The Challenge of Malaria Eradication in the 21st Century

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Issues to be covered

- An audacious goal announced in October 2007
- The feasibility of malaria eradication
- Key lessons in the history of malaria
- Recent successes
- The Gates Foundation malaria eradication strategy
- Research needs
- What lies ahead
An audacious goal set in October 2007

- Every life is of equal value; accepting malaria undervalues lives were it persists
- The cost of malaria control will continue indefinitely
- There will be an ongoing need to adjust control measures as the parasites and vectors adapt
- The time is right for charting a long-term course to eradication, knowing that it will take several decades, sustained commitment, and an array of new tools to reach such an ambitious goal
Extent of malaria transmission: 1945

Hypothetical phasing scenario

Source: Malaria Elimination: Geography, finance, and economics, presentation by Prof. Sir Richard Feachem, at ASTMH 7 Dec 2008 © 2010 Bill & Melinda Gates Foundation
Extent of malaria transmission: 2008

Hypothetical phasing scenario

Source: Malaria Elimination: Geography, finance, and economics, presentation by Prof. Sir Richard Feachem, at ASTMH 7 Dec 2008 © 2010 Bill & Melinda Gates Foundation
Is this possible by 2050?

Source: Malaria team projections
Malaria eradication is possible

- It is biologically feasible
  - There are multiple ways to attack transmission
  - Animal reservoirs absent or not significant
  - Much of the world freed of malaria during 20th century

- We must have the right interventions
  - For areas with low and moderate transmission, existing tools may suffice
  - For areas with high transmission, we will need new tools and approaches

- We must have adequate resources and commitment
  - Technical, operational, financial feasibility must be assessed
  - Long-term political and financial commitment is essential
The Gates Foundation strategy is guided by several assumptions

- The pathway to eradication is not clear, and we must clarify that pathway

- Existing tools are sufficient for elimination in some regions but not in all, and new tools and approaches will be needed

- A magic bullet is unlikely: a robust strategy requires multiple tools and approaches to interrupt transmission

- Malaria elimination should focus first on the two major human malaria species, *P. falciparum* and *P. vivax*; falciparum malaria will be the first priority and easier

- A 30- to 40-year time horizon for global eradication is reasonable because of the time needed to develop and deploy new tools
Global Malaria Eradication Program

- Started by WHO in 1955, intended to be time limited
  - Successful in several European Countries
  - North America and Australia are also free of malaria
- Major declines in malaria achieved in Asia and Latin America but short of elimination
- Africa with the greatest burden of malaria was not included
  - Unclear, even unlikely, that malaria elimination from Africa was feasible with the tools available
- The strategy was re-examined and ended by WHO in 1969
  - The beginning of over 20 years of stagnation
Recent history of malaria

- Chloroquine resistance first appeared in Thailand and Colombia in 1959-1960
  - Spread globally and reached Africa in 1979
  - Severe malaria and deaths increased with the lack of effective treatment
- Renewed commitment to malaria control in 1990s
  - 1992 – Amsterstam Ministerial Conference focused on reducing deaths
  - 1998 – Roll Back Malaria created by WHO
- April 2000 – Heads of State meet in Abuja, Nigeria
  - Committed to scaling up ITNs, IRS, effective treatment
  - MDGs and 2010 RBM targets
- At least 8 countries are actively pursuing elimination
  - UAE and Morrocco certified malaria free by WHO in 2007 and 2010, respectively
Current distribution of *P. falciparum* and *P. vivax*

Source: Shrinking the Malaria Map: a prospectus on Malaria elimination by Richard G.A. Feachem, Allison A. Phillips, and Geoffrey A. Targett on Behalf of the Malaria Elimination Group
Recent progress in controlling malaria, but overall malaria burden remains high

Important prevention tools are being successfully scaled up in some regions
- Enabled by a significant increase in financing, estimated to be ~15x since 1997

In areas where scale-up has been significant, an impact on burden has been achieved
- Notable examples are Zambia, Eritrea, Ethiopia, Kenya, Rwanda, The Gambia, and others
- In Zambia, surveys showed parasitemia rates in children under 5 declined by 53% 2006 - 2008

In 2008, there were an estimated 244M cases and 863k deaths from malaria
- 108 countries are endemic for malaria, with 1.2 billion people in areas of high risk
- 85% of malaria deaths are in children under 5
- P. falciparum accounts for the majority of the mortality; P. vivax burden is not well characterized
- Evidence suggests the potential for species replacement as P. falciparum declines

1. 2008 actual treatments projected from actual Novartis distribution of Coartem and assuming constant market share (BCG analysis, via MMV). WHO Malaria Report 2009 estimates 72m ACT treatment courses were delivered.
2. 580 cases estimated in 2008 Source: WHO Malaria Report 2008 and 2009, external interviews, and BCG analysis
Declines in deaths in 6 countries outside Africa
How do we go about eradication?

- Shrinking the map
  - Elimination in low and moderate transmission areas, primarily at the margins
  - *P. falciparum* will be a priority and easier than *P. vivax*, which is relapsing

- Aggressive control in areas of high transmission
  - Scale up available tools to achieve high coverage and reduce cases and deaths as much as possible
  - Sustain high level control
  - Prepare for elimination when it is feasible

- Research and development to protect and improve existing tools and to provide needed new tools
What the world needs to do to achieve eradication in ~40 years

1. Currently, existing control tools are LLIN, IRS, larviciding, treatment. The definition of existing tools will change over time.

**Model and test approaches to elimination and eventual eradication**

**R&D**

to improve existing tools and for transformative eradication tools

**Deploy toolkits for control**

**Scale up and sustain deployment of optimal toolkits**

*(Toolkits will change over time and by geography as new tools become available and transmission patterns change)*

**Deploy toolkits for elimination**

**Enabling Activities:** Increase funding and political will, and change policy and develop financing mechanisms; build capacity and capability, strengthen health delivery systems

We see the toolkits shifting increasingly over time from a focus on control to elimination. We have illustrated this shift in proportions with this line, recognizing that some countries now are entering elimination while the majority are still focused in control.

1. Currently, existing control tools are LLIN, IRS, larviciding, treatment. The definition of existing tools will change over time.
What are immediate challenges?

- **Parasite resistance**
  - Resistance to available drugs will almost certainly occur
  - **Confirmed** *P. falciparum* resistance to artemisinin on the Thai-Cambodian border, possibly in Eastern Myanmar and southern Vietnam, presents an immediate and serious threat

- **Vector resistance**
  - Various levels of resistance exist to available pesticides
  - Pyrethroids are the only pesticides currently used on ITNs

- **Human resistance**
  - People lose interest and become resistant to IRS and using nets when the threat of malaria is not perceived.
  - Sustaining political and financial commitment is hard if malaria is not seen as a priority
The long-term challenges in R&D

- Research and development were largely absent from the previous Global Malaria Eradication Program
  - Essential to the new effort
  - Long-term
  - Long lead times for development and deployment

- Malaria Eradication Research Agenda – malERA
  - An 2-year consultative process involving over 200 malaria and public health experts to identify new tools that could be needed for eradication
Some key malERA findings (1)

- **Vaccines**
  - Focus on vaccines that interrupt malaria transmission - VIMTs
  - Pre-erythrocytic and transmission blocking vaccines would attack the parasite when it is most vulnerable (fewest in number)

- **Drugs**
  - Ideal would be a drug given in a single encounter for radical cure and prevention or prophylaxis - SERCaPs
  - If not a single drug, we will need the following
    - Drugs to overcome resistance
    - Safer, better drugs to attack latent liver stages (hypnozoites)
    - Drugs suitable for mass drug administration
    - Safe, long acting drugs for prevention or prophylaxis
Some key malERA findings (2)

- New insecticides to avoid resistance
  - For both ITNs and IRS
  - New formulations for longer duration of action

- New vector control tools
  - Consumer friendly products to overcome human resistance
  - Interventions targeting outdoor biting and resting mosquitoes
  - Modified mosquitoes that permanently reduce vectoral capacity

- Diagnostics
  - To detect asymptomatic and low-level infections
  - To detect people who are infectious (with gametocytes)

- Basic science
  - Biology of liver stage and sexual forms (gametocytes)
  - Vector ecology and behavior
  - Immunology, especially for vaccines
Some key malERA findings (3)

- **Modeling**
  - Help identify and characterize key investments
  - Find optimal package of interventions for different settings

- **Health systems and operational research**
  - Strengthening key aspects of health services essential
  - Operational research to test financing and delivery systems, improve program performance, engage communities and political leadership, etc.

- **Monitoring and evaluation**
  - Granular and timely data to measure impact and manage programs
  - Test “surveillance as an intervention,” as with smallpox
The Gates Foundation is a major contributor in R&D funding

R&D Funding by Product Type in 2008

- Globally, the majority of R&D funds for malaria goes to Drugs, Vaccines, and Basic Research

Malaria R&D Funding Sources

- The Foundation is a contributor in every major area of malaria R&D
- The Foundation is the majority contributor in vaccines, vector control and appears to be the largest single contributor in drugs

Note: Analysis pending more detailed data

R&D and implementation funds needed

- **R&D funding**
  - In 2008, $542 million invested by multiple partners (foundations, US NIH and DoD, other governments, pharmaceutical and biotechnology industry).
  - Estimated total need for $500-800 million annually until needed tools have impact

- **Implementation funding**
  - In 2008, $2,560 million provided by Global Fund, USAID/PMI, other bilaterals, World Bank, and national governments
  - Estimated total need approximately $7 billion annually
It is up to us to make the future

- No more cycles of boom and bust
  - Malaria must remain a priority, as do childhood vaccines when vaccine preventable disease decline and even disappear
  - We must sustain our commitment to R&D and implementation

- We must address critical issues
  - Health services in the developing world must be able to deliver needed interventions
  - Communities should be engaged
  - We must understand and justify the costs of eradication

- If we don’t have the audacious goal of eradication, we will not challenge ourselves
  - Doubtful that countries can or will sustain control indefinitely
  - Available tools are unlikely to work indefinitely
Conclusions

- Malaria eradication is feasible but will require a long-term, sustained effort over several decades.

- Key lessons must be learned from the history of malaria:
  - Research must be a central component.
  - Efforts must be integrated into and build health services.
  - Surveillance will be key to monitoring and evaluation and to finding and attacking malaria where it persists.

- Recent successes are encouraging and offer new learnings.

- Research and development of new approaches and tools is key to the Gates Foundation malaria eradication strategy.

- Multiple partners and sustained commitment and financing will be essential.

- Without the challenge of eradication, we will consign too many to live with and die from malaria forever.
This is achievable by 2015

Source: *Malaria Elimination: Geography, finance, and economics*, presentation by Prof. Sir Richard Feachem, at ASTMH 7 Dec 2008 © 2010 Bill & Melinda Gates Foundation
This is possible by 2050