Introduction

A meeting of the Malaria Burden Estimation (MBE) Evidence Review Group (ERG) was convened by the Global Malaria Programme (GMP) of the World Health Organization (WHO) to:

- discuss updates on relevant work since the previous meeting,
- achieve consensus on the methods that should be used by WHO and in the World Malaria Report (WMR) to estimate malaria cases and deaths, and
- develop research agendas to improve estimates and address bottlenecks that prevent reconciliation of different methodologies/results.

This report summarizes:

- presentations given by meeting participants,
- major discussion points arising,
- recommendations on how WHO should proceed with malaria morbidity and mortality estimation, and
- recommendations for future work.
Summary of presentations and associated discussion

Updates on activities relating to case estimates

Update on the MAP Cube Pete Gething

The Cube

During the second ERG meeting, Pete Gething presented in depth on the methods and results of the Malaria Atlas Project (MAP) cartographic risk-based approach to modeling *Plasmodium falciparum* parasite prevalence among those age 2-10 years ($PfPR_{2-10}$). Using gridded population values and the relationship between incidence and parasite prevalence based on active case detection (ACD)-$PfPR_{2-10}$ pairs, MAP researchers generate estimates of cases across the globe by pixel (see the Report on the Second Meeting for additional details). Pete Gething announced during the second meeting that MAP was planning to extend its cross-sectional parasite prevalence mapping to generate a time series of gridded $PfPR$ estimates (known as the “Cube”).

Updates

Since then, MAP researchers have replaced their Markov chain Monte Carlo (MCMC) modeling structure with integrated nested Laplace approximations (INLAs), which speeds up the model runs by two orders of magnitude. The team is compiling additional $PfPR$ survey points for Africa (now up to 22 thousand, and will also include RTS,S data when available), generating the time-series covariates (such as the Enhanced Vegetation Index, Insecticide Treated Net – ITN – coverage, and use of different treatment types) needed to predict gridded parasite prevalence over time, and refining the prevalence-incidence model (including age stratification and exploration of ensemble modeling approaches). MAP plans to make available $PfPR$ and case estimates for 2000 to 2012 (even by month) by the end of 2013. Extending the estimates to year 2013 would also be possible, but would be accompanied by a large amount of uncertainty.

Support needed to access additional datasets

The MAP team appeals to the ERG for support in gaining access to 23 national surveys that are currently inaccessible (Table 1) and which would vastly strengthen MAP parasite prevalence estimates. Ana Carolina Santelli offered to provide support in accessing prevalence data from São Tomé and Príncipe. Roll Back Malaria (RBM) and GMP directors co-authored a letter to partners to help MAP obtain additional data, but there are still important holes in the database. Since WHO will change its methodology in 2014 to use MAP’s case estimates for high-transmission countries in the WHO African Region, WHO’s use of the estimates may help persuade some partners to augment MAP’s database. Stronger $PfPR$ and case estimates are imperative in order to accurately inform resource allocation.

Table 1: 23 national surveys that are currently inaccessible to MAP (source: Pete Gething)
Update on validation of WHO model assumptions regarding \( P/PR \) and care-seeking behavior

*Kathryn Andrews*

**Background on request to validate parasitaemia assumptions**

WHO uses a Health Management Information System (HMIS) case estimation method, for countries outside of the WHO African Region and countries in Africa with reliable surveillance data. Since HMIS data generally include data from public sector health facilities only, information on malaria cases that present for care in the private sector or do not present for care at all are estimated (i) using information from household surveys on the proportion of fever cases that attend private health facilities or do not present at all, and (ii) the propensity of these fever cases to be malarious. The propensity of fever cases attending private facilities to be malarious is assumed to be the same as that attending public health facilities based on a limited number of studies of patients attending private health facilities. For fever cases that do not seek care it is considered that the propensity to be malarious can vary from a low of zero (for countries with good access to care in which all malarious patients attend a health facility) to a high equivalent to the test positivity rate of fever cases attending public facilities (for countries with poor access to care in which patients not attending a health facility care are as likely to be as malarious as those that do attend). Given these extremes, the propensity of fever cases not attending a health facility to be malarious will, on average, be half that of those that attend public health facilities. The ERG recommended that household survey data on parasite prevalence stratified by type of care-seeking behavior be used to explore the validity of these assumptions.

**Results of survey analysis**

Based on an analysis of 10 Demographic and Health Surveys (DHS) and Malaria Indicator Surveys (MIS) from 9 African countries (2009-2011) with the variables of interest, parasite prevalence (as measured by rapid diagnostic test - RDT) is almost exactly equal among febrile children seeking care at a public facility, private facility, or not seeking care at all. The equality of parasite rates among patients attending public and private health facilities is consistent with the WHO method. The equality of parasite rates among patients attending public health facilities and those who do not seek care at all is less consistent – representing one extreme of the uncertainty range constructed by WHO. These results do not necessarily imply that the assumptions in WHO’s method be changed. Instead, the analysis outcomes merit further investigation of the applicability of the results given that this analysis only uses 10 surveys from only African countries where levels of immunity may be higher than outside of Africa (and the HMIS method is used primarily outside of Africa). In order to limit the biasing effect on parasite prevalence of receiving treatment, RDT results should continue to be used (rather than microscopy) in this analysis, and additional surveys should be incorporated (particularly if available from outside of Africa).

Update on varying the effectiveness of ITNs in the WHO model

*Richard Cibulskis*

**Background on request to validate ITN effectiveness assumption**

The WHO risk-based case estimation model (used for nearly all countries in the WHO African Region) assumes a protective effectiveness of ITNs of 50% (based on the efficacy value from the Lengeler et al Cochrane Review). In an effort to examine the extent to which this choice of effectiveness influences WHO’s case estimates, the ERG recommended that the assumption of 50% effectiveness be varied.

**Results of varying ITN effectiveness**

The resulting analysis (Figure 1) indicated that point estimates derived using effectiveness values from 0-100% all lay within the uncertainty intervals of WHO’s current estimates which use an effectiveness value of 50% (the upper and lower limits of cases for the WHO African Region are
110,000 and 242,000, respectively). Moreover, at other effectiveness levels, the bounds of the uncertainty intervals around point estimates mostly overlapped the uncertainty intervals of the estimates at 50% effectiveness. Given that modifying the effectiveness of ITNs results in a relatively moderate change, and that WHO is not aiming to make large changes before a full review of methods in 2014, the ERG does not recommend altering the value of ITN effectiveness for the burden estimation method to be used in 2013.

**Figure 1**: Effect of varying effectiveness of ITNs on case estimates in the WHO African Region (source: Richard Cibulskis)

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**HIV surveillance Txema Calleja**

After the second meeting, the ERG felt that it would benefit from hearing about HIV surveillance systems and ways in which malaria testing could be incorporated into preexisting HIV structures. During this third meeting, Txema Calleja, from WHO’s HIV Strategic Information and Planning unit, presented on HIV surveillance, surveys, burden estimates, and ways in which an RDT could potentially be added to existing HIV data collection systems.

*Nationally representative surveys*

DHS has collected data on HIV positivity since 2001. The non-response rate/refusal to be tested rate is high among some subpopulations e.g. those who already know their HIV status. Since the prevalence of HIV may be different among those who refuse the test as opposed to those who agree to it, the resulting national-level HIV prevalence may be biased. The AIDS Indicator Survey (AIS) was launched in 2003, and since then, 40 DHS/AIS surveys have provided HIV prevalence estimates for 32 countries. An RDT could feasibly be added to DHS/AIS biomarker survey modules, and since AIS test blood of people of all ages (unlike MIS), this could yield parasite prevalence among adults as well.

*Surveillance*

HIV serosurveillance is conducted among pregnant women in both urban and rural areas in selected countries every 1-2 years. Since antenatal care (ANC)-based surveillance targets a specific population (pregnant women with the means and ability to attend ANC visits) means these data are not representative of the entire population. When compared to DHS/AIS data, ANC data yield higher
prevalence of HIV on average, partly because ANC attenders represent a sexually active population. Unlinked anonymous testing (UAT) is also performed using leftover blood from syphilis tests. Recently, however, concerns about the ethics of finding HIV+ individuals and being unable to treat them due to the nature of anonymized data are causing a shift from the UAT seroprevalence surveillance to prevention of mother-to-child transmission (PMTCT)-clinic based surveillance. With the increase in antiretroviral therapy (ART) coverage, survival among HIV+ women is increasing (including those who are pregnant), making HIV seroprevalence data increasingly difficult to interpret. Finally, HIV sentinel surveillance in Africa includes over 4,000 sites (as of 2010). While the sites were initially all based in urban areas (because of easier access to ANC clinics), there have been efforts to increase data collection in rural areas as well.

**Modeling**

WHO’s estimates of HIV incidence and mortality are generated using the Spectrum model, whose inputs are HIV surveillance data, survey data, population estimates, programme coverage, and epidemiological assumptions (including a value of “natural death rate” from HIV based on pre-ART outcomes). The tools and methods have been published and are widely available to countries, which allows country programme managers to generate their own estimates of HIV burden and therefore reduces disagreement between numbers calculated by WHO headquarters and country offices. The HIV team conducted trainings on HIV surveillance starting in 2003, and continues to support analysts in country through online and phone communication.

**Potential for combining HIV and malaria surveillance**

Combining malaria diagnostic testing with preexisting HIV testing systems is feasible, but further examination into the cost-effectiveness of this is needed. An RDT could be added to ANC clinic HIV testing, but the resulting estimates of parasite prevalence may be biased downward compared to an annual average because HIV seroprevalence surveillance through ANC clinics is primarily done during the dry season. PMTCT clinic data will be collected year-round, which would be more appropriate for malaria testing, but there could be a higher prevalence of HIV among those attending a PMTCT clinic, meaning that these individuals would be more susceptible to malaria, and the resulting malaria prevalence biased upwards.

Parasite prevalence data from HIV surveillance could be incorporated into current mapping initiatives as long as information on age range and type of diagnostic test was also available. The more important question is whether this type of endeavor is cost-effective. The low-hanging fruit in gaining new PfPR data is access to parasite prevalence surveys that are already in existence but not shared publicly. An investment in ensuring that surveys include recording of GPS coordinates is also potentially a more cost-effective step. It is also important to consider the potential stigma associated with HIV testing; linking a test for malaria (which, to date, has little if any stigma attached to it) with a test for HIV has the potential to result in a spill-over of stigma to malaria.

**Retrospective parasite prevalence**

In theory, countries should have retained stored samples of dried blood from both historic ANC surveillance and DHS, which could potentially be examined for parasites. If it is cost-effective, the availability of these stored samples could be explored in countries such as South Africa and Democratic Republic of the Congo (DRC) to see whether they can be used to examine malaria prevalence retrospectively.
Update on activities relating to mortality estimation

Update from CHERG Li Liu

The Child Health Epidemiology Reference Group (CHERG) is working on updating their cause-specific child mortality estimates, and hopes to have new estimates available in September. The inclusion of the MAP Cube covariate will remove the need for the post-hoc adjustment of malaria deaths for ITN coverage. The CHERG appeals to the ERG members to help supplement their list of included studies (particularly VA). Ana Carolina Santelli has agreed to help supplement the verbal autopsy (VA) data from Brazil (currently CHERG only has 6 VA studies from Brazil, 4 of which are in areas with no malaria).

Update on WHO Mortality and Burden of Diseases Colin Mathers

The WHO burden of disease estimates for 2011 were recently completed and the country consultation process will take place in July and August. UNICEF and WHO will publish all-cause child mortality estimates in September. WHO burden of disease will be using the malaria mortality estimates generated by CHERG/GMP.

Update on IHME malaria mortality estimation Caterina Guinovart

As part of the Global Burden of Disease (GBD) 2.0, IHME will be producing new estimates for all diseases over the course of the next few months. As soon as the Cube is available, it will be incorporated into the suite of covariates used in the malaria mortality covariate selection process in CODEm. IHME has agreed to rerun the malaria model without redistribution of deaths assigned to garbage codes to examine the impact on the estimated deaths. Caterina Guinovart will be working on malaria at IHME for the foreseeable future, and looks forward to continued discussions with WHO and responding to feedback on IHME data and methods.

Update on generation of malaria treatment time series Thom Eisele

The objective of the analysis, undertaken by Thom Eisele, Adam Bennett, and Josh Yukich, is to estimate the annual proportion of children with uncomplicated malaria (fever + parasite infection) receiving treatment with antimalarials (CQ, SP, ACT separately) for all countries in sub-Saharan Africa, from 2001-2011. The data to be used are MIS, DHS, and Multiple Indicator Cluster Surveys (MICS). The methodology that will be employed is still under construction, but will likely involve establishing a predictive model of the outcome of parasitic fever treated with antimalarials using covariates such as gross domestic product (GDP), artemisinin combination therapy (ACT) policy, and random effects on country and year. As of yet, there is no clear end date deadline for the generation of this malaria treatment time series. This time series could be used as a covariate in CHERG’s malaria mortality model.

Trends over time in age structure of deaths Richard Cibulskis

As background on how the age pattern of malaria deaths may change over time, Richard Cibulskis examined the change in number and percent of all-cause deaths by age group over time. In all WHO regions, the fraction of deaths in those under age 5 years has declined from 1990 to 2011, and the corresponding fraction of deaths in those age 5 and over has increased by about 5% every 10 years in high burden malaria countries. If all other things remained equal then this trend, would suggest that the percent of malaria deaths in older children and adults may increase over time simply because the distribution of mortality is shifting to older ages. However, the changes in age structure of overall mortality may also be due in part to decreases in malaria deaths at young ages.
Update on deaths from malaria among those age 5 years and over, by endemicity level

Kathryn Andrews

The traditional understanding of the relationship between PfPR and deaths by age is that as parasite rate increases, the percent of deaths that are among young children increases and the percent of deaths among adults decreases. Given that the IHME death estimates show an unexpected age pattern (with a large number of deaths among individuals aged 5 years and above), ERG members requested during the second meeting that the proportion of malaria deaths that are among adults be plotted against malaria endemicity to investigate whether this shows the expected pattern.

The 2010 values of mean population-weighted country-level PfPR from MAP were plotted against the proportion of malaria deaths that are among those aged 5 years and older, for all countries (Figure 2). While the IHME estimates show a funnel pattern, WHO’s estimates are calculated using traditional assumptions about the relationship between PfPR and age distribution, so show an expected pattern. The age structure of deaths in IHME estimates continues to raise concerns among ERG members.

Figure 2: Proportion of malaria deaths that are among those aged 5 and over vs. population-weighted PfPR, for both IHME and WHO estimates (source: Kathryn Andrews, Pete Gething)
Adult deaths due to malaria using hospital data *Malcolm Molyneux*

**Background on hospital data for malaria**

Given that estimates of malaria mortality in Africa are primarily reliant upon VA data, it is worthwhile to consider alternative data sources. The advantages to using health facility data to monitor severe malaria include that hospitals are likely to: attract a large percent of cases of varying ages (enough to generate a reasonable sample size and for staff to become familiar with the condition), have microscopy available and quality lab staff (allowing for quantification of parasitaemia), have the capacity to make other diagnoses, and be amenable to chart reviews and additional research. The downsides of using facility data to quantify severe malaria are that there is still rarely proof of diagnosis, patients may have received prior treatment before arriving to the facility, and the population presenting in hospital may be very different from the population as a whole (considering issues of access, transport, etc.). The denominator to be used in calculating severe malaria rates is often unclear with hospital data, and health facility staff may have many demands on their time and be unable to prioritize quality data collection.

**Study in Queen Elizabeth Central Hospital**

Queen Elizabeth Central Hospital (QECH) serves as a district hospital for Blantyre, Malawi, which has a population of 1 million. From 2011-2013, adult malaria admissions were monitored at QECH using an electronic data system. RDTs were performed for suspected malaria, and microscopy was done for positive RDT cases. During 7 sentinel weeks during the year, RDTs and microscopy were done on all admissions, and a detailed file review was conducted of all severe malaria cases. During these sentinel weeks, of 70 adult RDT positive cases, 36 cases of uncomplicated malaria and 28 cases of severe malaria were observed. The main defining clinical feature of severe malaria was prostration (23 of 28 cases), while only 9 of 28 cases had parasitaemia >250,000/µL. These data indicate the difficulty of diagnosing severe malaria.

**Severe malaria in prospective studies**

In connection with IHME’s estimate of the percent of malaria deaths occurring among those age 70+ of almost 7%, Nick White combined data from prospective studies in 7 countries over 30 years, and found only 0.7% of deaths occurred among those age 70+ (Figure 3).

**Figure 3**: Proportion of severe malaria mortality occurring in various age groups (source: N J White et al, letter to *The Lancet* 380, August 11, 2012)
Hospital deaths in Kilifi
Richard Cibulskis presented on behalf of Kevin Marsh on data from Kilifi’s Health and Demographic Surveillance System (HDSS) in Kenya. It is part of the INDEPTH network and collects data on malaria deaths in hospital by age. While the data cannot be described in depth because they are not yet published, they show that, of 37 patients who died and who had a positive parasite test, 33 were between the ages of 1 and 10 years, and only 4 parasite positive deaths occurred over the age of 10. These results further support the traditional understanding of the age pattern of malaria mortality.

Estimating malaria mortality using VA data Peter Byass

Background
Historically, and at least for the near future, VA will continue to be the main source of malaria mortality data in Africa. VA for malaria remains challenging and inaccurate, and even gold standard data have flaws. VA for malaria is particularly difficult because there are no definitive history/symptoms and many ill-defined diseases have the same symptoms as malaria. VA will likely remain a poor tool to identify a malaria death on an individual level, but may yet have the potential to generate population-level estimates of the number of deaths that can be attributed to malaria.

InterVA
InterVA is a VA interpretation model that produces posterior distributions of the probability of causes given symptom patterns, and is compliant with WHO’s Verbal Autopsy Standards. It is downloadable from [www.interva.net](http://www.interva.net) and is being designed for an Android hand-held tool.

InterVA was used to generate mortality rate ratios of various causes of death based on HIV positivity vs. HIV negativity (Figure 4). If INDEPTH data have a sufficient number of records with RDT results, this same analysis should be repeated for malaria. Examining the causes of death among those who are RDT+ but do not die of malaria would help assessing the extent to which malaria influences mortality from other causes (indirect malaria mortality).

Figure 4: Ratio of cause-specific mortality among HIV+ vs. HIV- patients (source: Peter Byass)
IHME’s PHMRC gold standard study
The malaria results from the Population Health Metrics Research Consortium (PHMRC) gold standard VA study generate concern among some malaria VA experts. None of the 4 study sites have a high burden of malaria, and the 4 sites combined (India, Philippines, Tanzania, Mexico) yielded only 100 deaths in individuals over 5 years of age and 117 deaths under 5 years from malaria. Although the IHME malaria model does not use the PHMRC data to generate the main results, it does use the data in a sensitivity analysis to support the finding of a large number of adult malaria deaths. Conducting another gold-standard validation study in settings of varying transmission intensity would help strengthen the current findings, but may be prohibitively expensive.

Estimating malaria mortality form exposure-response relationships Tom Smith

Case-control approach
Given the challenges of estimating malaria mortality directly from VA data, alternative methods should be examined. The relative risk and population attributable fraction of deaths associated with parasitaemia could be assessed through a case-control study. Cases could be defined as admissions with severe febrile illness (who subsequently die), and controls could be either admissions with clearly non-malaria disease (i.e. accidents) or matched individuals in the community. The admissions would be given an RDT upon arrival, and the prevalence among the controls from the community could be taken from MAP estimates. The challenges with case-control studies are in finding well-matched controls, accruing enough data from a range of settings, and determining the indirect or delayed effects of parasitaemia.

Cohort approach
Malaria mortality could also be estimated by way of cohort studies, where exposure is measured in the community (i.e. a DSS site) at the individual level, and the members of the cohort are followed up to observe their mortality. A strength of this method is that it also accounts for indirect deaths as well as direct deaths from malaria. The Malaria Transmission Intensity and Mortality Burden across Africa (MTIMBA) study used geostatistical models of entomological inoculation rate (EIR) in space and time for 4 DSS sites to estimate excess risk of mortality as a function of EIR, by age group. The shortcomings of using EIR as the exposure measure (that it is imprecise, available from only a few sites, is difficult to relate to MAP prevalence, etc.) were a weakness of this study.

Current status of a prospective study
Tom Smith and Salim Abdulla are planning a workshop for the INDEPTH meeting in October, during which representatives from INDEPTH sites will bring all available individual-level and geolocated prevalence data and covariates (i.e. ITN and treatment coverage over time). The goal is to use these data to create virtual cohorts for prospective analysis of the relationship between rates of excess age-specific all-cause mortality and history of exposure as measured by parasite prevalence. The analyses could be conducted using both current exposure and history of exposure, and supplemented by sensitivity analyses to explore how the estimated relationship depends on uncertainties in the history of exposure. Currently, there is no funding for this project, so would rely mainly on the willingness of INDEPTH sites to share their data and the availability of a statistician to work quickly.
Ways forward for malaria case estimation *ERG members*

**Conclusions and recommendations for MAP**

1. Given that most household surveys measure parasite prevalence in the 6-59 months age group, the ERG requests that MAP generate *PfPR* estimates for this age range (in addition to the 2-10 age range, which is what is currently reported).

2. For explicit analyses assessing impact (i.e. examination of the relationship between coverage of interventions like ITNs and parasite prevalence), intervention coverage covariates cannot be used in generating the estimates of *PfPR*. At the same time, it is important to generate malaria parasite prevalence estimates that are of the highest quality and that incorporate the effects of recent changes in interventions even if there is not a recent *PfPR* survey. This requires that intervention coverage covariates be used in the model. Given the potential different uses of the modeled it was agreed that estimates should be generated for both situations.

3. MAP researchers may want to further examine the relationship between microscopy and RDT results to determine whether an additional term in the model is required to take into account any differences in prevalence associated with diagnostic test type.

4. MAP researchers may want to consider doing an analysis to generate a curve of diminishing rate of return with regard to addition of new data; this would help determine the cost-effectiveness of obtaining additional prevalence data, and provide an evidence-based case for increased funding if necessary.

**Conclusions and recommendations for WHO**

1. For the 2013 WMR, WHO should use the same methodology for case estimation as currently used. In 2014 and after, WHO should use MAP’s case estimates from the Cube for African countries without strong surveillance systems.

2. WHO will need to continue to present time series of cases and deaths in each WMR so that journalists and other consumers of the information will not create their own time series by extracting annual estimates from different WMRs (which will be different due to changes in methodology and data validation).

3. WHO should discuss with partners to determine the feasibility of collecting prevalence data through MIS on all age groups (not just 6-59 months) so that the age pattern of *PfPR* can be further examined. The sample of older children and adults available at home at the time of the survey may not be an accurate representation of the population on the whole, but the data would still be useful.

4. The assumptions about parasitaemia and different care-seeking behaviors would benefit from further validation. To do so, the analysis examining parasite prevalence stratified by type of care-seeking behavior should be supplemented with more recent surveys and surveys from outside of Africa, if available (such as from the WHO Eastern Mediterranean Region). If the analysis indicates highly variable results by region, the assumptions used may need to be country- or region-specific. Ashwani Kumar and Nick White agreed to follow up on the possibility of designing a study to determine the characteristics of populations in India that are missed by WHO’s surveillance method.

5. The ERG feels that it is highly desirable to increase the amount of malaria prevalence data available by linking with other ongoing activities. There was some concern that about the broader ramifications of adding an RDT to PMTCT HIV testing or to HIV testing done in national AIS surveys (i.e. that the stigma associated with HIV would begin to include malaria as well). Rather than linking explicitly with HIV, the ERG recommends that women receive an RDT when they present for their first ANC visit. Data from this subset of the population
could be adjusted for any lack of representativeness. The ERG also recommends that adding an RDT to measles immunization timing should be explored.

6. The ERG recommends that WHO report on parasite prevalence as one of their key indicators (in addition to cases and deaths). As with cases and deaths, the WMR will show country-reported parasite prevalence values and modeled parasite prevalence (from MAP). WHO will need to consider the complicating factors of reporting parasitaemia: since prevalence changes by season, presenting a static annual value may be misleading; in some areas outside of Africa, estimates of cases may be of higher quality than MAP prevalence estimates, so WHO will need to decide whether to convert case data into prevalence values in order to generate estimates of \$PfPR\$ for the entire globe. WHO will need to determine whether country consultations on \$PfPR\$ will be required, as with cases and deaths.

7. WHO should follow the HIV team’s lead in generating user-friendly and transparent methodologies for generating estimates of prevalence, cases, and deaths. This will increase country ownership over the estimates, which, in turn, should encourage more investment in data quality.

**Ways forward for malaria mortality estimation**  
*ERG members*

**Conclusions and recommendations for partners**

1. Thom Eisele, Azra Ghani, Tom Smith, and Kathryn Andrews have agreed to share and compare their coding of care-seeking behavior and treatment variables. This will ensure consistency and help Thom Eisele’s team generate their antimalarial treatment covariate, which will be used by CHERG and others in malaria mortality estimation.

2. Given the striking difference between the percent of malaria deaths among those age 70+ from the IHME model as opposed to Nick White’s analysis of prospective study data, ERG members recommend that WHO use the STPH model to calculate deaths by the same age groups as IHME and Nick White’s analysis and compare the results.

3. The ERG requests that Malcolm Molyneux reach out to 10 hospitals in endemic areas to determine whether they would be willing to share their data on the age distribution of severe malaria. The goal is to develop a list of hospitals in Africa that could serve as sentinel hospitals (like QEHC and Kilifi) for adult malaria mortality research. The results of analyses on hospital data should still be considered in the context of their being a biased sample of the general population. Community-level parasitaemia (such as from MAP or RTS,S sites) could be used to determine the level of incidental parasitaemia.

4. Over the next 9 months, the universe of available data to examine adult deaths from malaria should be assembled. This should include a literature search for hospital and other studies, and include the RTS,S trial data when made available. Tom Smith and WHO will spearhead this work.

5. The ERG recommends that Peter Byass send a sample of INDEPTH records (half with a classification of malaria and half without) to Malcolm Molyneux to determine whether, based on his field experience in hospital, he would code the deaths the same. This would serve as a validation of the InterVA methodology.

6. Ashwani Kumar and Nick White have agreed to produce a draft protocol for a study in India using hospital data on mortality and RDT results. They will circulate the draft to the ERG for comment.
Conclusions and recommendations for WHO

1. WHO should use the same methodology for the 2013 WMR malaria mortality estimates as presently used. Once further research is conducted, WHO may want to change their death estimation methodology, but there is no evidence that this should be done at the present time.

2. WHO should also use the same assumptions (of case fatality rate – CFR-, ITN effectiveness, etc.) in the 2013 WMR as presently used. While this approach is necessary for mortality estimates outside of Africa owing to limited data on malaria mortality WHO should not apply a fixed CFR to the estimated cases in Africa in order to generate mortality estimates. ERG members felt that changes over time in case management would not be reflected by a static CFR, and that identifying a valid CFR would be challenging.

3. WHO and the malaria community should consider eliminating the under-5/over-5 dichotomy; the message is confusing because “over-5” is often termed “adult”.

4. Given that the malaria mortality research agenda is just in its beginning stages, additional meetings of the MBE-ERG may be required in order to evaluate new methodologies. The MPAC may decide that the Surveillance Monitoring and Evaluation Technical Expert Group (SME TEG) should take over the functions of the current ERG, in which case many ERG members may transition to membership of the TEG instead.

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