Shifting the paradigm on evaluating interventions

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Project BITE is working to shift the paradigm on protection from mosquito borne diseases

1. Understanding gaps in protection
2. Taking a staged approach to intervention evaluation
3. Evaluating interventions based on their mode of action
Understanding the problem and defining the question

Cambodia: Persistent transmission among forest goers, forest dwellers, and forest rangers

How do we target and tailor our intervention strategies to forest malaria transmission?
Understanding gaps in protection

Where and when are people getting exposed to mosquito bites? Answering this question allows for:

- Targeting and tailoring
- The use of multiple intervention paradigms and products
Definition of “gap in protection”

Used to describe a circumstance when an individual and/or household is potentially exposed to malaria infection (i.e., an infective mosquito bite) due to a lack of effective and/or adequate protective or preventive intervention in place to reduce that exposure to mosquito bites.
Forest transmission as an example

Where are people spending time?

What are they doing?

When are the mosquitoes biting?

What products fit in these spaces and times?
Forest pack that addresses each / all spatial and temporal exposures

<table>
<thead>
<tr>
<th>Exposure space and activity</th>
<th>Intervention type</th>
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</table>
| Temporary structure (sleeping, resting) | - Passive Volatile Pyrethroid Spatial Repellent (VPSR)  
  - Spatial Repellent spray  
  - Treated clothing  
  - Topical repellent |
| Outside temporary structure (eating, resting, work) | - Passive VPSR  
  - Spatial Repellent spray  
  - Treated clothing  
  - Topical repellent |
| Forest (work, foraging) | - Treated clothing  
  - Topical repellent |
Taking a staged approach to intervention evaluation

- WHO considerations – evidence-based decision-making
- Responsible and ethical
- Cost effective
- Allows the evaluation of multiple paradigms and products
- Allows for targeting and tailoring
- Allows community input
- Understanding remaining gaps in protection
Staged approach to evidence generation within Project BITE


- **Stage 1**: Semi-field studies: entomological protective efficacy and modes of action (Thailand)
- **Stage 1-2**: Formative assessment and user acceptability studies with target populations (Cambodia)
- **Stage 2**: Entomological field study: entomological protective efficacy with wild vector populations (Cambodia)
- **Stage 3 - 4**: Implementation research: acceptability, appropriateness, reach, use, operational feasibility, cost, willingness-to-pay
- **Stage 3 - 4**: Impact assessment (future work): epidemiological protective efficacy, cost-effectiveness
- Transmission modeling
Evaluating interventions based on their mode of action – secondary endpoints

- Fair to the intervention
- Targeting and tailoring
- Understanding intervention-related gaps in protection
### Secondary endpoints

<table>
<thead>
<tr>
<th></th>
<th>Immediate</th>
<th>24-hours</th>
<th>48-72 hours</th>
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<tbody>
<tr>
<td>Seek</td>
<td>Host</td>
<td>Rest</td>
<td>Alive 48h</td>
</tr>
<tr>
<td>Land</td>
<td>Blood</td>
<td>Alive 24h</td>
<td>Alive 72h</td>
</tr>
<tr>
<td>Blood feed</td>
<td>Rest</td>
<td>Alive 24h</td>
<td>Eggs</td>
</tr>
</tbody>
</table>

The diagram shows the process from immediate to 24-hours, and then 48-72 hours, including stages such as seeking, landing, blood feeding, resting, and various survival stages.
Outcome measures and associated MoAs (Thailand)

INCREASED RISK
- Diversion

PERSONAL PROTECTION
- Repellence
  - HLC Landing inhibition
- Disarming
  - HLC landing + no feeding
  - Knock down
  - Resting (recapture) + no feeding

COMMUNITY PROTECTION
- Feeding inhibition
  - Resting (recapture) + no feeding
- Mortality
  - 24 hour mortality

NOT just landing!!!
Paradigms integrated:
- Understanding gaps in protection
  - Cambodia forest transmission
  - Product MOAs fit these gaps
- Taking a phased approach
  - Problem / question understood
  - Controlled SFS data supports evaluation
- Evaluating interventions based on their mode of action – secondary endpoints
  - Not just biting
  - Community impact with multiple interventions
Results from the entomological field study

Figure 1. Risk of mosquito landing for each intervention compared to control

- All six interventions significantly reduced risk of landing by at least 50%
- The VPSR1 alone and the combination of three products reduced mosquito landings by nearly 95%

Figure 2. Cumulative Anopheles captures, by intervention or control

I1 – VPSR1 new
I2 – ETO x0wash CIVILIAN (short sleeves, long trousers) + PICARIDIN20%
I3 – ETO x20wash RANGER + PICARIDIN20%
I4 – Control
I5 – ETO x0wash RANGER + PICARIDIN20%
I6 – ETO x20wash CIVILIAN (short sleeves, long trousers) + PICARIDIN20%
I7 – Combined interventions: PE (new) + ETO x0wash CIVILIAN + PICARIDIN20%
Next steps for Project BITE

1) Understanding gaps in protection

2) Taking a staged approach to intervention evaluation
   a) SFS (complete), b) Field (Complete)

3) Evaluating interventions based on their mode of action
   a) SFS (learning by doing), b) Gaps in protection,
Implementation research in Cambodia
Sep 2022 – Feb 2023

- Distribution by local government / implementation partners (high transmission Sep – Dec 2022)
  - Forest pack:
    - topical repellent and passive VPSR; etofenprox treatment for clothing
    - delivered by local government / implementer
  - Active *P. falciparum* hotspots (Cambodia)

**Primary aim:**
To assess intervention reach, fidelity, acceptability, appropriateness, coverage, and use of BITE tools among high-risk populations

**Secondary aims:**
Exposure risks, safety, gaps in protection, economic studies, operational feasibility, facilitators and barriers to potential scale-up