Vector resistance studies in Uganda in relation to insecticide use in public health and agriculture

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RBM 9th VCWG Meeting, Geneva
20 February 2014
Pyrethroid Resistance Management Project

Objectives

- To evaluate the role of IRS using carbamates or organophosphates in pyrethroid resistance management to prolong the usefulness of LLINs
- To understand the role of insecticides used in public health and agriculture in the spread of vector resistance
- To understand the impact of resistance on effectiveness of interventions
- To support MOH to develop resistance management strategies to maintain coverage of effective malaria interventions
## IRS target districts

<table>
<thead>
<tr>
<th>Year</th>
<th>Implementer</th>
<th>No Districts targeted IRS</th>
<th>Insecticide used</th>
</tr>
</thead>
<tbody>
<tr>
<td>2006</td>
<td>PMI (RTI)</td>
<td>1 District South</td>
<td>Lambda-cyhalothrin</td>
</tr>
<tr>
<td>2007</td>
<td>PMI (RTI)</td>
<td>2 Districts South,</td>
<td>Lambda-cyhalothrin</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3 Districts North</td>
<td></td>
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<tr>
<td>2008</td>
<td>PMI (RTI)</td>
<td>5 Districts North</td>
<td>DDT</td>
</tr>
<tr>
<td></td>
<td>NMCP</td>
<td></td>
<td>Alpha-cypermethrin</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1 District East</td>
<td></td>
</tr>
<tr>
<td>2009</td>
<td>PMI (RTI/Abt)</td>
<td>5 Districts North</td>
<td>Alpha-cypermethrin</td>
</tr>
<tr>
<td>2010</td>
<td>PMI (Abt)</td>
<td>10 Districts* North</td>
<td>Alpha-cypermethrin</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Bendiocarb</td>
</tr>
<tr>
<td>2011</td>
<td>PMI (Abt)</td>
<td>10 Districts* North</td>
<td>Bendiocarb</td>
</tr>
<tr>
<td>2012</td>
<td>PMI (Abt)</td>
<td>10 Districts* North</td>
<td>Bendiocarb</td>
</tr>
<tr>
<td></td>
<td>NMCP</td>
<td>1 District East</td>
<td></td>
</tr>
</tbody>
</table>

* In 2010, large districts underwent district subdivision
Historical distribution of LLINs per site (2001-2011)
Study site selection

45 sites in 3 groups of districts:

**Group A** Districts that had undergone several rounds of IRS and received LLINs (Apac, Gulu, Pader)

**Group B** Districts where LLINs had been distributed but no IRS had taken place (Kayunga, Kiboga, Mbale)

**Group C** Districts that had not received IRS or LLINs as part of a large campaign (Bugiri, Mayuge, Soroti)

During our survey in September of 2012, LLINs were distributed in Mayuge and Bugiri districts as part of a LLIN mass distribution campaign. In Soroti, nets were distributed a couple of months before the survey.
Study components

- Entomological surveys
- Household and malirometric surveys
- Health facility-based morbidity studies
- Intensity of insecticide use in public health
- Intensity of insecticide use in agriculture
Entomology survey

- WHO susceptibility tests

- Pyrethrum Spray Catches (PSC)
  - 12 houses in each site x 2 rounds

- Molecular analysis:
  - Species
  - Sporozoite rates
  - Molecular markers of resistance
Household and maliometric surveys

- Household interviews
  - Ownership of ITNs
  - Use of ITNs by household members
  - Spray status of houses
  - Socio-economic status

- Malaria infection rates
  - Infection rates linked with use of interventions by households and household members
Health facility-based morbidity studies

- Trends in morbidity from a geographically defined area (health centre data) over about 10 years:
  - How is the trend associated with the intensity of use of interventions?
  - Is the trend of malaria in any way related to variation in resistance levels?
Intensity of insecticide use: public health

- Use of IRS over the years
- ITNs distributed over the years
- Current use of IRS
- Current use of LLINs
Intensity of insecticide use: agriculture

• Agricultural chemicals supplied at district and sub-district levels

• Agricultural offices

• Pesticide suppliers/shops (Agro-dealers)

• Use of agricultural pesticides by farmers (household surveys)
Malaria prevalence (Sep 2012)

- Group A: 5%
- Group B: 5%
- Group C: 25%

Malaria prevalence
Malaria prevalence by age

- Group A
- Group B
- Group C
LLIN use during survey

![Box plots showing mean number of LLINs used per household and proportion of LLINs used. The plots are labeled A, B, and C.]
Entomology Results
Indoor resting densities of *A. gambiae* s.l. and *A. funestus* s.l.
Susceptibility tests

- Insecticide-susceptibility tests were performed following WHO guidelines
- Deltamethrin, permethrin and bendiocarb
- *A. gambiae* s.l. and *A. funestus* s.l.
- The main challenge was low mosquito densities
Susceptibility tests

- Resistance status determined according to current WHO guidelines:

  **S**: susceptible populations
  (≥98% mortality: GREEN)

  **SR**: suspected resistant populations
  (90-<98%: ORANGE)

  **R**: resistant populations
  (<90% mortality: RED)
Resistance mechanisms Uganda

- Metabolic resistance *An. funestus* (Morgan et al. 2010)

- L1014S *kdr* mutation observed in *An. gambiae* s.s., less common in *An. arabiensis* (Verhaegen et al. 2010, Ramphula et al. 2009, Maweji et al. 2012)

- Ace-1R mutation absent *An. gambiae* s.s. (Ramphula et al. 2009)

- Metabolic and target site resistance testing ongoing by ABT/PMI/CDC
Tentative conclusions

• Resistance to pyrethroids is widespread in Uganda

• Bendiocarb resistance was not detected in any of the IRS districts

• The apparent reversion of pyrethroid resistance in Apac requires confirmation

• Apart from Apac, in the other bendiocarb-sprayed districts, pyrethroid resistance does not seem to have reverted

• In the districts with less historical coverage of nets, malaria prevalence is relatively higher compared to areas with high ITN coverage – this indicates that nets seem to be providing protection despite widespread resistance

• Next steps: molecular analysis and further data analysis
Acknowledgements

• Study participants
• Vector Control Officers and field staff
• Ministry of Health/ NMCP
• Malaria Consortium staff
• UK Aid
www.malariaconsortium.org

Thank you