

## **Minutes MERG Mortality Trends Task Force meeting**

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### Present:

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### **Objective of the meeting (TW, chair)**

To make recommendations for (African) countries on the monitoring of the mortality impact of malaria control under the RBM programme (as outlined in the Abuja targets) and of the progress towards the Millennium Development Goal (MDG) targets.

### **UNICEF/WHO/WB method for estimating under-5 mortality trends (GJ)**

GJ presented a method developed by UNICEF together with Johns Hopkins University to estimate mortality trends for all countries, for infants and for under-fives. It involves, first, identifying and graphing all mortality data for each country, separately for U5MR and IMR; and second, fitting a line to both those datasets, which results in a reasonable time series of mortality estimates over the period 1960 to present. All available data sources for a given country are considered, including household-based surveys such as MICS and DHS, censuses, sample registration systems (SRS) and vital registration systems (VR). Different weights are applied to the different data according to the estimated data quality, e.g. certain censuses, SRS and VRs with low coverage get lower weight.

This method has been used by UNICEF since 1989 and was also used for the End-Decade Assessment for progress toward the World Summit for Children goals (see 'Trends in child mortality in the developing world: 1960 to 1996' by K. Hill, R. Pande, M. Mahy (JHU) and G. Jones (UNICEF); and [www.childinfo.org](http://www.childinfo.org) for methodology and updated individual country estimates).

Previously, WHO (for the global burden of disease project) and WB used slightly different mortality estimates than UNICEF; for example, WHO gave more weight to VR even if coverage was only 50%. Some differences arose because the different agencies report at slightly different timepoints, and the agencies applied slightly different lifetables to the same overall numbers of deaths. The WB has now started implementing the same approach as UNICEF, and there remain few differences in their estimates. WHO and WB recently agreed to use the same method for tracking progress toward the MDG goal for under-5 mortality reduction. Much progress has been made toward producing a common set of estimates between the three agencies and at present only slight differences remain.

Much of the data used is 'indirect' mortality estimates, which are available more widely (from many surveys including shorter, non-birth history surveys such as MICS) than 'direct' estimates (which need more time-consuming birth histories with accurate reporting on the timing of births and deaths). Disadvantages to indirect estimates are that, for infants and neonates they are sensitive to the assumed lifetable, and they tend to overestimate mortality for the most recent period (due to underreporting of recently born surviving children). The availability of both "direct" and "indirect" estimates is desirable for estimating levels and trends in under-five mortality.

A concern with survey-based mortality estimates is that orphans, on whom no biological mother is reporting, are underrepresented and this may deflate mortality estimates; an adjustment for this is being considered.

Comments:

- EB: WB has had some problems selling this method within the Bank and to countries' statistical offices, more outreach with education and explanation is needed.
- AR: There may be a need to emphasize the uncertainty in the estimates, e.g. a difference in 5q0 between 154 and 151 does not represent a significant decline but is often seen as such.
- For RBM monitoring, a focus on 6-59 months might be more specific and sensitive than 0-59 months, since neonatal mortality is not due to malaria. Birth-history surveys (like DHS) can provide estimates for such alternative age groupings. Six months would be a better lower cut-off than 12 months or 1 month, because of age heaping at '1 year' (and at '1 month'?). For non-birth history surveys (like MICS), estimates for the age group 6-59m are less straightforward: they require assumptions on the age pattern among under-ones on top of the applied lifetables. The age group chosen is thus a trade-off between complexity of the mortality estimation and complexity of the interpretation from the malaria perspective.

### **Bellagio paper no.2 on estimating malaria-attributed and avertible mortality (GJ)**

*(Lancet 2003, 362:65-71)*

Based on a causal distribution of under-5 deaths and a review of the efficacy and current coverage of key child health interventions, the proportion of deaths avertible by different interventions was estimated, for Africa and SE Asia. The causal distribution of deaths is described by a CHERG working group in *Int.J.Epid.* 2003 (in press). Malaria caused an estimated 9% of deaths (24% in Africa, and <1% in SE Asia); of this, 7% could be averted with full coverage of ITNs, or 5% might be averted with full coverage of prompt effective antimalarial treatment. Combinations of interventions were not evaluated; for simplicity malaria interventions are assumed to attain their full effect by averting exclusively malaria-attributed deaths.

Comments:

- AR: The model used to estimate the 'baseline' causal distribution of deaths had limitations. In particular, it was based on a subset of mortality studies, namely those that reported:
  - the proportions of deaths due to all main causes (malaria, ARI and diarrhoea) separately.
  - and a number of covariates (e.g. % of births attended by skilled birth attendant) that were used to subsequently apply the model for country-level predictions.
 These selection criteria may have biased the data included; for example for measles, studies that had found high measles mortality were underrepresented. In general, the model overestimated for large causes, and underestimated for smaller causes.
- CS: Additional methodological problems included the use of studies with extremely small sample sizes and skewed response variables which were modelled as multivariate normal variables, which led to the fact that at present only 1 WHO department would find the model acceptable for use in GBD. Moreover, when constructing GBD, WHO/EIP typically triangulates across multiple different models and methods, of which this study could be only one, if acceptable.

### **CHERG estimation of malaria-specific mortality in African under-5s (AR)**

An estimation of malaria mortality in under-5s in Africa for feeding into the 2002 Global Burden of Disease is nearing finalization, under WHO/CHERG and CDC, with input from RBM. The estimates is constructed from mortality rates for 4 strata:

- Rural endemic areas: based on DSS that performed VA, using either a simple average or a multivariate model that accounts for the increase in malaria mortality between the 1980s and the 1990s and geographical variation that correlates with sociodemographic characteristics that will allow subsequent nation-wide predictions that are country-specific.
- Southern Africa (only endemic areas considered): a simple average from demographic surveillance (DSS) systems that performed verbal autopsies (VA).
- Urban areas: adjusting the malaria mortality rates estimated for rural endemic areas as estimated above by the urban-to-rural ratio in all-cause under-5 mortality.
- Deaths occurring during epidemics: an across-Africa calculation based on the periodicity of epidemics and the typical incidence of clinical illness and case fatality rate.

The resulting rates are multiplied with populations at endemic and epidemic malaria risk (from MARA) and population sizes living in rural and urban areas (from UNPD) to give numbers of deaths. The latest estimates for year 2000 are 530,000-840,000 deaths or 12%-19% of all under-5 deaths. Several limitations in the source data and estimation methodology are recognized, but there is consensus that this represents the best possible synthesis.

Comments:

- RS: The current model for endemic Africa does not include parasite prevalence or any other indicator of transmission intensity. Adding parasite prevalence (after solving the problem of apparent falling mortality at highest parasite prevalence) would improve the model by adjusting for differences in endemicity between DSS sites, and it would allow for more country- (and time?) specific predictions.
- SR/EK: In the model for endemic Africa, in the weighting between studies the imprecision due to VA may need consideration (*Lancet Inf Dis 2003, 3:349*); this may have deflated mortality estimates.
- CS: The presented problems with trying all-cause mortality as a covariate hold true also for other diseases.
- EB: The lower % of under-5s in urban areas should be considered in the estimation.
- EK: Although these estimates are not intended to indicate time trends at the country level, the inclusion of covariate ‘% of births attended by skilled birth attendants’ and possibly parasite prevalence might allow some estimation of time trends.

### **WHO/EIP’s model for estimating malaria-specific mortality (CS)**

For the GBD causal distribution of deaths, EIP uses VR (if coverage >90%), SRS, DSS, epidemiological studies and expert opinion, provided by WHO control programmes, member states, CHERG, MERG, public health agencies like UNICEF & UNAIDS and contracted academics. The primary input to GBD is the proportion of deaths attributed to each cause, by age and sex. For each cause, if available, multiple sources are triangulated, which are then subjected to checks of validity (checking of predictions for specific countries against their SRS and VR data) and plausibility (face validity according to consulted experts, regional offices & countries, and estimates published in the literature).

Results are then applied to a total ‘envelope’ of all deaths in each age and sex group for each country. The envelopes usually derive from VR (if coverage >90%), SRS or DSS, which if necessary are disaggregated using pre-defined life tables. For the few countries with no all-cause

mortality data at all, EIP uses data from the 'nearest neighbor'. The envelope assures that the deaths attributed to the different causes according to cause-specific models do not exceed the total number of deaths. The correct adding-up is obtained by shrinking either the proportions of deaths due to all cause by an equal proportion (which is the current approach), or the deaths due to some causes for which estimates are more uncertain than for others disproportionately much. Because of the adjustment to the overall envelope, EIP estimates sometimes differ from countries' estimates. For countries without cause-specific data, the envelope is first distributed over 3 groups, using a model called CoDMod: (1) infectious, maternal, perinatal and nutritional causes; (2) chronic diseases, (3) injuries and other external causes; then the causal distribution within each group is approximated from local research studies.

GBD is not primarily concerned with measuring trends. Changes between numbers for one year to the next usually reflect population growth, newly available evidence or the use of changed methods.

Malaria-estimates of GBD 1990 up to year 2000 were based, for Africa, on the 'Snow model'. Overall, malaria accounted for 9-10% of all-age deaths. In Afro-D and Afro-E, respectively, 22.8% and 18.2% of under-5 deaths were attributed to malaria. For Latin America and the Caribbean, 0.003% of all deaths were estimated to be due to malaria, of which 50-77% in under-5s. The model was based on the incidence of acute fever combined with positive malaria smears, as recorded in clinics and some community-based studies. This fluctuated somewhat between 1998 and 2001, probably reflecting some uncertainty in recording. For Asia and the Middle East, 0.4% of all deaths were estimated to be due to malaria. Estimates relied on (the few complete) VR and SRS in India, Bangladesh and China and fluctuated considerably over the years, probably in part due to overestimation of malaria deaths in 1998 in India.

EIP recognized as problems in these malaria estimates:

- poor direct country data
- changes in epidemiology of malaria not accounted for
- fitting into the all-cause envelope was proportional for all causes, whereas malaria may be one of the more-ill defined causes and hence get either over- or underestimated.
- little validation (no reference data available for Africa!) & plausibility checks
- changes over years merely reflect changes in the all-cause envelope.

Next steps could potentially be:

- improve models (including, for under-5s in Africa, from CHERG)
- increase VR coverage, esp. in Africa ( )
- set up additional sentinel sites with VA to infer time trends
- nationally representative VA surveys
- improve routine HMIS / monitoring ( ).

Comments:

- Add malaria prevalence (by blood smears) to future national surveys? For DHS, this idea was previously discarded, because infection prevalence does in endemic areas with largely immune populations not equate disease, and surveys are commonly conducted in the dry season when infection prevalence is at its nadir. However, the clear & strong association between infection prevalence and under-5 malaria mortality in the DSS included in the CHERG analysis, and the impact of ITNs on parasite prevalence in trials provide a rationale for collecting nation-wide prevalence data. Estimating malaria-mortality at national level by applying the CHERG model multiplied with national-level malaria prevalence may be more

feasible than improving measurement of malaria mortality via the )s above. Given the seasonality in parasitemia, however, inclusion of prevalence in malaria may be more useful in malaria stand-alone surveys than in DHS or MICS. Malaria prevalence can explicitly *not* be used to apply case/fatality rates to.

- BN: Are SRS as in Bangladesh cost-effective (in comparison to African DSS)?
- VA was previously in some DHS, but has been discarded, because the number of deaths recent enough in a cross-sectional to avoid recall bias is very small and makes the VA unsatisfactory. VA is included in the World Health Survey (WHS) for all deaths in the two years preceding the survey, but in such a simplistic way as to allow the exclusion but not the exact identification of malaria deaths.
- BN/CS: WHS measures all-cause under-5 mortality as well as adult mortality (by the sibling method) and may – if repeated – contribute data for time trends. This year, WHS were conducted in 40 countries of which 18 in sub-Saharan Africa.
- SR: Why does WHO/GBD always report numbers of deaths rather than rates? The numbers increase almost by definition (reflecting population growth); rates are more stable. The information is available for both but numbers speak better for advocacy and for lay audience who often ‘think in millions’.
- TW/KM: The inevitable uncertainty in malaria mortality estimates from CHERG & EIP should be communicated on a half pager to UN/MDG (Michael Doyle).

#### **Precision of trends in all-cause under-5 mortality from birth history surveys (EK)**

An assessment of sampling errors on direct mortality estimates in the African DHS conducted between 1986 and 2002 revealed that the country-level time trends in mortality observed over subsequent surveys are often not statistically significant. The precision depends on the number of women interviewed, the number of births per woman, the mortality level and the design effect, which is the extent by which sampling in a selected subset of ‘clusters’ increases the error as compared to a random, one-stage sample.

At mortality levels seen in recent African surveys, DHS at current typical sample size of 7,000 women would be able to statistically detect mortality reductions of 15% or more (e.g. as in Malawi between 1992 and 2000). To conclude on more subtle mortality changes (e.g. the recent increases in Tanzania and Uganda), sample sizes of up to 20,000 would be required. Detection of trends at subnational level or in sub-age groups among the under-5s would also require larger sample size. Sample requirements for evaluating mortality trends are much larger than for indicators like ITN coverage or anemia prevalence.

This analysis focused on mortality estimates for the 0-4 year preceding each survey. A somewhat more powerful analysis could be done if multiple mortality estimates for earlier periods from the same survey were included, which would by definition be for the same clusters so that the design effect could then be ignored.

A disadvantage of using the estimates for the 5-9 years and 10-14 years preceding a survey is that these are sometimes inconsistent with estimates for the same period from next surveys, suggesting recording bias in the more historic estimates. On the other hand, assessing trends between estimates from only the most recent period across subsequent surveys assumes that other errors would be constant across all surveys or be unimportant. (The latter argument was key for UNICEF, as outlined by GJ above, for synthesizing all different types of biases in different surveys and different estimation procedures in one unifying approach.)

Comments:

- RS: Based on evidence from intervention trials, a 15% reduction in all-cause under-5 mortality is a realistic expectation for the impact of RBM in countries with increased efforts. To achieve the overall MDG goal of reducing all-cause under-5 mortality by half-to-two-thirds, a 15% contribution from improved malaria control is a minimum requirement. So this analysis confirms that DHS are adequate to detect meaningful impact.
- SR: Trend testing would be more robust if subsequent surveys sampled the same clusters, as was done in Morocco and in Kenya (because the design effect then falls away). Retaining of clusters across surveys is, however, not common practice in DHS, because it may compromise the national representativity of the 2<sup>nd</sup> survey, due to population growth and the risk that countries focus programmatic efforts in clusters that they know will be covered in next surveys.
- RS: Would increasing survey frequency be an alternative to increasing sample size? But 0-4 year back estimates will start overlapping at between-survey intervals of less than 5 years...
- EB: Statistical precision is a concern, but it has limited value in the context of the international reports like the UNICEF one described above, because lay people and politicians only cite exact numbers, not confidence intervals.
- GJ: For the UNICEF estimations from the different sources, precision estimates could theoretically be produced also for indirect mortality component as from MICS data. But this is complex and likely not worth the effort, since these errors would not even represent the total uncertainty which includes non-sampling errors on top.

#### **The role of country programmes in monitoring malaria mortality (BN)**

Recommendations from this task force to country programmes on whether and how to monitor their mortality impact are urgently needed. Currently there exists confusion due to the use of the MDG-indicator malaria-specific mortality. The note by RS (attached as appendix here) provided an excellent description of the problems inherent to monitoring malaria mortality, and a rationale for proposing an action plan that the MERG can put against resources.

#### **Proposed plan for country-level monitoring**

Overall question:

By 20??, has RBM achieved its goals?

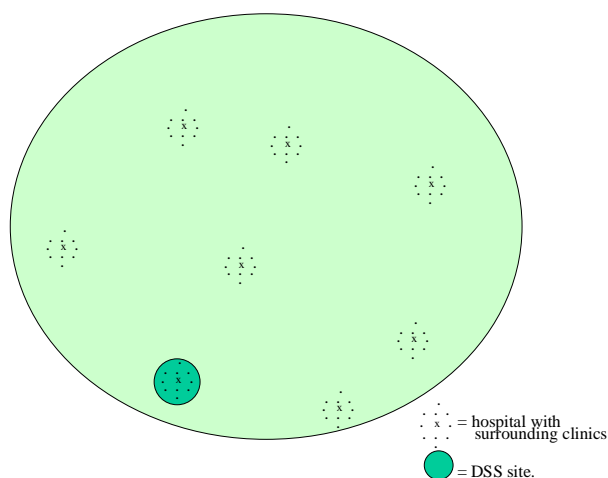
- By  $T_x$ , how many countries have achieved 60% for the three key RBM interventions?
- By  $T_{x+1}$ , what was the mortality impact in the countries with 60% coverage (for the three interventions, or at least for ITNs)?

The task force proposes different intensities of monitoring for (African) countries with advanced and less advanced malaria control programmes (Table and Figure):

| <i>Country (of Africa)</i>   | <i>Household surveys</i>   | <i>DSS/SRS</i>   | <i>Sentinel health facilities ('HMIS')</i>  | <i>Remarks</i>   |
|--|--|--|---|--|
| 3-5 countries with highest international funding for RBM interventions | Every 2-3y:<br>- Coverage<br>- All-cause under-5 mortality<br>- Malaria-specific mortality?<br>- Anemia? | - Coverage<br>- All-cause under-5 mortality<br>- Malaria-specific mortality? | Outpatient visits, admissions and deaths due to malaria and anemia, with and without parasitological confirmation, as a proportion of all causes and providing CFR. | To be selected by RBM partnership secretariat (and GFATM?) |
| 9-11 remaining   | Every 2-3y:<br>- Coverage  | ''<br>(if existing)  | ?   |  |

|  |   |  |  |
|--|---|--|--|
| countries of RBM's 14 priority countries | Once coverage $\geq 60\%$ :<br>- All-cause under-5 mortality<br>- Anemia?   |  |  |
| Next tier of countries                   | Every 5y:<br>- Coverage (Once coverage $\geq 60\%$ :<br>- All-cause under-5 mortality<br>- Anemia?)                     | '' (if existing)   | ?  |
| Remarks                                  | Sampled clusters to include the sentinel health facilities. Include questions on treatment seeking for fatal illnesses? | To be used if existing (typically 1 or 2 sites in targeted countries), but no new sites to be funded by RBM. | E.g. 10 per country, each consisting of a hospital and surrounding clinics, with a defined catchment area. To include the DSS/SRS area(s). |

CFR=case fatality rate. DSS= demographic surveillance site. SRS=sample registration system, GFATM=Global Fund Against Aids, TB, Malaria.



Notes:

- Although HIS currently fulfills no role in RBM monitoring in Africa and improvement in data quality cannot realistically be expected without additional regional or global support apart from RBM, inclusion of a facility-based component in the monitoring plan is desired to emphasize the importance of a working HMIS especially for local planning.
- If a main distribution channel for ITNs is going to be ANC & EPI clinics, coverage with ITNs might be indicative of coverage with IPT for pregnant women.
- Q. What to conclude if despite adequate intervention coverage, all-cause mortality is rising, e.g. due to decreasing EPI coverage and HIV/AIDS?

- Anemia: Under the Anemia Task Force, work is underway to assess the utility of haemoglobin as measured in national surveys among under-fives (or a subgroup) as an additional impact indicator to complement all-cause mortality.

### **Recommendations to countries**

- The primary impact indicator to be monitored by all countries is all-cause under-5 mortality, as measured by household surveys. Malaria-specific mortality is not to be monitored routinely, as this can in malaria-endemic Africa not well be measured. Symptoms and signs (such as anemia) are not specific and sensitive, making autopsy and verbal autopsy inaccurate; and many deaths, especially in young children, may be malaria-related rather than attributable to malaria exclusively without concurrent infections. Moreover, a majority of deaths do not occur in hospitals and are not routinely recorded in HMIS, and these are unlikely to be picked up in the – usually incomplete - vital registration. (Addendum CS: This view was not shared by EIP who believe that child mortality alone is a poor indicator of the success of very specific interventions, which would not resolve the issue of whether coverage of those interventions was actually effective).
- These limitations hold true now and in the future and irrespective of measuring a rate, number or a proportion. They imply that verbal autopsy, HIS-data on malaria mortality and vital registration will tend to underestimate the impact of malaria control, because they pick up only a subset of true malaria deaths (those with fever & seizures).
- Greater emphasis must be placed on process (and input and output) indicators, before embarking on impact measurement. Process monitoring should include household surveys of intervention coverage, and input measures such as whether there is an UNICEF distribution programme or a Worldbank loan. Only countries where coverage with the three key interventions, or at least with ITNs, has reached the 60% target should embark on impact measurement.
- Given current coverage levels and rates of increase in coverage, the GFATM request to demonstrate mortality impact within e.g. 1 year of increasing intervention coverage is not realistic. Mortality measured from cross-sectional surveys always reflects the level of several years back, so that mortality impact can earliest be detected starting several years after coverage has increased.
- (Impact on) the malaria-specific mortality may be estimated from the measured trend in all-cause under-5 mortality rate in combination with the measured coverage of the three key interventions.

Appendix. **Roll Back Malaria Monitoring and Evaluation Reference Group  
Monitoring Mortality – Rick Steketee, July 10 2003.**

**Issue:** Methods and feasibility for monitoring all-cause or malaria-specific child mortality at Global, Regional, Sub-regional, and Country level

*All-cause mortality and malaria-specific mortality*

All-cause mortality can be measured via DHS & MICS and other similar surveys with precision determined by the sample size. Estimates may underestimate neonatal mortality, but are otherwise likely to be valid

Malaria-specific mortality can be assessed using verbal autopsy (VA) with or without additional diagnostic criteria and adjustment. However, given the nature of VA methodology, this method for malaria will always be insensitive (e.g., missing anemia associated deaths) and nonspecific (e.g., potentially including sepsis, meningitis, respiratory illnesses, HIV and other causes of death as malaria). Quality control and adjustment techniques may or may not reduce this inherent imprecision. And, similar to the estimates for all-cause mortality, precision will also be determined by sample size.

RBM has the flexibility to establish recommendations for measurements and, despite stating that the goal is reduction of malaria burden (e.g., malaria mortality), RBM may choose all-cause mortality as the principle measurement. In contrast to this, the Millenium Development Goals have stated that they seek a reduction in malaria-specific mortality.

*Methods for assessing mortality*

Child mortality may be assessed via nationally representative household surveys (e.g., DHS, MICS), by demographic surveillance systems (DSS), and by using or enhancing national-level or multiple (sentinel) district health information systems (HIS) that report health facility information including deaths and disease-specific cause of death. Each of these has developed in ways that address different aspects of all-cause or malaria-specific mortality.

DHS, MICS, and similar nationally representative surveys are based on their national representativeness, but do not collect disease-specific causes of death. It is currently deemed not feasible to expand these surveys to assess disease-specific causes of mortality.

DSS methods are focal in nature, covering geographically defined populations of approximately 50,000 – 150,000 and are not nationally representative. The monitoring allows for detailed and repeated assessments of births and in-migration and deaths and out-migration – thus allowing for sufficient time to conduct VA to evaluate disease-specific causes of mortality. Typically, a variety of disease interventions are evaluated in these settings, making them even more non-representative of national events.

HIS systems typically report admissions and cause of deaths at in-patient health facilities. In recent years, there has been limited and often diminishing support for HIS in African countries and reporting may be inconsistent and may use varying definitions and techniques in different districts and facilities. However, with expanded support and training, HIS systems have been used in the past for national or sentinel site data on frequency and causes of in-patient admissions and deaths – and this could be done again. The integrated disease surveillance (IDS) methods do not routinely include the in-patient admission and cause of death data, and no other multi-country effort is supporting this at present.

Options for monitoring all-cause or malaria-specific child mortality at Global, Regional, Sub-regional, and Country level

With the above preamble, there are limited options for RBM mortality measurement and these include:

|                            | Global   | Regional         | Sub-regional  | Country   |
|----------------------------|--|------------------|---|---|
| All-cause mortality        | DHS/MICS -<br>? increase frequency and increase sample size to detect changes in all-cause mortality   | Same as “Global” | Same as “Global” unless support is available to standardize methods across all countries in the sub-Region per “Country” column | DHS/MICS (see “global” column) HIS either nationally or as representative sample sites may be supported to supplement and compare to DHS/MICS DSS may or may not be able to do this depending on representativeness |
| Malaria-specific mortality | No Options - methods are typically not nationally representative, not identical across countries and are not done in sufficient numbers of countries | Same as “Global” | Same as “Global” unless support is available to standardize methods across all countries in the sub-Region per “Country” column | HIS either nationally or as representative sample sites may be supported to conduct VA and this data could supplement and compare to DHS/MICS DSS may or may not be able to do this depending on representativeness |

The feasibility of these options is important to consider. There currently exists support for DHS and MICS surveys to be done in many countries in the coming years, however to increase the frequency and sample size will require substantial additional resources. Given the poor state of many country HIS and the lack of regional or global support for this, there is concern that RBM cannot mount sufficient support to reconstitute HIS infrastructure in a large number of countries to allow for good data and cross-country comparisons within the next decade. If another global effort to reconstitute HIS were developed rapidly, RBM could/should actively engage with this effort to address country-level and sub-regional level evaluation of malaria-specific mortality – with full understanding and caution due to the limitations of VA methodologies (noted above).