecticide-treated nets/indoor residual spraying (ITN/IRS). Examples might include identifying the existence of antibiotic-resistant strains and differentiating falciparum vs. vivax (malaria). The E-SRS would increase the impact of full supportive care for prematurity by differentiating between stillbirths from early neonatal deaths, and prematurity from small gestational age. Interventions that would have higher impact when informed by information on geographic disparities include Oral Rehydration Salts (ORS), Antiretroviral therapy (ART), Labor and delivery management and full supportive care for neonatal sepsis/pneumonia. HIV interventions are not cost-effective enough to be universally deployed in highly budget constrained environments, though some (including ART) are amenable to re-allocation or scale-up based on more real-time assessments of burden. Better-informed delivery of bags and masks can prevent neonatal deaths from asphyxia. Greater precision on infection rates and locations could inform a more targeted rollout of the new WHO treatment protocol for Possible Serious Bacterial Infection. Considering the pathways through which E-SRS can contribute to saving lives, we undertook a modeling exercise to simulate estimates of the potential impact of an E-SRS network in reducing under-5 mortality.

METHODS

Study setting

To assess potential impact of establishing E-SRSs, subnational and national-level estimates of lives saved for children under age 5 were simulated for Ethiopia, Bangladesh, and Mozambique. Child mortality has declined in each of these countries over the past decade, but remains higher than the SDG target under-5 mortality rate of 25 per 1,000 live births.(15) National level estimates in 2021 ranged from 27.7 under-5 deaths per 1000 live births in Bangladesh, 47.2 under-5 deaths per 1000 live births in Ethiopia, and 68.4 under-5 deaths per 1000 live births in Mozambique.(16) Yet detailed understanding of national and subnational child mortality is impeded by limited or nonexistent civil registration in these countries.(5) In their 2021 report on global health data systems and capacity, the WHO reported nascent capacity for full birth and death registration in Ethiopia and limited capacity in Bangladesh and Mozambique.(17, 18, 19) The WHO further reported nascent capacity for certification and reporting of cause of death in Ethiopia and Mozambique; Bangladesh was rated at moderate capacity. While their capacity for nationwide registration of births and deaths remains limited, each of these countries have some CHAMPS and/or COMSA activities already in place,(20, 21) hence their selection as example countries for our simulation.

Nine interventions related to seven of the top causes of death in children under five and neonates (birth asphyxia, diarrhea, HIV/AIDS, lower respiratory infections, malaria, neonatal sepsis, and premature birth) were selected for simulation modeling (see Figure 1 for country specific cause of death distributions).(22, 23) To establish a modeling baseline, subject experts within Program Strategy Teams (PST) from the Bill and Melinda Gates Foundation were consulted to identify interventions that would benefit from better data as well as provide estimates of potential magnitude of intervention scale up that could occur with improved surveillance, which are summarized in Table 1. Preliminary simulations were modeled upon these recommendations.

Preliminary simulations focused on subnational estimates of potential lives saved in a given year, which were then summed to generate national-level estimates over time. Subnational cause of death estimates were calculated by multiplying region specific prevalence of a given cause of death (as reported by the DHS) by the corresponding region-specific population to obtain the estimated number of cases for a given region. A burden weight was then calculated by taking the estimated number of cases for a given region and dividing by the total number of estimated cases for the entire country. The burden weight was then multiplied against national level estimates of deaths attributable to a given cause (as reported by IHME) to generate subnational cause of death estimates. Subnational coverage levels for each of the interventions listed in Table 1 were obtained from the Lives Saved Tool (LiST).(24, 25) The number of covered cases was calculated as the number of cases multiplied by the coverage percentage. A coverage weight was then calculated by taking the estimated number of covered cases for a given region and dividing by the total number of estimated covered cases for the entire country. Disparity in burden vs. coverage was calculated by subtracting the coverage weight from the burden weight for a given region; disparity units were calculated by multiplying the burden vs. coverage disparity by the total number of covered cases in a given country.

The simulation proceeded by first modeled for subnational regions. Based on estimates of the difference between coverage and illness, experts provided their estimates of the likely magnitude and timing (immediate, three years, or five years) of coverage scale-up. In cases where subnational coverage exceeded subnational burden, coverage levels were maintained. Once disparities in coverage were addressed, remaining coverage units were allocated to high-burden areas. Reductions in mortality translate directly to lives saved based on extrapolated deaths due to a specific cause. In order not to erroneously include the contributions of secular improvements in health systems and socioeconomic factors, the model incorporates projected coverage for each intervention through 2030; an upper limit for intervention coverage increases due to E-SRS data is then estimated. An intervention is assumed to affect only a single cause of death. 2016 deaths are used as the baseline for future annual deaths through 2030. If data for a particular indicator were not available, data for the nearest proxy, identified by expert opinion, are substituted. Additional simulations were carried out using the Lives Saved Tool (LiST).(24, 25).

Overview of the Lives Saved Tool (LiST)

LiST is a free, publicly available software (including an online version) for modelling simulation estimates of the number of lives saved by the scaling up of interventions related to child and maternal health.(24) LiST was developed in an effort to improve the ability of global health policy makers, practitioners/program managers, and scholars to "assess the differential mortality impact of a comprehensive set of maternal and child health interventions." (26) The modeling tool developed as an extension of several articles in a Lancet Series that sought to estimate the impact of scaling up coverage of evidence-based interventions on child and neonatal mortality as well as nutrition related interventions for mothers and children.(27, 28, 29) Throughout the process of developing LiST, the tool's developers aimed to overcome limitations associated with prior estimation tools that were perceived as either too narrowly focused or lacking in rigor by generating a tool that could simulate estimates of lives saved when multiple interventions were increased simultaneously. This capacity was facilitated in part by integrating LiST within the

SPECTRUM suite of projection models.(26, 30) Over the past twenty years, the tool has undergone several iterations of revision and expansion to assess the impact of interventions related to under-five mortality,(28) neonatal mortality,(27, 31) wasting and stunting,(29) HIV/AIDS,(30) birth outcomes and stillbirths,(32) and pneumonia and diarrhea incidence.(33) Development and maintenance of the tool was funded in part by the Bill & Melinda Gates Foundation and in collaboration with the Child Health Epidemiology Reference Group (CHERG).(24)

Scholars have used LiST in multiple studies to estimate reductions in child and maternal mortality and the corresponding number of lives saved by scaling up interventions. In these studies, scholars used LiST as a means to quantify the benefits of a given intervention at the population level, as an aid for focusing intervention priorities, and as a means for setting target goals.(24) Global health policy makers and practitioners/program managers have also incorporated LiST as a strategic planning tool in developing countries.(34) A benefit of the tools is the ability to generate multiple simulations of intervention in order to assess the potential impact on mortality due to various combinations of scale-up scenarios.(24) Several studies have documented that the lives saved estimates generated with LiST were accurate predictions in settings where child and maternal health interventions were scaled up and the actual number of lives saved were assessed.(35, 36)

A general overview of the underlying algorithms and data inputs that LiST utilizes were summarized by Walker et al. (24) with additional detail provided by Winfrey et al.(26) LiST allows for interventions to have both direct and indirect effects on a specific cause of death. Accordingly, increasing intervention coverage may cause a reduction in multiple causes of death. Indirect effects are modeled to operate through intermediate risk factors or other characteristics that impact mortality. Calculated outcomes include neonatal, infant, child, and maternal mortality rates; numbers of stillbirths; cause specific death counts; and the number of deaths averted by cause of death and intervention. Outcomes of intervention scale up can be obtained through evaluating the impact of scaling up a given intervention in isolation or evaluating scenarios in which multiple interventions are scaled up simultaneously. For simulations where multiple interventions are scaled up simultaneously, LiST first estimates mortality reductions for each individual intervention in isolation. Complete mortality reduction for a suite of interventions is then estimated by sequencing the impact calculations, e.g., the first intervention affects the current level of mortality, while subsequent interventions affect the mortality that remains after the effects of previous interventions have been removed.

Results

Using baseline data inputs, estimates from LiST indicate 47,263 lives could be saved across Ethiopia, Bangladesh, and Mozambique between 2016 and 2030 (see Figure 2). The lives that could have been saved between 2016 and 2022 represent missed opportunities to improve child health in these countries. Upper and lower bound estimates based on either a five percent increase or decrease in intervention scale-up set the number of lives that could be saved during this period at 55,001 and 32,390 respectively. The largest number of lives estimated to be saved in the baseline simulation were from Ethiopia (27,161 lives), followed by Mozambique and then Bangladesh.

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Figures

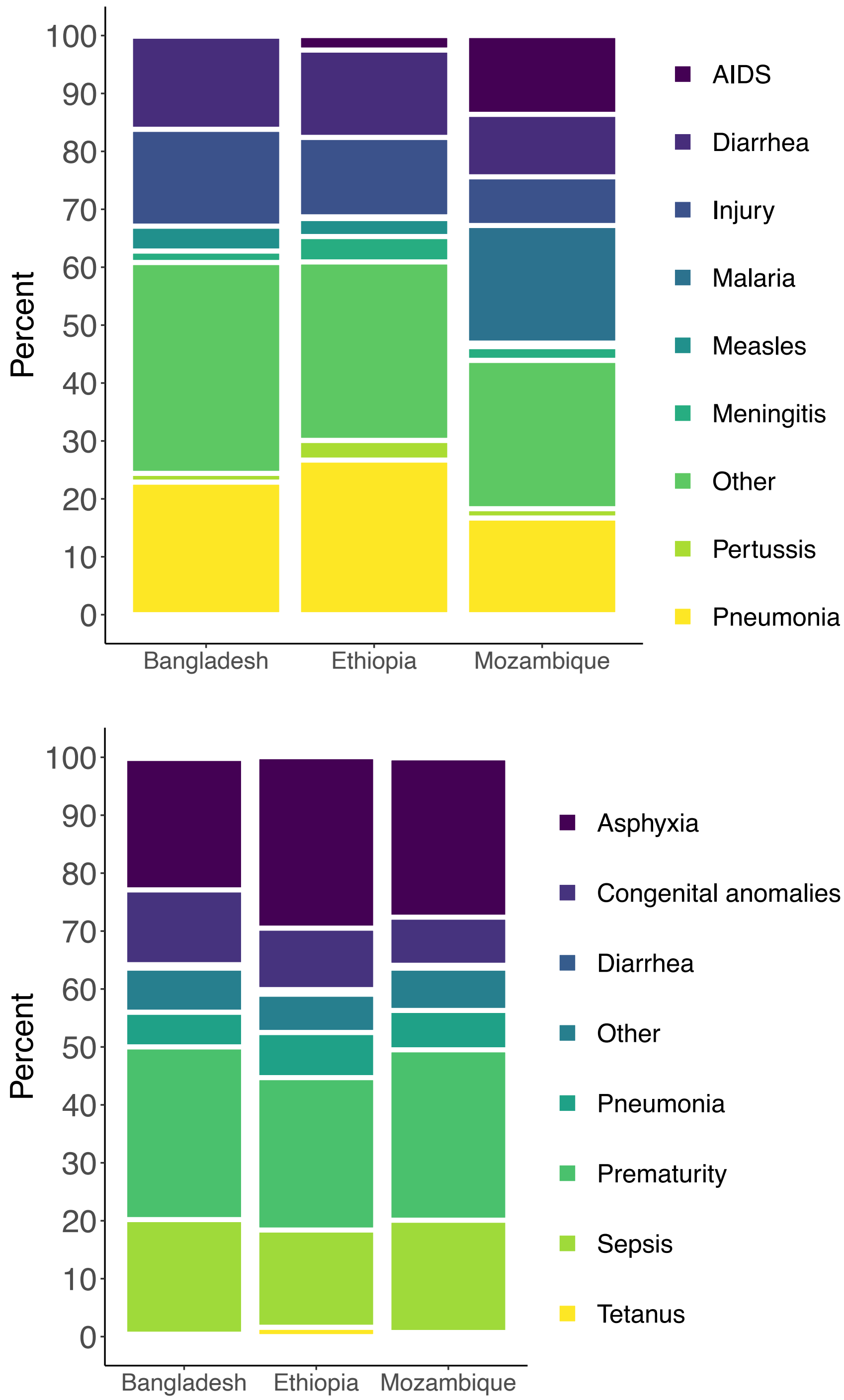

Figure 1. Distribution of Major Causes of Death in Children Under-5 and Neonates in Bangladesh Ethiopia and Mozambique. Data source: World Health Organization.(22) These estimates are used within LiST to inform simulation estimates of lives saved by the scaling up of child and maternal health interventions.

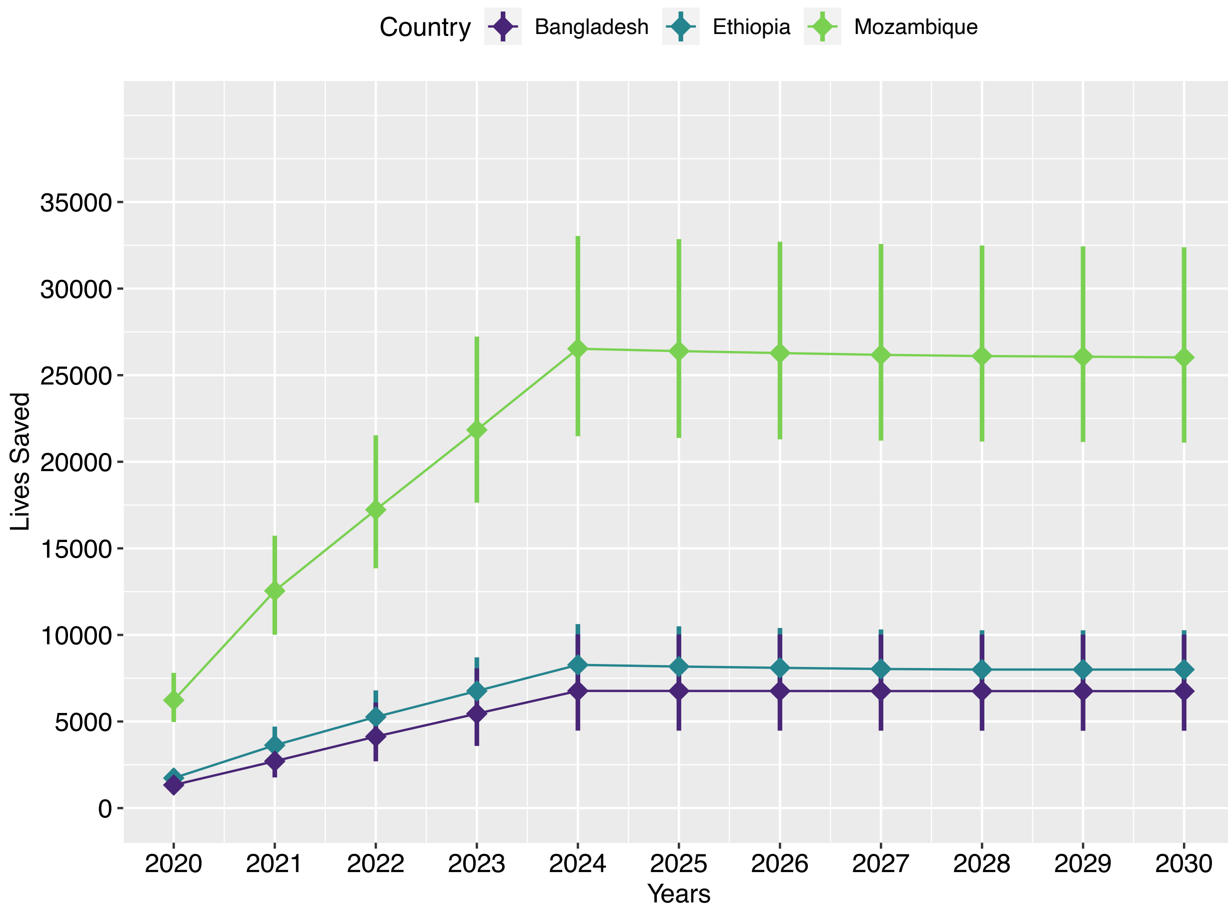

Figure 2. Estimates of Lives Saved By Country over Time. Estimates for 2020 through 2024 represent "Missed Opportunities" with regards to the potential lives saved had these systems been in place to inform intervention policy.

Tables

Table 1. Pathways to Impact for Nine Interventions (Original)

Intervention	How increase was generated	Coverage increases		
		Ethiopia	Bangladesh	Mozambique
Pneumococcal vaccine	Expected coverage in 2030 based on current trends assumed achievable by 2024 (five years after implementation) with E-SRS	36%	-	-
Oral antibiotics for pneumonia	Expected coverage in 2030 based on current trends assumed achievable by 2024 (five years after implementation) with E-SRS	27%	43%	28%
Rotavirus vaccine	Expected coverage in 2030 based on current trends assumed achievable by 2024 (five years after implementation) with E-SRS	29%	85%	9%
Oral rehydration salts (ORS)	Expected coverage in 2030 based on current trends assumed achievable by 2024 (five years after implementation) with E-SRS	36%	9%	19%
Antiretroviral therapy (ART)	Assumption that E-SRS could drive coverage five percentage points above estimated coverage in 2024 by 2024. Estimated coverage projections based on exponential decay examining past ART coverage trends and expected coverage of 85% in 2030 per reduction to UNAIDS 90-90-90 goal	23%	-	36%
Insecticide-treated nets/indoor residual spraying (ITN/IRS)	Acceleration of difference between projected coverage estimates for ITN for 2015 and 2030; consultation of Mozambique's Malaria Strategic Plan	-	-	39%
Labor and delivery management (L&D)	Acceleration of difference between projected coverage estimates for SBA for 2020 and 2030	15%	16%	9%
Full supportive care for prematurity	Acceleration of difference between projected coverage estimates for institutional delivery for 2020 and 2030	13%	17%	8%
Full supportive care for neonatal sepsis/pneumonia	Acceleration of difference between projected coverage estimates for institutional delivery for 2020 and 2030	13%	17%	8%