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Comparison of Lives Saved Tool model child mortalit estimates against measured data from vector control studies in sub-Saharan Africa

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4.7 6.2 (22% 25%).

Conclusions:

Background

Malaria was estimated to have directly caused over 715,000 child deaths in 2008 in sub-Saharan Africa [1]. Its indirect influence on mortality is likely even higher [2,3]. Fortunately, vector control interventions, such as insecticide treated mosquito nets (ITNs) and indoor residual spraying (IRS), have been shown to be highly effective in preventing malaria morbidity and mortality among children in malaria endemic settings [4,5]. These interventions have been scaled-up across sub-Saharan Africa as part of international efforts to control malaria and have the potential to significantly impact child mortality.

Unfortunately, vital registration data to measure changes in child mortality are not available across most sub-Saharan African countries. While birth histories within national surveys are useful for obtaining trends in all-cause child mortality at the national level, they do not typically measure cause of death using a linked postmortem verbal autopsy. Most demographic surveillance system sites lack sufficient external validity to estimate child mortality rates or causes at the national level. The Lives

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Saved Tool (LiST), a part of the Spectrum policy modeling package, was developed to provide national or regional estimates of cause-specific mortality based on the extent of intervention coverage scale-up. Several interventions specific to malaria can be modeled with LiST, including vector control (ITNs and IRS), intermittent preventive treatment to prevent malaria in pregnancy (IPTp), and appropriate malaria case management. LiST can be used to estimate historic changes in child mortality in countries where vital registration data are not available or to estimate the potential impact of future programs that affect child mortality.

While mortality reductions estimated by LiST have performed well when compared against measured data following the scale-up of packages of child survival interventions in various settings [6-8], the model has not been compared specifically to studies that measured changes in child survival following the scale-up of vector control interventions for preventing *Plasmodium falciparum* malaria. Here we compare the percent reduction in all-cause child mortality estimated by LiST against

Table 1 Characteristics of Studies included in validation analysis

Country	Study Area	Years	Study Design	Intervention	Relative Risk cited by the studies (95% CI)
9		1991-92			0.95[a] (0.71 – 1.28) 0.55 (0.30 – 1.01)
10		1994-96			0.85 (0.70 – 1.04)
11		1997-99			0.84 (0.70 – 1.00)
12		2004-06			0.58 (0.35 – 0.98)

a: Measured all-cause mortalit in children aged 1-2 ears comparing intervention to controls.
b: Measured all-cause mortalit in children aged 3-4 ears comparing intervention to controls.
c: Measured all-cause mortalit in children aged 6-59 months comparing intervention to controls.
d: Measured all-cause mortalit in children aged 0-5 ears comparing 1999 to 1997.
e: Measured all-cause mortalit in children aged 1-59 months comparing exposed to unexposed.
CI: Confidence interval.

ITN possession. The estimates from these studies were therefore not based on whether children under the age of 5 slept under an ITN the previous night.

Data used for comparison between LiST and study estimates

We began by using the standard demographic projection available for each country in LiST included in the analysis. We then used measured data for three key parameters in LiST for each comparison of modeled and measured estimates: household vector control coverage, proportion of post-neonatal mortality due to malaria, and baseline child mortality rate. The coverage of all other child survival interventions in LiST were held constant to ensure that only the effect of vector control on rates of all-cause child mortality was being modeled. The inputs used in LiST for each study comparison, as well as their sources, are detailed below (Table 2).

Three of the 4 studies measured all-cause child mortality as a rate of death (deaths per 1,000 person years), while the LiST model uses survival probabilities (probability of dying between birth and a child's 5^{th} birthday [$_5q_0$ in years], or between 1 month and a child's 5^{th} birthday [$_{59}q_1$ in months]). The fourth study measured all-cause child mortality as the probability of dying. Mortality rates per 1,000 person-years reported by the studies were therefore converted to survival probabilities using a life table analysis. Comparisons between LiST and the measured study estimates were done with unadjusted percent reductions in all-cause child mortality. Confidence intervals about mortality reduction estimates in the studies were calculated proportionally to the confidence intervals about the reported relative risk in each study.

The Gambia: The study was conducted in 1991-1992 and included 19,561 children in 104 villages matched on size and then randomly assigned to intervention or control [9]. The entomological inoculation rate (EIR), or number of infective bites per person per year, ranges from 1-10 in this area [9]. Villages were analyzed in pairs to account for correlated data. As the original study published the mortality rate among children 6-59 months, the all-cause child mortality rates 1-59 months were obtained from a Cochrane review on insecticide treated materials that included data on children 1-5 months from this study [4]. The neonatal mortality rate input into LiST was calculated by the difference between the <5 survival probability in 1991 ($_5q_0$) published by the Interagency Group on Child Mortality Estimation (http://www.childmortality.org/cmeMain.html) and the $_{59}q_1$ in months reported by the study. In the study publication, it was assumed that 80% of nets utilized in intervention villages were ITNs, thus the published coverage estimates of household possession of any mosquito net were multiplied by 80%. The baseline year coverage was set at 0%, as ITNs were unavailable in the control villages. The proportion of post-neonatal deaths due to malaria used in LiST was set to 34.8%, being the mean of 2 different studies measuring 35.0% in the upper river division of Gambia from 1989-1993 among children aged 1 to 59 months [15] and 34.6% along the southern bank of the Gambian river near the coast from 1988-1990 [16]. This second study from 1988-1990 included neonatal mortalities in its estimate of the proportion of child deaths due to malaria, and so the original figure of 25.3% was inflated by 26.9%, assuming that 26.9% of total child mortality occurred in the neonatal period in this area [15] and that malaria was not a significant cause of neonatal mortality.

Burkina Faso: The study was conducted from 1994-1996 and included 16,540 children in 168 villages aggregated to 16 randomized clusters [10]. The EIR averaged 300-500 per person in the area [17]. As the original study published the mortality rate among children 6-59

months, the all-cause 1-59 month child mortality rates were obtained from a Cochrane review on insecticide treated materials that included data on children 1-5 months from this study [4]. The neonatal mortality rate from the Platuea-Central region was used from the rural strata of the 1998-1999 DHS [18]. A demographic surveillance system in the Nouna Health District, which lies to the west of the study province, from 1997-1999 estimated the proportion of child deaths due to malaria

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study of socially-marketed ITNs reported the smallest reduction in all-cause child mortality of 7.9% (95% CI: 0.0% - 14.8%).

After matching the baseline child mortality rate, proportion of post-neonatal mortality due to malaria and vector control intervention coverage in LiST to each study site to the extent possible, all four LiST-modeled estimates of the percent reduction in all-cause child mortality following vector control scale-up were within the 95% confidence intervals reported by the studies and quite close to the measured reductions (Figure 1). Similarly, the estimated reductions in mortality from the studies all fell within the uncertainty produced by the LiST model. The LiST-modeled estimates of the percent reductions were within ± 5 absolute percentage points of the measured reduction in The Gambia and Tanzania (relative difference between LiST estimates and measured data were 22% and 35%, respectively) (Table 3). The percent reductions in all-cause child mortality estimated by LiST were overestimated by 6.1 and 4.2 percentage points (33% and 35% relative to the measured estimates) in Burkina Faso and Tanzania respectively and underestimated by 4.7 and 6.2 percentage points (22% and 25% relative to the measured estimates) in the Gambia and Kenya respectively.

Discussion and conclusions

The percent reductions in all-cause mortality as a result of vector control (ITNs and IRS) scale-up estimated with the LiST model were all within the published 95% confidence intervals from measured study data; all four studies had modeled estimates of child mortality reductions that came within 6.5 absolute percentage points of the measured changes. Furthermore, all of the study estimates fell within the uncertainty bounds of the reduction in child mortality calculated with the LiST model. The LiST model did not systematically under- or overestimate the impact of ITNs on all-cause child mortality, underestimating the impact for 2 studies while overestimating the impact for the other 2 studies. These results are consistent with LiST validation studies of other child survival interventions, suggesting that the 55% protective effect used in the model is a reasonable estimate of the potential impact of vector control on child mortality due to malaria, when matched with the population-level vector control indicator at the household level.

A potential reason that the LiST model estimates of reductions in all-cause child mortality differed slightly from measured reduction from studies is that only vector control was scaled-up in the LiST model; all other child survival interventions (e.g. exclusive breastfeeding and access to oral rehydration therapy) were held constant in the model due to a lack of data on their population coverage in the study sites. This is likely an inaccurate reflection what actually happened in the study sites, as even small changes in access to child survival interventions could have affected changes in measured rates of all-cause child mortality, which would not have been captured in the LiST estimates.

The LiST model estimate (17.1% reduction in 1-59 month all-cause child mortality) came closest to the measured results from the Gambia study (21.8% measured reduction in 1-59 month child mortality), underestimating the reduction by 4.7% (relative difference between measured and modeled estimates = 22%). A potential reason for the underestimation of LiST is that the proportion of post-neonatal mortality used in this analysis reflected only 2 of the 5 study areas, but did not include the study area with the highest measurements of malaria incidence. This area also saw the greatest reduction in child mortality. As such, the envelope of child malaria deaths that could potentially be

possible reasons for this underestimation. First, the mea-

Mali from 2001 to 2005, matching mortality rates and intervention coverage measured through household surveys [8]. LiST-estimated all-cause child mortality rates fell inside the confidence interval of measured mortality