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The Lancet Commission on Malaria Eradication Summary of the 2nd Meeting

Malaria Elimination
Initiative



University of California
San Francisco

The Lancet Commission on Malaria Eradication 2nd Meeting

Hosted by the UCSF Global Health Group's Malaria Elimination Initiative

Wiston House, Steyning, UK

May 7 – 10, 2018

This was the second meeting of the **Lancet Commission on Malaria Eradication**, formerly the Malaria Eradication Group (MEG 2.0). Commissioners serve in an individual capacity and do not represent their institutions. This report includes highlights from the plenary presentations and discussions and is not comprehensive.

Meeting Objective: to develop an outline for the Lancet Commission on Malaria Eradication (LCME), which will identify the scientific, financial, and operational requirements for malaria eradication in the coming decades.

Meeting Highlights:

- The Commission, comprised of 24 experts from around the globe, will develop a seminal Report on the scientific, financial, and operational requirements for malaria eradication in the coming decades. This Report is expected to be published in Summer 2019. The UCSF Global Health Group's Malaria Elimination Initiative will serve as the Secretariat for the Commission.
- In consideration of the plenary presentations and discussions, including a presentation by *The Lancet* on features of a great Commission, the group discussed and deliberated on a draft outline that investigates the feasibility and rationale of malaria eradication. This outline will be finalized in the coming months.
- The Commission Report will summarize why malaria eradication is necessary, what is required to achieve eradication, and aims to address sources of skepticism using rigorous, evidence-based research.
- The meeting concluded with a group discussion on a draft outline that has since been refined and shared with Commissioners and co-authors. The following elements were

considered important for inclusion in the Report:

- *Overview and conceptual framework:* A definition of malaria eradication, differentiation between malaria eradication and other vaccine-based eradication campaigns, and the importance of countries and regions in driving eradication.
- *Review of the malaria eradication imperative:* Malaria eradication is possible and worthwhile based on plausible trajectories, current and new tools, and an attractive ROI.
- *Assessment of the technical, operational, and financial requirements for eradication, including:* Review of the current strategy and progress to date, important issues that will likely have a significant effect on short- and long-term milestones, possible endgame challenges and last battlegrounds, and present costing projections and plausible financing scenarios.
- Embedded throughout the Report will be important links to health systems, universal health coverage (UHC), leadership, management, and accountability.

The **Malaria Elimination Initiative (MEI)** at the University of California, San Francisco (UCSF) Global Health Group believes a malaria-free world is possible within a generation. As a forward-thinking partner to malaria-eliminating countries and regions, the MEI generates actionable evidence through operational research, shares new tools and approaches to help countries eliminate malaria more efficiently and effectively, documents and disseminates elimination best practices, assesses the costs and benefits of elimination, fosters regional initiatives for malaria elimination, and strengthens political and financial commitment to shrink the malaria map. With support from the MEI's highly skilled team, countries around the world are actively working to eliminate malaria—a goal that nearly 30 countries will achieve by 2020.

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Session 1: Welcome and Overview

Presenters: Richard Feachem, Ingrid Chen

- The purpose of the Commission Report is to fully explore the technical, operational, and financial requirements to achieve malaria eradication in the medium term.
- This work is complementary to the World Health Organization's Strategic Advisory Group on Malaria Eradication (WHO SAGme), which is investigating eradication with the intention of informing the WHO Director-General on whether the WHO should update their current stance on eradication in 2020. The Report will be one of several inputs into the SAGme position statement on malaria eradication.
- The objective of this meeting is to develop a detailed outline of the Report. This includes consensus on which topics the Report will cover, key messages, and the analyses that must be conducted to generate a compelling Report with evidence-based conclusions.
- The Commission will next meet in December 2018 in California to review a working draft of the Report. The current aim is to submit the Report to *The Lancet* in early 2019 and publish in Summer 2019.

Highlights of Session 1 discussion

- To optimize information sharing and ensure that efforts are coordinated and harmonized, it is important for the LCME and SAGme to remain in frequent contact.
- Countering sources of skepticism may be a potential way to frame the Report. There are members of the malaria community that do not believe malaria eradication is possible or necessary, and it is imperative that the Report acknowledge sources of skepticism.
- Similarly, most policymakers support the eventual eradication of malaria but question when to start. The Report must address the issue of timing for the launch of a malaria eradication campaign.
- The intended audience for the Report includes national-level stakeholders and global

policymakers and influencers; well-balanced content and messaging is critical.

- To reach policymakers, the Report should feature an expanded executive summary followed by detailed sections. Policy briefs could be developed on important topics covered in the Report.
- Past *Lancet* Commissions have continued work after their reports were published. Potential future work for this Commission could include applying the conclusions of the Report to specific regional and national level contexts.
- Community engagement and country ownership should be included as topics in the Report as they are integral to malaria eradication.

Session 2: What do we mean by malaria eradication?

Chair: Altaf Lal

Current knowledge on transmission of *Plasmodium knowlesi* malaria between macaques and humans and from humans to humans, presented by Balbir Singh

- *Plasmodium knowlesi* is a simian malaria parasite that primarily infects long-tailed and pig-tailed macaques indigenous to the Southeast Asia region. Evidence of naturally-occurring infections among humans was first discovered in 1965.
- The first large focus of *P. knowlesi* infections was discovered in Sarawak state in Malaysian Borneo in 2002. Between 2000 and 2017, 55% of the 3,448 malaria cases in Malaysia were diagnosed through PCR as *P. knowlesi* infections. In 2017, *P. knowlesi* / *P. malariae* (which are morphologically similar and difficult to distinguish by microscopy) made up nearly 90% of infections in Sarawak and Sabah states in Malaysian Borneo.
- Due to the natural habitat of hosts and incriminated vectors, risk of *P. knowlesi* is widely distributed across Southeast Asia, and infections have increasingly been reported in Cambodia, Indonesia, Malaysia, Myanmar, Philippines, Thailand, and Vietnam. However, naturally-occurring human-to-human

transmission of *P. knowlesi* has not been demonstrated and questions remain on how to obtain evidence for such transmission.

- The current WHO definition for eradication is “the permanent reduction to zero of the worldwide incidence of malaria infection caused by all species of human malaria parasites.” As human malaria decreases in Southeast Asia and beyond, simian malaria and other zoonosis that can infect humans is likely to complicate elimination efforts. An alternate definition to the current WHO definition was posed as: “the reduction to zero of worldwide incidence of malaria in humans.”

Highlights of Session 2 discussion

- The increase in *P. knowlesi* infections can likely be attributed to a combination of factors, including loss of habitat for macaques, changes in the local ecology, changes in vector bionomics, and changes within the parasite.
- Risk of *P. knowlesi* seemingly stops at Bangladesh. India has screened rhesus macaques, the predominate local species, and has not detected any *P. knowlesi*. This is likely a combination of two factors: rhesus macaques are not natural hosts for *P. knowlesi* and long-tailed and pig-tailed macaques are deterred from migrating westward into India by the presence of rhesus macaques which are aggressively territorial.
- Regarding the definition of malaria eradication, monkeypox continues to cause morbidity and mortality throughout Africa, but smallpox is still considered to be eradicated.
- The LCME will use the WHO definition for malaria eradication, a caveat being that simian malaria should be actively monitored for evidence of human-to-human transmission.

Session 3: Confronting the hardest cases

Chair: Caroline Buckee

A malaria heat map in 2040 based on continuation of current trends, presented by Pete Gething

- The Report will feature outputs of a model combining 2000-2018 data on prevalence, intervention coverage, and micro-environmental factors (e.g. housing quality, land surface temperature) with plausible future macro-environmental scenarios (based on climate change and socioeconomic development) in order to project potential future malaria trends.
- This analysis will review the background effects, or “megatrends,” on malaria, which may dictate feasibility, timeline, and the optimum strategy for eradication. The model will identify likely trajectories for malaria eradication and will ultimately identify the hardest cases and endgame regions.
- The outcome of this work will be a pixel-level projection map of future malaria prevalence across the globe. The scope will be expanded to include additional intervention scenarios and a more comprehensive suite of variables. The methods will be refined to account for sub-national patterns including urban expansion, deforestation, and land use change.
- Important elements that will likely have a significant influence on future malaria trends, but which are not currently included in this model, include operational factors, drug resistance, complex emergencies, and conflict.
- The uncertainties and limitations inherent in the model used to produce the risk maps must be well-articulated for readers.

Malaria transmission in holoendemic Africa: addressing the biggest challenges, presented by Fred Binka

- Effective tools are available to diagnose, treat, and prevent malaria; the biggest challenge is access. As such, the “hardest cases” are a result of operational challenges, not biological factors. The hardest cases are not the same across or even within countries. Sub-national stratification is a necessary first step in optimizing malaria interventions.
- Elimination and eventual eradication will require improved access to quality health care. Integrated Community Case Management is an evidence-based strategy proven to significantly

reduce mortality from malaria, pneumonia, and diarrhea. However, it should not be a blanket policy across any one country, and it has the greatest effect in providing free care in hard-to-reach communities.

- Strengthening the private sector's role in malaria case management is critical. The public health system should provide standard commodities to private sector providers to ensure consistency and quality of care; in exchange, private providers should be expected to share data so that the public health sector can monitor implementation and progress.
- It is imperative that health information systems be expanded and strengthened early in the elimination process to monitor implementation, document progress and impact, inform problem-solving, and ensure that timely and tailored feedback is provided to malaria service providers working on the ground.

Highlights of Session 3 discussion

- There is overlap between health system strengthening, UHC, and malaria eradication. Malaria eradication should not be viewed as a standalone cost but as an incremental cost on top of health system strengthening.
- There is a need to invest more in community-based approaches as these are generally the most functional units through which to work and are primarily responsible for implementation. Community health workers should be compensated for their work, which is a challenge in resource-limited settings where precedent relies on a largely unpaid workforce. Additionally, the delivery of health services should be optimized with innovative approaches to data collection, implementation, and logistics.

Session 4: The broader context for malaria eradication

Chair: Bruno Moonen

Malaria eradication: benefit to Universal Health Coverage or expensive distraction? presented by Muhammad Pate

- Malaria eradication and UHC are not mutually exclusive. Eradication can accelerate progress towards UHC but the effort will require a well-crafted, integrated approach that is country-led and tailored to the local context. Central to both efforts is political commitment to ensure that both efforts are adequately prioritized.
- Polio eradication has demonstrated that disease eradication is achievable but can be a protracted, expensive undertaking. The short-, medium-, and long-term goals of malaria eradication should be aligned with country and regional priorities and contexts.
- Shared country-based platforms necessary to achieve eradication and promote UHC include: (1) health financing policies that can efficiently mobilize necessary resources, (2) effective healthcare system with an adequate workforce, equitable infrastructure and functioning supply chain system, (3) health information systems linked to accountability mechanisms, (4) community engagement and mobilization, and (5) the private sector.
- Multi-stakeholder governance at the global, regional, and national levels will be important, and independent monitoring mechanisms should be established to ensure credibility and transparency of the substantial investment.

Malaria eradication: benefit to drug resistance or jeopardized by drug resistance? presented by Arjen Dondorp

- In high transmission areas, there are natural barriers to antimalarial drug resistance including multiple infections, large numbers of asymptomatic infections, increased immunity, and lower coverage of antimalarial drugs. Antimalarial resistance always emerges in low transmission settings first. As transmission declines, Africa will be more prone to antimalarial drug resistance.
- Monitoring molecular markers is a helpful surveillance method for assessing antimalarial drug resistance risk. *PfKelch13* propeller mutations confer artemisinin resistance and have been documented in the GMS; there is no evidence to date of *PfKelch13* change in Africa.

- In the absence of new compound drugs, other options with currently available drugs include triple artemisinin-based combination therapy (TACT), changing from a 5- to 7-day drug regimen of ACTs, drug rotation, or sequential use of two different ACTs.
- In Africa, drug efficacy and molecular markers of resistance should be closely monitored and multiple first line treatments should be used. The continent should prepare for the arrival of multi-drug resistant falciparum through registration of multiple ACTs, development of a mechanism for rapidly changing first-line drugs, potential use of TACTs as a preventative measure, and consideration of new drugs.

Highlights of Session 4 discussion

- UHC has the potential to bypass the private sector, and determining how to balance the two is an important aspect of UHC. The provision of basic health services is a fundamental responsibility of public health, but the private sector can and should play a role in the provision of services and in innovation.
- The group should consider two questions during analysis: (1) In countries that have successfully eliminated, was the provision of health services mainly public with minimal contributions from the private sector? Or did public services have a strong grip on the private sector? (2) Can we eliminate where private providers play a significant role in the health system and where these providers regularly misdiagnose and mistreat malaria?
- Following clinical trials, there is a lengthy WHO registration process for new drugs. These regulatory pathways should proceed at the same time as academic studies and trials to avoid delays in the uptake of new drugs.
- Drug resistance is related to the counterfactual: if we do not eradicate, drug resistance will persist. Resistance occurs as a byproduct of increased exposure to drugs and insecticides; as such, it is likely to occur in either scenario (maintain the status quo versus the dedicated pursuit of eradication). Whether there will be significant differences in the rate and spread of resistance between the two scenarios is

unknown and an important topic to consider for further analysis.

Session 8: Writing a successful Lancet Commission Report

Chair: Jeny Wegbreit

Manifesto of Lancet Commission tips and best practices, presented by Rebecca Cooney

- A commission is a scientific review, inquiry, and response to an urgent, and perhaps neglected or understudied, health predicament. It is science-led, multidisciplinary, and aims for transformational change.
- There are several features of a great commission: (1) Write a bold message, (2) Develop a compelling story, (3) Devise an original idea, (4) Offer a critical review, (5) Be forward looking, (6) Provide actionable conclusions, (7) Create an active afterlife, (8) Convene great people, (9) Give yourself time, (10) Be inspiring and optimistic, (11) Think big.
- The review process for commission reports can take about 3 months. To publish in July, the Commission should strive to submit in March.

Working Group Sessions

The remainder of the meeting was spent in small working group sessions tasked with identifying key messages and necessary analyses and developing section outlines. On the final day, the group came together to review a proposed draft Commission Report outline. The following issues were identified as requiring further refinement and consensus:

- Defining the counterfactual.
- Clarifying the term “hardest cases.” There may be technical and biological challenges, but many Commissioners feel that operational challenges are the most critical.
- Many potential overlaps exist between the proposed sections, which will need to be addressed as the outline gets finalized, and throughout the writing process.

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