Results from a 2-year trial of 4 rounds of mass treatment for malaria
2014-2016

Southern Province, Zambia

Dr Busiku Hamainza

National Malaria Elimination Program, Zambia
Overview of MDA/fMDA campaign

Study design
- **Community randomized controlled trial** to assess impact of MDA/fMDA-with dihydroartemisinin-piperaquine (DHAp) vs. standard of care (control)
- 60 health facility catchment areas (HFCAs) randomized, stratified by higher (>10% PfPR) and lower (≤10% PfPR) malaria transmission
  - Study Area for MDA/fMDA Trial
    - population = ~330,000
    - Malaria = highest prevalence within Southern Province

Zambia population = ~16 million

Southern Province
- population = ~1.6 million
- Malaria = lowest prevalence nationally
MDA & fMDA trial in Southern Province, Zambia

- Trial from 2014-2016 in Southern Province to evaluate the contribution of mass-drug-administration (MDA) or focal (household) drug administration (fMDA) compared to control to further accelerate or “bend the curve” to achieve low levels of transmission that would facilitate case investigation as a final push for elimination.

- All areas got a standard “package of interventions” per the Ministry of Health:
  - Improved information to direct the implementation
  - Vector control: LLINs and targeted IRS (introducing Actellic insecticide)
  - Case management: facility staff and community workers (CHWs)
    - This led to ↑ care seeking, assured supplies of diagnostics and treatment
  - Case investigation of household/neighbors when possible (few enough cases to investigate)
All areas received improvements in the “intervention package” across Southern Province

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<tr>
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<tbody>
<tr>
<td><strong>Vector control</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Insecticide-treated mosquito net ownership</td>
<td>73%</td>
<td>73%</td>
<td>82%</td>
<td>78%</td>
</tr>
<tr>
<td>Indoor residual spraying (with Actellic*)</td>
<td>20%</td>
<td>15%</td>
<td>*36%</td>
<td>*48%</td>
</tr>
<tr>
<td>Any LLIN or IRS</td>
<td>79%</td>
<td>80%</td>
<td>*92%</td>
<td>*87%</td>
</tr>
<tr>
<td><strong>Case management</strong></td>
<td></td>
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</tr>
<tr>
<td>Febrile children seeking care/treatment</td>
<td>61%</td>
<td>70%</td>
<td>70%</td>
<td>79%</td>
</tr>
<tr>
<td>Care-seeking children going to CHW</td>
<td>4%</td>
<td>11%</td>
<td>15%</td>
<td>15%</td>
</tr>
<tr>
<td>Passive malaria cases reported by CHWs</td>
<td>5%</td>
<td>20%</td>
<td>50%</td>
<td>55%</td>
</tr>
<tr>
<td>Febrile RDT+ children recently treated</td>
<td>14%</td>
<td>56%</td>
<td>54%</td>
<td>58%</td>
</tr>
<tr>
<td>Febrile RDT+ adol/adult recently treated</td>
<td></td>
<td>51%</td>
<td></td>
<td>62%</td>
</tr>
<tr>
<td><strong>Training/supervision/quality improvement</strong></td>
<td>√</td>
<td>√</td>
<td>√</td>
<td></td>
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<tr>
<td><strong>Community engagement</strong></td>
<td>√</td>
<td>√</td>
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Treatment choice

- **DHAp (dihydroartemisinin+piperaquine)**
  - Currently the alternate first-line antimalarial treatment in Zambia for uncomplicated malaria
  - Excellent safety profile, comparable to AL
  - Offers extended prophylaxis period (~5 weeks at therapeutic level) post treatment administration compared to AL (~1.5 weeks)
  - Less complicated dosing: adult dose is 3 pills one time per day versus 4 pills twice daily for AL, suggesting improvements in adherence
Results

Compared to control, MDA had consistent and substantial impact after first 2 rounds

Lower transmission setting:
• 87% relative reduction in parasite prevalence in children
• 70% relative reduction in cumulative infection incidence (NS)
• 50% larger decline in confirmed case incidence

Higher transmission setting:
• 59% relative reduction in cumulative infection incidence
• 15% larger decline in confirmed case incidence (marginally significant)
Results

Compared to control, MDA had consistent and substantial impact after 4 rounds

Lower transmission setting:
• 72% relative reduction in parasite prevalence in children
• 61% relative reduction in cumulative infection incidence (NS)
• 50% larger decline in confirmed case incidence

Higher transmission setting:
• 49% relative reduction in cumulative infection incidence (marginally significant)
• 15% larger decline in confirmed case incidence (marginally significant)
Prevalence surface in study area (May 2014)
Prevalence surface in study area (May 2015)
Prevalence surface in study area (May 2016)
Prevalence surface in study area (May 2017)
5 (8%) of 60 HFCA had 0 infections
Prevalence by study arms (survey May 2015)

29 (48%) of 60 HFCA had 0 infections
Prevalence by study arms (survey May 2016)

32 (53%) of 60 HFCA had 0 infections

- All but 5 had <10% prevalence

Outlier – 14 infections among 42 kids (evidence An funestus remaining)
## Deaths and hospital admissions 2014–2016

<table>
<thead>
<tr>
<th>Year</th>
<th>Study site</th>
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<th>Non-study site in Southern</th>
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<tbody>
<tr>
<td></td>
<td>Deaths</td>
<td>Hospitalizations</td>
<td>Deaths</td>
<td>Hospitalizations</td>
</tr>
<tr>
<td>2014</td>
<td>32</td>
<td>1,825</td>
<td>87</td>
<td>3,547</td>
</tr>
<tr>
<td>2015</td>
<td>5</td>
<td>787</td>
<td>36</td>
<td>1,432</td>
</tr>
<tr>
<td>2016</td>
<td>1</td>
<td>398</td>
<td>11</td>
<td>1,301</td>
</tr>
<tr>
<td>Change 2014→2016</td>
<td>↓97%</td>
<td>↓78%</td>
<td>↓87%</td>
<td>↓63%</td>
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So what happened?
What we know/observed

- Very high IRS and fresh LLIN coverage achieved
  - 50% IRS (Actellic) coverage in 2016
  - Vector population shifted from primarily *An funestus* to *An arabiensis* (less competent vector)

- Lots of investment was made in community mobilization and capacity strengthening for malaria elimination

- Increasing access to diagnosis and treatment via community case management (CCM)
  - Coverage of appropriate treatment among children with malaria increased from 14--30% before community case investigation (in 2012) to 58% in 2016

- Improved surveillance occurred province wide, including at community level

- 336,821 courses of DHAp distributed across 4 rounds in mass treatment areas
What we do not know/cannot quantify at this time

• Specific reasons for large decline in malaria in control areas

  ▪ Still working to directly quantify attribution or contribution of exposure to interventions other than MDA to declines in malaria outcomes

  ▪ We expect that the greater than expected benefit reflects a combination of overall enhanced delivery of the full package of malaria interventions plus some potential contribution from “community effect” of the MDA/fMDA.

• Whether we could have achieved the same results with more efficient approaches to MDA (E.g., single high-coverage round, less training/supervision, community engagement, alternative to house-to-house delivery, no RDTs)

• Can we maintain these gains, and achieve elimination, going forward with good vector control and case management/case investigation?
MALARIA FREE ZAMBIA

MALARIA ENDS WITH ME.
Thank you