

Malaria Burden Estimation Methods Evidence Review Group

Meeting report



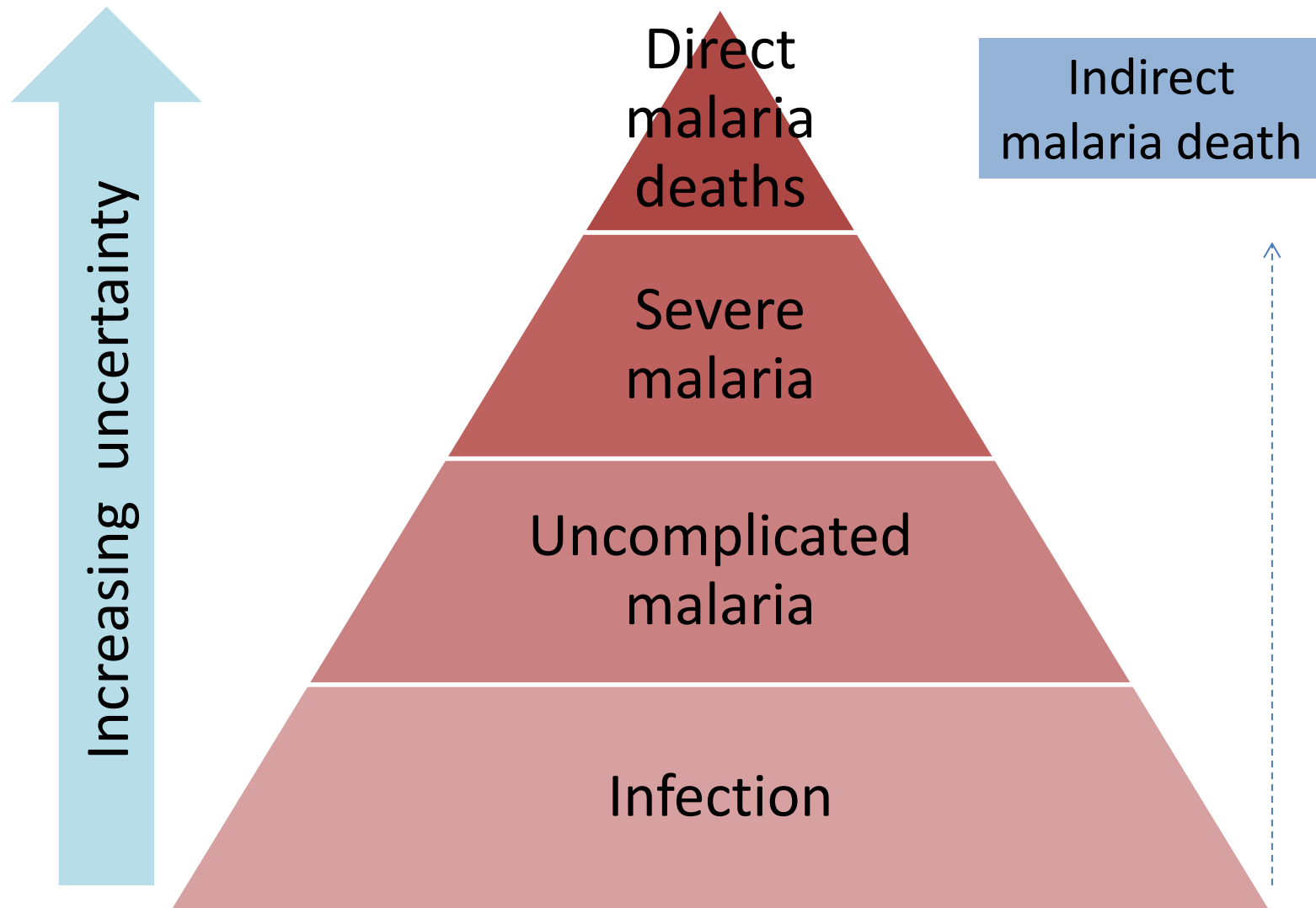
Abdisalan M Noor,
Team Leader, Surveillance , Monitoring and Evaluation
Burden ERG Meeting, 11-13 April 2018

Global **Malaria** Programme

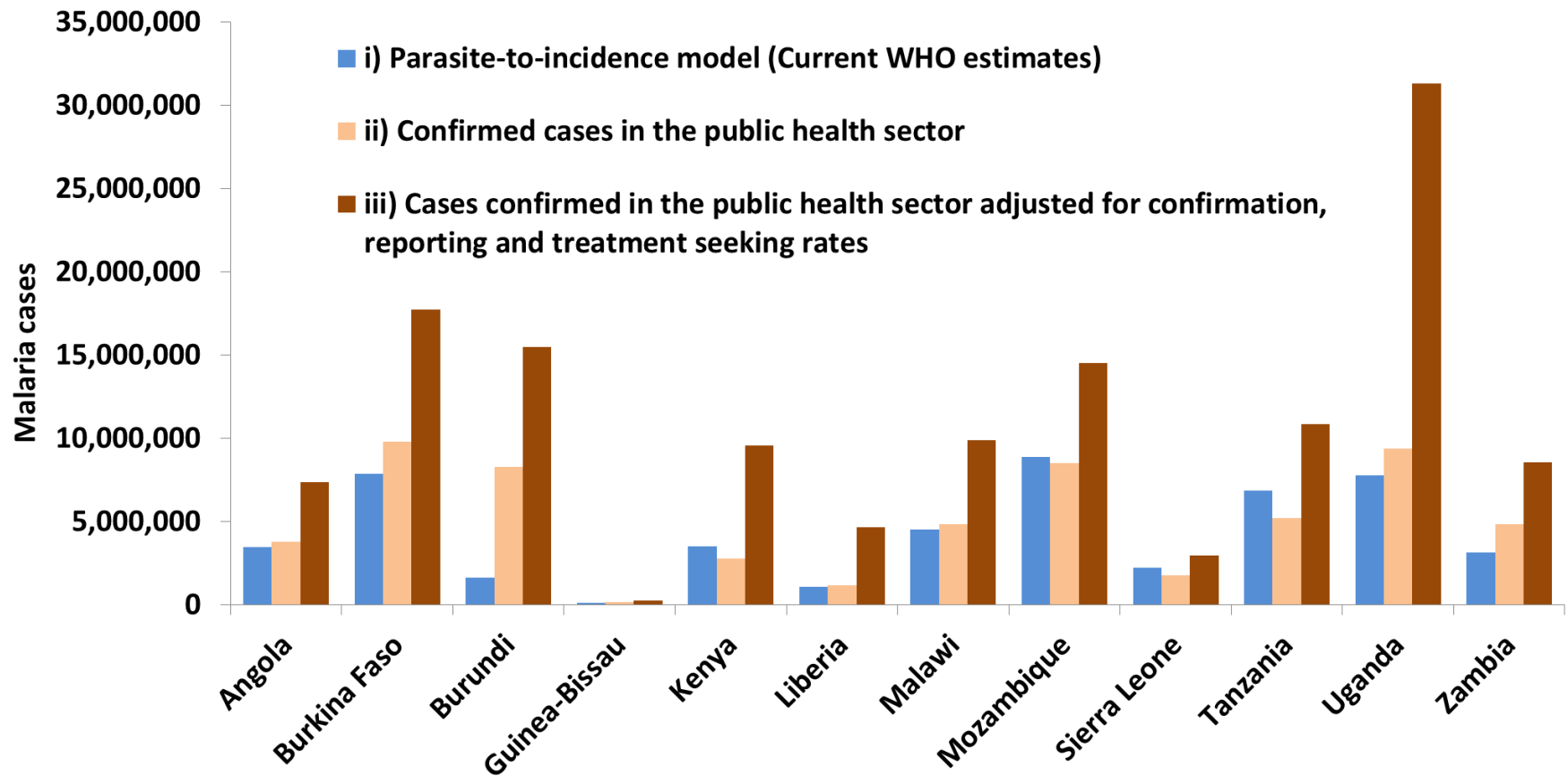


**World Health
Organization**

Malaria burden



Comparisons of parasite rate-to-incidence vs adjusted routine data model estimates - 2016

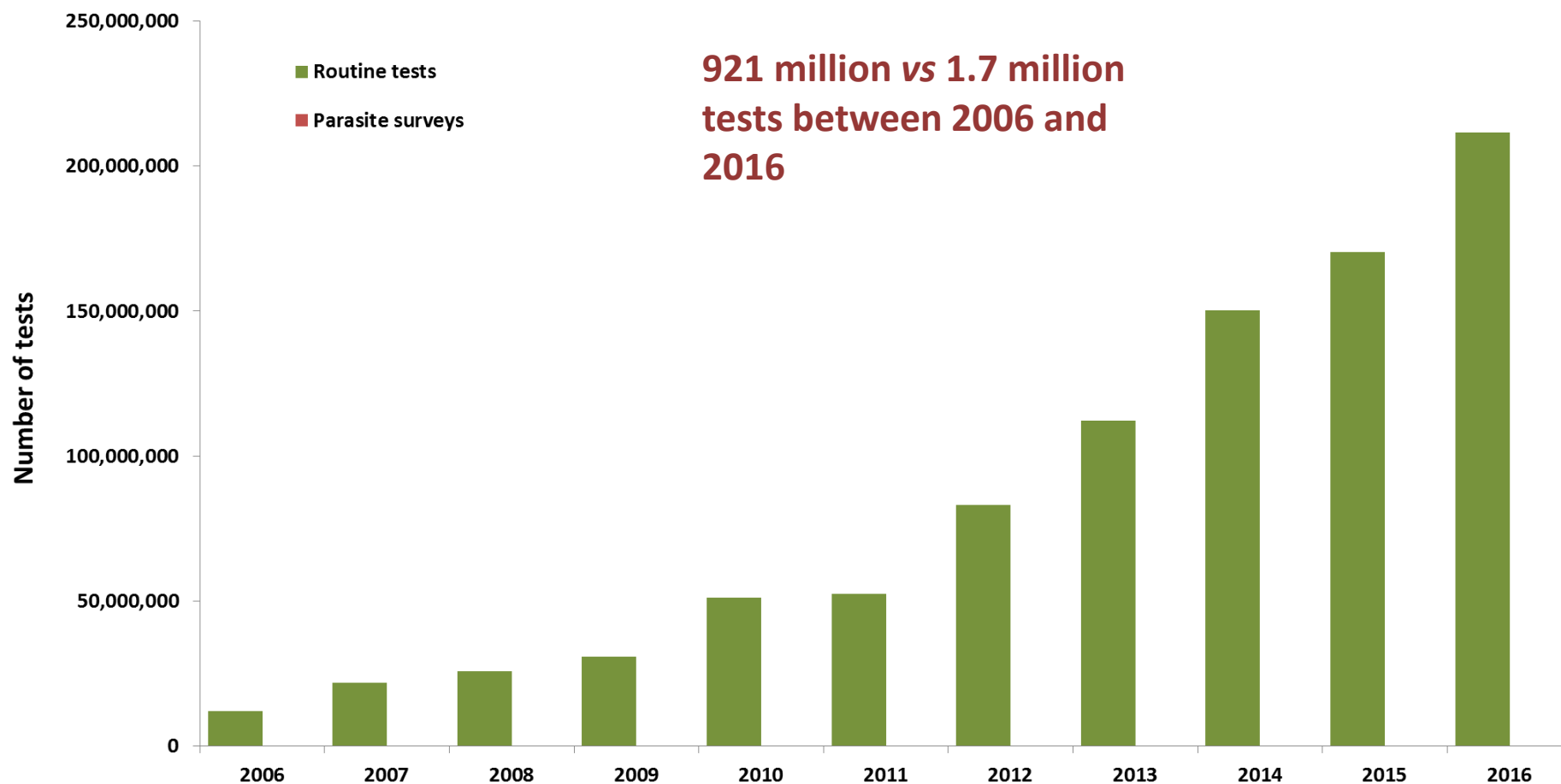


80 million more cases from the adjusted routine data compared to the *PfPR* to incidence model

Uncomplicated malaria



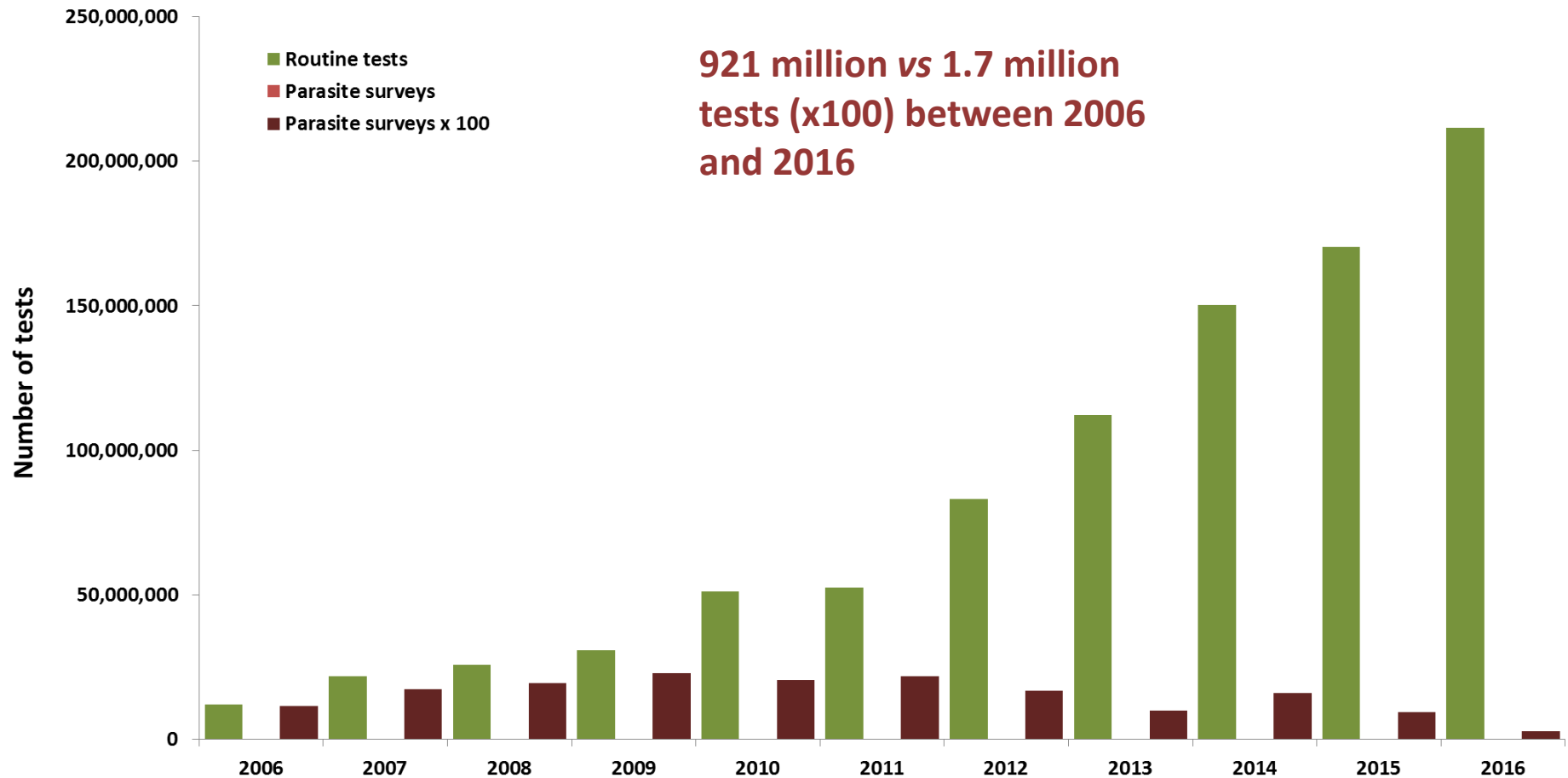
Number of persons tested, household surveys vs routine data, SSA



Uncomplicated malaria



Number of persons tested, household surveys vs routine data, SSA





Approve terms of reference for Malaria Burden Estimation (MBE) Evidence Review Group (ERG):

- Review existing methods for morbidity and mortality estimation. Focus on addressing issues related to use of routine data, temporal trends in case fatality rate (CFR), age attribution of malaria mortality, and the role of geospatial approaches to modelling mortality estimation;
- Revisit the pending recommendations from the ERG 2012–2013 in light of any new data, and develop proposals for best approaches to ensure those recommendations are fulfilled;
- Re-focus on the indirect burden of malaria infection.



Members

- Prof Fred Binka (Co-chair)
- Dr Richard Steketee (Co-chair)
- Prof Joana Armstrong-Schellenberg
- Prof Azra Ghani,
- Prof Simon Hay
- Prof Li Liu
- Prof Christophe Rogier
- Dr Alexander Rowe

Rapporteur

- Dr Gillian Stresman

Observers

- Dr Scott Filler
- Dr Bruno Moonen

Collaborating centres and presenters

- Prof Peter Gething
- Prof Thomas Smith
- Prof Clara Menendez (by phone)

WHO – GMP and IER

- Dr Pedro Alonso
- Dr John Grove
- Dr John Aponte
- Dr Richard Cibulskis
- Dr Kim Lindblade
- Dr Colin Mathers
- Dr Abdisalan Noor
- Dr Maru Aregawi Weldedawit

Estimating malaria case incidence

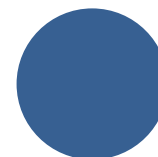


Unadjusted routine data



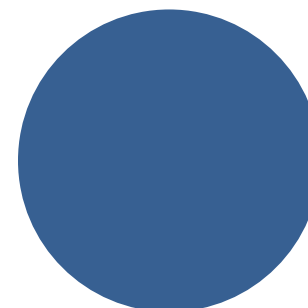
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Adjusted routine data



14%

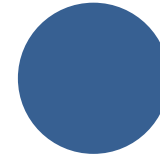
Parasite rate –to-incidence



86%



Adjusted routine data



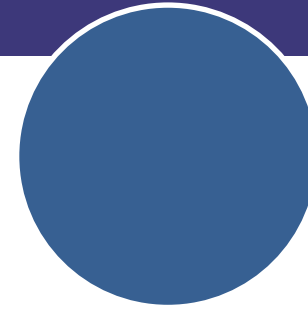
14%

- Data mainly from the public health sector adjusted for:
- Confirmation rate
 - Country reported, not validated consistently
 - Can be highly variable between years
- Reporting rates
 - Country reported, sometime not clear if % HF or % district
 - Some countries do not know actual number of public health facilities and increase over time
- Proportion seeking treatment in the private sector
 - Based on self-reported fever – not validated, not clear on subsequent action, may be higher in non-malaria but highly populated areas
- Proportion not seeking treatment at all
 - Based on self-reported fever – not validated, not clear on subsequent action

Estimating malaria case incidence



Parasite rate –to-incidence



86%

- Considerable temporal gaps in parasite prevalence data that may affect recent estimates
- Estimates are based on an epidemiological model that quantifies the proportion of infections that are likely to be clinical cases, and may not be the same as symptomatic individuals who were tested and treated at health facilities
- Considerable differences in magnitude and trend compared with routine data

Direct malaria deaths - 2016



Unadjusted routine data



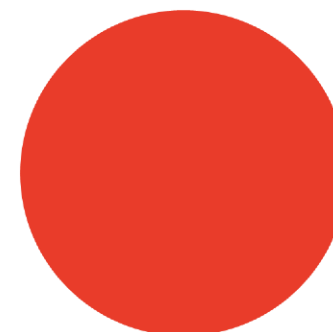
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Adjusted routine incidence data x CFR



11%

U5 mortality data x malaria CoD fraction
+ fraction over 5,
PfPR a variable in CoD model



89%



Adjusted routine incidence data x CFR



11%

- Affected by problems of computing cases from imperfect routine data
- Static case fatality rates (CFR) for both *P. falciparum* and *P. vivax*

Direct malaria deaths - 2016



Adjusted routine incidence data x CFR



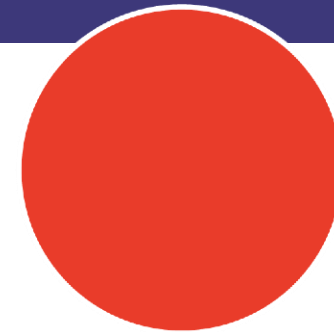
11%

Study	Place	Year	CFR	CFR Hospital
Mendis (summary)	Multiple (SE Asia, Africa)	1980s-1990s	0.1%-0.3%	
Nyarango	Eritrea	2000-2004	0.14%-0.21%	
Luxemburger	Thailand (Western)	1992	0.19%	
Meek	Thailand (Southeastern)	1983-1985	0.31%-0.42%	
Zucker	Kenya	1991		11%-33%
Dzeing-Ella	Gabon	2000-2002		9
Reyburn	Tanzania	2002-2003		7% (6%-13%)
Marsh	Kenya	1989-1991		3.50%
Schellenberg	Tanzania	1995-1996		3%
Greenberg	Kinshasa	1985-1986		21%

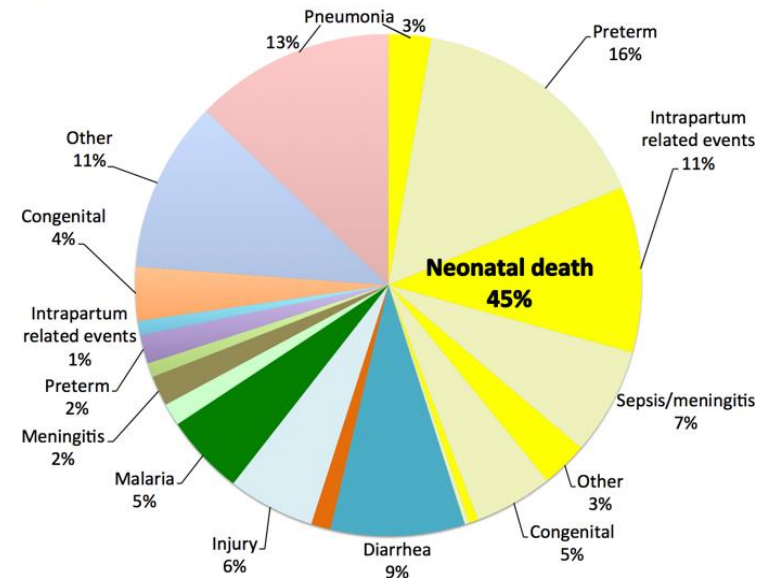
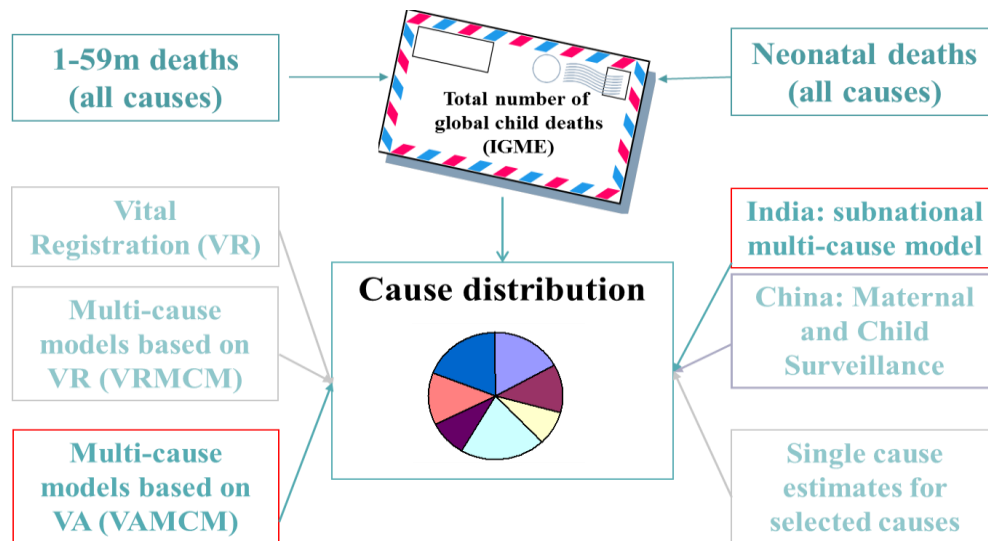
Direct malaria deaths - 2016



U5 mortality data x malaria CoD fraction
+ fraction over 5,
PfPR a variable in CoD model



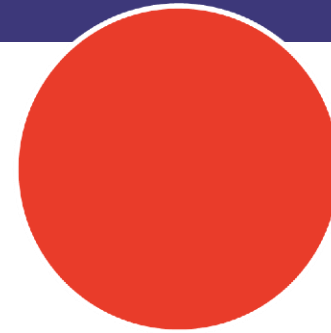
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Direct malaria deaths - 2016



U5 mortality data x malaria CoD fraction
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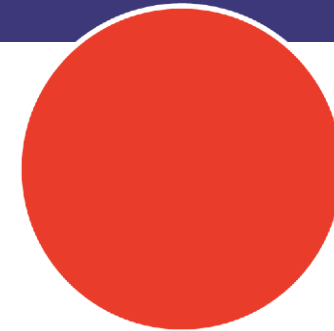
89%

- *PfPR* a covariate in quantification of CoD fraction for malaria, but there are some limitations in estimates and trend in *PfPR*
- *PfPR* discordant with confirmed cases from routine systems
- A fixed over 5 fraction is applied to U5 malaria estimates across a wider range of highly variable epidemiology

Direct malaria deaths - 2016

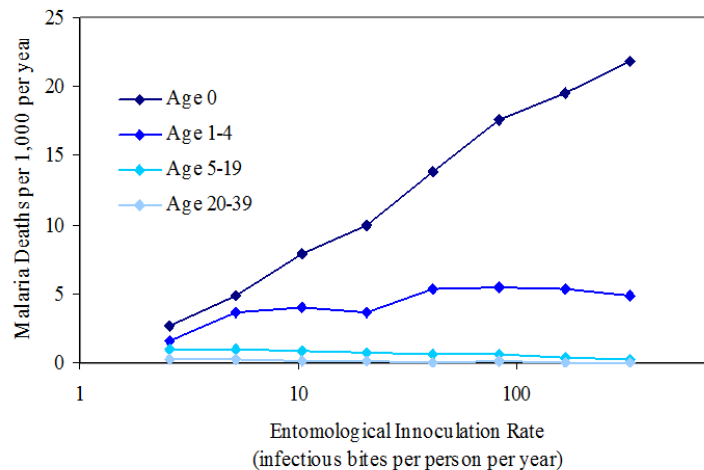


U5 mortality data x malaria CoD fraction
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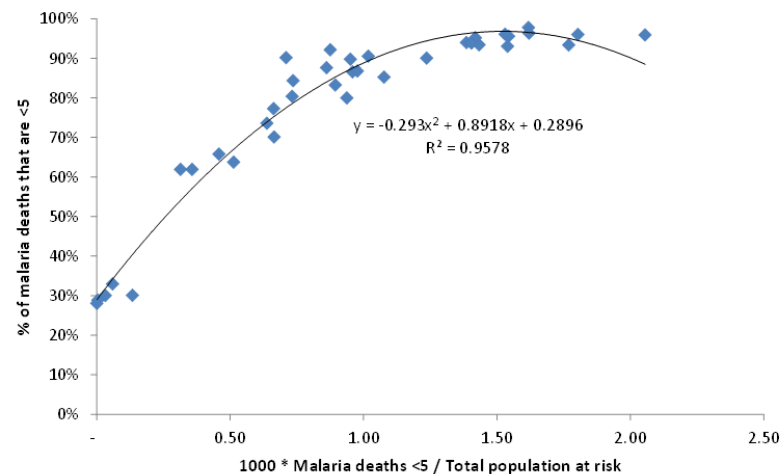
89%

Relationship Between Intensity of Malaria Transmission and Malaria Specific Death Rates



From Ross *et al* 2006.

Relationship between death rates under 5 and % deaths under 5 years of age



Relationship also used to infer % of deaths <5 outside of Africa

$$y = -0.2289x^2 + 0.8233x + 0.2239$$



Some countries submit inpatient malaria data

Indirect malaria deaths



Consequences of malaria in pregnancy



Anemia



- Countries report population in high risk (in areas where incidence is ≥ 1 case per 1000 population), and low risk (<1 case per 1000 population)
- These are scaled to UN population estimates for a given year
- We assume PAR used to computed incidence = high risk + $(0.5 * \text{low risk})$



1. What are the criteria for the use of routine data from sub-Saharan Africa? What levels of diagnoses and reporting rates over how many years would qualify a country in sub-Saharan Africa to transition from the parasite rate-to-incidence model to one based on adjustment of routine data. How does one apply these data to inform trends back to 2000?
2. What is the relationship between treatment-seeking for any fever, as used in routine reports of malaria data, and treatment-seeking for malaria fever?
3. What data are available to best quantify CFRs for *Pf* and *Pv* across different transmission and case management settings?



4. If routine data estimates are used for sub-Saharan African countries whose estimates were previously based on the parasite prevalence-to-incidence model, how do we integrate these into the analysis of the cause of death fraction for malaria?
5. How do we define populations (at risk) denominator to compute incidence from case estimates?
6. What are the best approaches for quantifying the severe and indirect burden of malaria?



General issues in malaria burden estimation

Estimation of malaria morbidity

**Estimation of all cause mortality and
quantification of cause of death fractions**

Estimation of malaria mortality

Discussion and recommendations



Immediate action (3-12 months)



1. Clear definition and purpose of metrics: currently, the following metrics of malaria morbidity are produced through various estimation processes:

- i. Parasite prevalence** (proportion of population with *Plasmodium* parasites in their peripheral blood following a test using microscopy or standard rapid diagnostic test. Data mostly from household surveys interpolated in time and space using statistical methods);
- ii. Fever with infection** (standard case definition in treatment guidelines and reported by routine health information systems);
- iii. Fever attributable to infection** (a model estimate based on the relationship between parasite prevalence and clinical episodes of malaria, defined as parasite density >5000 p/ul by age).



2. Improvements to PfPR models:

- i. Revisit current assumptions on the relationship between determinants and PfPR, which are important for filling gaps in space and time and have a major influence on trends, especially in years without data. Assembling new data, preferably sub-nationally, on intervention coverage is required to improve assumptions.
- ii. Where there is substantial divergence in trends between PfPR and routine reports, incorporate routine data to adjust trends, particularly in countries without recent parasite rate (PR) surveys.



3. Improvements to the *Pf*PR-to-incidence model:

- i. Identify and assemble recent active case detection surveillance data in sub-Saharan Africa in order to update the model.
- ii. Identify and assemble other contemporaneous *Pf*PR and clinical data from studies in order to add to the information that can be used to improve the *Pf*PR-to-incidence model.
- iii. Use the *Pf*PR-to-incidence model to estimate infections among fevers in addition to the current estimates of infections among fevers that are likely to be due to malaria.



4. Use of routine data – assessment of biases in routine data:

- i. Implement detailed surveillance assessments of select countries, with strong emphasis on the quality and completeness of routine data. Focus on countries with significant recent improvements in surveillance systems.
- ii. Assemble subnational data that are disaggregated by age over several years, preferably from 2010 when the large scale-up of diagnostics began in some countries, but where possible from 2000.
- iii. Where available, collect additional data on changing policies and quality of care over time in order to understand case management practices that may influence trends in routine data.
- iv. Based on the assessment data and confidence in the stability of the surveillance system, use routine data for MBE.
- v. Develop methods that will allow the use of routine data back to 2000.

5. Improvements to assumptions and methods for mortality estimation:

- i. Use updated and improved PfPR estimates to inform the magnitude and trends in the cause of death fraction for malaria in moderate to high transmission countries.
- ii. Assemble new data to update assumptions regarding over-5 mortality fractions applied to the under-5 mortality estimates.
- iii. Assemble new CFR data for low transmission areas in southern Africa and outside Africa for both *Pf* and *Pv*.
- iv. Examine MAP-implied CFR against current estimates used in the WMR and compare magnitude and trends.



6. Anaemia and malaria morbidity and mortality:

- i. Assemble available data to assess the relationship, and implement exploratory analysis of distribution and the relationship with malaria for the next WMR.
- ii. Develop a mechanism for developing a comprehensive repository of data and a mechanism for analysis for future WMRs.



7. Comparative clinical and prevalence studies across different transmission settings, including pathways of treatment-seeking:

The ERG acknowledged that there were gaps in the understanding of community parasite prevalence and the clinical cases seen from health facilities used by these communities. This relationship is critical to the joint interpretation of parasite prevalence and case reports and is influenced by levels of transmission, malaria interventions, seasonality of fevers, socioeconomic status, access to care and the pathways for treatment-seeking for fevers. Primary studies that reflect different endemicities, health systems and socioeconomic contexts should be conducted across sub-Saharan Africa.



8. Risk factor analysis in relation to malaria mortality:

Given the uncertainty of defining malaria mortality even under high-quality case management conditions, the ERG suggested that an analysis of changes in potential risk factors for malaria mortality would strengthen the interpretation of the trends in malaria burden and should be explored for future WMRs.



9. Ways of incorporating emerging tissue sample autopsy data from moderate to high transmission countries:

There are a few studies that are ongoing, and the ERG recognized that such data may provide opportunities for improving VA-based mortality models. In addition, they may serve as a concrete source of data for adult malaria mortality quantification. Data from these studies should be explored as they emerge.



10. Severe disease due to malaria:

It was recognized that the quantification of the burden of severe disease was a critical gap in the WMR. The ERG also recognized emerging new opportunities, such as community health worker referral data on severe disease in areas where rectal artesunate has been scaled up; and ongoing sentinel studies of inpatient facility data for severe disease and hospital CFR estimation. The ERG recommended that WHO explore the possibility of working with partners to assemble these data for future quantification of severe malaria burden.



- 11. Roadmap and resources
- 12. Communication
- 13. Next meeting

Please check out the WMR App



App Store Preview

This app is only available on the App Store for iOS devices.

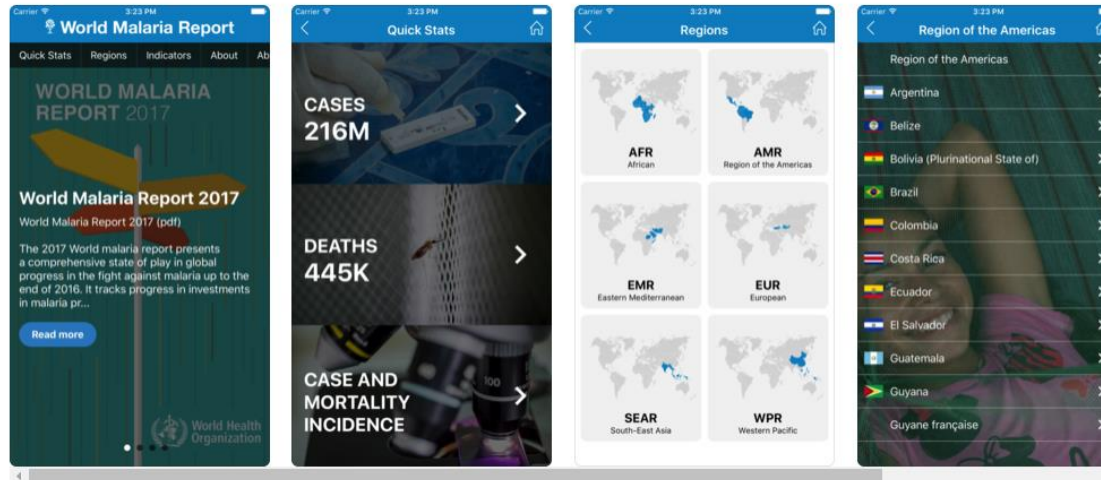


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