Malaria Burden Estimation – Evidence Review Group (MBE-ERG)

Peter Smith - Chair MBE-ERG
(with thanks to Kathryn Andrews for drafting slides)

MPAC meeting
13th March, 2013

World Health Organization

GLOBAL MALARIA PROGRAMME
To review approaches to burden estimation and make recommendations to MPAC on:

1. Approaches WHO should use to:
   a) Estimate the number of malaria cases and deaths to prioritize countries for resource allocation
   b) Understand trends over time to assess global strategies
   c) Prioritize malaria in comparison with other health conditions

2. Approaches endemic countries should use to:
   a) Estimate the number of malaria cases and deaths nationally and sub-nationally
   b) Understand which populations are most affected
   c) Improve the quality of input data for malaria burden estimation
MBE-ERG: Membership

- Salim Abdulla (Tanzania)
- John Aponte (Spain)
- Zulfiqar Bhutta (Pakistan)
- Peter Byass (UK)
- Azra Ghani (UK)
- Brian Greenwood (UK)
- Patrick Kachur (CDC-US)
- Aswan Kumar (India)
- Seth Owusu-Agyei (Ghana)
- Ana Carolina Santelli (Brazil)
- Peter Smith (UK)
- Richard Steketee (PATH)
- Jane Thomason (HMN)
- Nicholas White (Thailand)

MPAC Members
MBE-ERG: Timetable

Meeting 1: (June 2012):
Review the issues and determine key questions

Meeting 2: (January 22-24, 2013, Geneva):
Individuals (Thom Eisele, Peter Gething, Li Liu, Christopher Murray and Tom Smith) representing major groups involved in malaria burden estimation presented their approaches to the ERG and answered questions on their methods

Meeting 3: (Second quarter 2013)
Review evidence gathered and formulate recommendations to MPAC that address questions posed (after follow-up ERG teleconference, this may no longer be necessary)
Morbidity estimation methods

Malaria Atlas Project (MAP)

- Cartographic approach uses geo-referenced PfPR surveys (~22,000 up to 2010) and environmental covariates, adjusts for age groups and years, but not seasonality (substantial increase in PfPR surveys in recent years).
- Prevalence is converted to incidence using population estimates and relationship between PfPR and case incidence from ~140 longitudinal studies with active case detection (ACD) – considerable variability in the relationship in different surveys.
- Results are considered most reliable in Africa and least reliable in India, China, and Myanmar (fewer prevalence data).
- Future work: research to generate infection prevalence and case incidence time series for 34 high-endemicity countries in Africa, using additional covariates - i.e. will produce estimates of cases by year.
Morbidity estimation methods

WHO

- Surveillance/HMIS approach: used for countries outside the WHO African Region and low transmission countries in Africa
  - Number of reported malaria cases adjusted for completeness of reporting, likelihood that cases are parasite-positive, and extent of health service use
  - Model assumptions should be tested using MIS data
- Risk approach: used for high-transmission countries within the WHO African Region
  - Uses MARA map for estimates of malaria risk (high, low or no), and adjusts post-hoc for ITN coverage using efficacy value from Cochrane review ($\text{ITN} \uparrow 1\% \Rightarrow \text{Inc.} \downarrow 0.5\%$)
  - Advantage = simplicity: Disadvantage = crude.
  - MARA should be updated with MAP, and ITN efficacy may be unrealistic
Ways forward for malaria morbidity estimation

Recommendations for WHO

1. For 2013: WHO should continue to estimate cases as currently, but should vary/test assumptions regarding value of ITN effectiveness and test positivity among febrile children seeking care vs. those not seeking care.

2. In 2014 and beyond:
   - Sub-Saharan Africa: WHO should derive case estimates based on time-series of PfPR assembled by MAP and a refined model of relationship between prevalence and incidence (including survey data, seasonality information, new covariates)
   - Outside Africa and in countries with robust surveillance data: estimates should be based on reported cases; as surveillance systems become stronger, more countries will be able to use HMIS method

3. Uncertainty around estimates should always be presented with mean values, and country consultations should remain integral to estimate generation in order to understand data quality and anomalies, and to validate results

4. Generation of a more user-friendly cartographic methodology should be explored
Ways forward for malaria morbidity estimation

Recommendations to improve the science

1. Explore methods of collecting additional prevalence data should be collected (through RDTs at antenatal visits (method used to monitor HIV prevalence), EPI visits, or in school deworming campaigns), which would improve MAP estimates.

2. More data on relationship between incidence and prevalence must be gathered
   - Concerns about possibility of bias in longitudinal surveys with ACD
   - ERG members have agreed to compile a list of data that could supplement the MAP database.
Mortality estimation methods

Institute for Health Metrics and Evaluation (IHME)

- Cause of Death Ensemble Model (CODEm - weighted average of different models) used to estimate mortality from nearly 300 causes of death, including malaria; model is data-driven, and chooses an ensemble of models based on out-of-sample predictive validity.

- Uses VAs and environmental data. Details of methods used is a little opaque at present and not all data in public domain.

- High estimates for adult deaths driven empirically by Verbal Autopsy (VA) data in older age groups and by redistribution of deaths from unspecified causes to malaria.

- Additional research is required to resolve disagreement between modeled adult mortality results and clinical experience – especially assessing validity of VA data.

- Likely that IHME estimates (for all causes of death, including malaria) will be updated annually.
Mortality estimation methods

**CHERG: age under 5y deaths**

- Multi-cause model of 8 child causes of death, including malaria
- Uses VA to partition all cause death rate between causes (only 20 VA data points in Africa).
- Exclusion criteria may have eliminated some high-quality VA studies from the analysis
- Post-hoc adjustment for effect of ITNs may improperly influence estimates

**WHO: age 5y+ deaths**

- CHERG’s under-5 deaths in Africa used to estimate deaths age 5+ via relationship between age-specific malaria death rate and intensity of malaria transmission (from 1 study!)
- Outside of Africa, CFR of 0.3% is applied to total number of estimated cases of *P. falciparum*
Ways forward for malaria mortality estimation

Recommendations for WHO

1. For 2013: WHO should continue to estimate malaria deaths as currently, but should also estimate *P. vivax* deaths separately.

2. In 2014 and beyond: the recommended approach has not yet been decided. There appear to be substantial weaknesses in all the current methods.

3. Uncertainty around estimates should always be presented with mean values, and country consultations should remain integral to estimate generation in order to understand data quality and anomalies, and to validate results.
Recommendations to improve the science

1. Existing data should be assembled to examine evidence base for IHME’s high adult death estimates (e.g. INDEPTCH)

2. Novel research should be conducted to examine age patterns in malaria deaths and relationship between PfPR and mortality (case-control studies comparing parasite prevalence in those dying of any cause and controls; prospective cohort studies of all-cause mortality in relation to malaria exposure)

3. To explore reasons for differing results, CHERG should rerun its model using less restrictive VA inclusion criteria, and IHME should rerun its model without redistribution of unassigned VA deaths

4. Consider possible need for an MPAC standing committee to evaluate new estimation methods for both morbidity and mortality, as methods evolve.