Accelerate to Zero: Malaria Strategy

Presentation for the RBM-VCWG

Janice Culpepper, PhD
February 21, 2014
A 25+ year arc to achieve our ambitious eradication goal

A world free of Malaria

<table>
<thead>
<tr>
<th>...in 7 yrs</th>
<th>...in 8-15 yrs</th>
<th>...in 15-25 yrs</th>
<th>...in 25+ yrs</th>
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<tbody>
<tr>
<td><strong>Stage set for adoption of global eradication agenda:</strong></td>
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<tr>
<td>• New drug and vector interventions needed to accomplish Pf and Pv elimination available and approved for use</td>
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<tr>
<td>• Foundation Accelerate to Zero strategies are proven to achieve elimination</td>
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<td>• Global community mobilized around a common eradication goal</td>
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<tr>
<td>• Delivery of current interventions with new strategies optimized</td>
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<tr>
<td><strong>Eradication effort gathering momentum:</strong></td>
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<tr>
<td>• New vaccine and Anopheline replacement interventions to complete elimination available and approved for use in some settings</td>
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<td>• Global leadership, financing, and policies needed to advance eradication galvanized</td>
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<tr>
<td>• Evidence from technical and operational feasibility studies of delivery models incorporated into or used to inform approved delivery policies</td>
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<td><strong>Eradication efforts rolled out everywhere:</strong></td>
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<td>• Proven tools &amp; delivery models deployed at scale in all endemic countries</td>
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<tr>
<td>• Financing and policy in place for sustained deployment of eradication effort</td>
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<tr>
<td>• Any additional interventions needed in global last mile settings developed and deployed</td>
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<td><strong>Eradication achieved:</strong></td>
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<td>• Global Pf and Pv prevalence reduced to 0</td>
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The world has three potential future trajectories for malaria...

...in our strategy, we have chosen to 'Accelerate to Zero', which leads to three overarching goals for the period (2014-2020)

Global annual malaria parasite incidence

Goals
1. Accelerate to Zero Now (new strategies using current tools)
2. Prepare for the Future (new strategies using new tools)
3. Sustain Progress (current strategies using current tools)

“Bend the Curve”
Our three overarching goals for 2014-2020 are to accelerate to zero now, prepare for the future and sustain progress

<table>
<thead>
<tr>
<th>Goal</th>
<th>Rationale</th>
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<tbody>
<tr>
<td>1. Accelerate to Zero Now</td>
<td>- Prove we can <strong>accelerate</strong> the trajectory to elimination (bend the curve) by applying interventions and strategies based on the five principles of the Analytic Framework</td>
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<td>- Convincingly demonstrate at scale that we can eliminate malaria in settings that are unlikely to achieve elimination with current control strategies in the next 7 years</td>
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<td>2. Prepare for the Future</td>
<td>- <strong>Prepare</strong> the next generation of interventions, strategies, and delivery models to enable improved implementation of elimination efforts</td>
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<td>- Widespread recognition and adoption of Accelerate to Zero approach by global normative and funding bodies to enable country implementation</td>
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<td>3. Sustain Progress</td>
<td>- <strong>Sustain</strong> progress by preventing resurgence in countries that are nearing elimination and helping them to achieve and sustain their current elimination goals</td>
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<td>- Support universal scale up of current interventions for disease burden reduction until countries are ready to implement Accelerate to Zero strategies</td>
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Eradication Principles

1. Malaria eradication is the elimination of plasmodium parasites from the human population.

2. On an individual level, complete cure is necessary for a successful malaria eradication effort.

3. At the population level, targeting the human transmission reservoir in asymptomatic people is necessary for successful eradication.

4. The principles of evolutionary medicine should be the foundation of science, product development and operational deployment.

5. Think global and act local.
We have organized our work around six initiatives

Our three strategic goals...

Accelerate to Zero Now  Prepare for the Future  Sustain Progress

...will be supported by the six initiatives that organize our work

Eliminate

Infection Detection  Achieve Radical Cure  Prevent Transmission  Last Mile

Mobilize
Success in 2020 will require working towards specific initiative objectives (I)

<table>
<thead>
<tr>
<th>Initiative</th>
<th>Objectives</th>
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<tbody>
<tr>
<td>Eliminate</td>
<td>▪ Accelerate the path to elimination at scale in diverse geopolitical and transmission contexts</td>
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</tbody>
</table>
| Infection Detection         | ▪ Develop high sensitivity diagnostic tools and real-time data transfer methods to guide campaign  
                                  ▪ Understand epidemiological patterns to determine significance of asymptomatic infection to elimination                           |
| Achieve Radical Cure        | ▪ Develop first generation Single Encounter Radical Cure (SERC) drug  
                                  ▪ Develop strategies for treating special populations  
                                  ▪ Develop NCEs for second generation SERCaP using novel in vitro and in vivo platforms  
                                  ▪ Optimize the use of existing tools and prevent loss to resistance                                                                             |
| Prevent Transmission        | ▪ Develop / evaluate tools that prevent mosquitoes from biting people  
                                  ▪ Develop / evaluate tools that interrupt parasite development in mosquitoes  
                                  ▪ Develop / evaluate tools that immunize against infection  
                                  ▪ Create decision making framework for the prevent transmission toolbox                                                                              |
Success in 2020 will require working towards specific initiative objectives (II)

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<th>Initiative</th>
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<tr>
<td>Last Mile</td>
<td>▪ Develop appropriate tools for measuring &quot;zero&quot;</td>
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<td>▪ Update criteria for assessing and certifying zero</td>
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<td>▪ <strong>Develop strategies for the use of people-independent solutions (e.g. HEGs)</strong></td>
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<td>▪ Develop context-adapted delivery mechanisms</td>
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<td>▪ Learn from other eradication programs (e.g. smallpox, polio)</td>
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<td>Mobilize</td>
<td>▪ Maintain current levels of global funding for malaria community to sustain progress</td>
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<td>▪ Advocate for sustainable financing for malaria elimination</td>
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<td>▪ Leverage partners to support elimination targets in prioritized regions</td>
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<td>▪ Cultivate a supportive global agenda for malaria elimination</td>
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<td>▪ Ensure interventions are implemented efficiently and effectively</td>
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<td>▪ Support the development of an affordable, sustainable supply of commodities for elimination</td>
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P. falciparum 2013: Clinical Cure and Incomplete Prevention

Three types of people in malaria endemic areas

- Not infected
- Infected Asymptomatic
- Infected Symptomatic

Interventions

- LLINs
- IRS

Outcome: Infectious asymptomatic reservoir

Goal: Prevent death and severe disease

RDT + ACT

No effect on gametocytes

Ignored Transmission reservoir remains untouched

Outcome: Vector Escape

Mosquitoes infected
Future *P. falciparum* Eradication Paradigm?

- **Not infected**
  - LLINs
  - IRS
  - New Tools
  - Outcome: Complete Prevention (Vector +/- Vaccine)

- **Infected Asymptomatic**
  - ACT + PQ
  - Transmission reservoir eradicated
  - Target Population
  - RDT + ACT + PQ
  - Kill gametocytes
  - Prevent death and severe disease
  - Interventions

- **Infected Symptomatic**
  - Three types of people in malaria endemic areas

- **Outcome:** Un-Infected Asymptomatic reservoir

- **No parasites to infect mosquitoes**
Broad set of potential vector control tools using various mechanisms and applied in various settings

<table>
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<tr>
<th>Individual Interventions</th>
<th>Household Interventions</th>
<th>Community Interventions</th>
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<td><strong>Environmental Modification</strong></td>
<td><strong>Biological Control</strong></td>
<td><strong>Chemical Treatment</strong></td>
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<tr>
<td>• Screening windows, household improvements</td>
<td>• Draining wetlands and ditches</td>
<td>• Larvivorous Fish</td>
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<tr>
<td></td>
<td></td>
<td>• Bacterial pathogens (<em>Bacillus thuringiensis</em>)</td>
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<td>• Fungal pathogens</td>
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<tr>
<td></td>
<td></td>
<td>• Endosymbionts (<em>Wolbachia</em>)</td>
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<tr>
<td><strong>Personal protection</strong></td>
<td><strong>Attractive Toxic Sugar Baits</strong></td>
<td><strong>Long lasting Insecticide treated bed nets</strong></td>
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<td></td>
<td></td>
<td>• Spatial repellents</td>
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<tr>
<td></td>
<td></td>
<td>• Long lasting indoor residual spraying (LLIRS)</td>
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<tr>
<td><strong>Genetic Modification</strong></td>
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Not infected

Asymptomatic
Residual transmission – Mind the Gap

Our new strategy requires new vector control tools that can deliver complete transmission prevention

**Current approach**  
*(Incomplete prevention)*

**Tools**
- Universal Long Lasting Insecticide Treated Nets (LLINs), Indoor Residual Spraying (IRS), as appropriate

**Delivery**
- Community delivery of LLINs, IRS

**Outcome**
- Residual transmission due to outdoor / early evening biters and insecticide resistance

**Accelerate to Zero**  
*(Complete prevention)*

**Tools**
- LLINs and IRS with new AIs, new tools to address outdoor biters, transformative tools for universal prevention

**Delivery**
- Modeling to determine context-adapted package of interventions
- Community delivery of ideal combinations of tools

**Outcome**
- Complete transmission prevention
We are working with partners to build a toolkit that addresses current limitations and "fills the gap"

Limitations of current toolkit

- LLINs and LLIRS are effective, but there is increasing evidence of insecticide-resistance
- We have no tools to effectively address outdoor biters

Our approach to "fill the gap"

- We will explore new AIs to reduce the threat of resistance
- We will broaden our portfolio to prevent outdoor biting
  - Novel vector control measures – spatial repellents and attractive toxic baits
  - Personal protective measures – protective clothing and personal repellents

While we are pursuing these projects, we do not have all the answers yet and we are committed to exploring novel vector paradigms, such as homing endonuclease genes, as well as transmission blocking drugs and vaccines
Thank You!
The Accelerate to Zero approach requires complete detection, cure and prevention, using new delivery strategies, to fill current gaps

**Current (Incomplete)**

- **Detect**: Current Rapid Diagnostic Tests (RDTs)
- **Cure**: Artemisinin Combination Treatments (ACTs)
- **Prevent**: Universal Long Lasting Insecticide Treated Nets (LLINs), Indoor Residual Spraying (IRS), as appropriate
- **Delivery**: Treatment at health care facility (HCF)
- **Outcome**: Gametocyte persistence and residual transmission

**Proposed interventions**

- **Detect**: Not being done
- **Cure**: Not being done
- **Prevent**: Universal LLINs, IRS, as appropriate
- **Delivery**: Community delivery of IRS, LLINs
- **Outcome**: Parasite reservoir persistence, residual transmission

**Accelerate to Zero (Complete)**

- **Detect**: Current RDTs
- **Cure**: ACT + PQ (or new tools, e.g. SERCap)
- **Prevent**: LLINs, IRS + new tools (including vaccines and chemophylaxis)
- **Delivery**: Treatment at HCF and community delivery of Targeted Parasite Elimination (TPE) strategies
- **Outcome**: Total parasite elimination (complete cure) and complete transmission prevention

**Proposed interventions**

- **Detect**: High sensitivity diagnostic
- **Cure**: ACT + PQ (or new tools, e.g. SERCap)
- **Prevent**: LLINs, IRS + new tools (including vaccines and chemophylaxis)
- **Delivery**: Community delivery of IRS, LLINs + TPE strategies
- **Outcome**: Total parasite elimination (complete cure) and complete transmission prevention

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1. Residual transmission is defined as the gap in transmission that remains in the community after LLINs and IRS, usually as a result of outdoor human–mosquito contact and early evening biting.
2. Targeted Parasite Elimination is a portfolio of strategies (e.g. focused Mass Drug Administration, Mass Screen and Treat, active case detection) pursued in a population depending on parasite prevalence, transmission level and other local conditions.