Evaluation of the effectiveness of topical repellent distributed by village health volunteer networks against *Plasmodium* spp. infection in Myanmar: A stepped-wedge cluster randomised trial


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An open stepped wedge cluster-randomised controlled trial to test effectiveness of repellent distributed by village health volunteer (VHV)

- **Primary Objective:** To determine effectiveness of distributing repellent to villagers through VHV in high risk geographically isolated populations to reduce the incidence of *P. falciparum* and *P. vivax* infections.
- **Primary outcome:** Incidence of *P. falciparum* and *P. vivax* infections (in village) by Rapid Diagnostic Test (RDT)
- **Secondary outcome:** Incidence of PCR detectable *Plasmodium* spp. infections (from dried blood spot)
- **Intervention:** Mosquito repellent cream (N,N-diethyl-benzamide – 12% w/w, cream)

Townships included in trial

- Conducted in 2015 - 16
- Delivered malaria services to geographically isolated populations:
  - Early diagnosis; quality treatment, behavior change communication, malaria prevention
- 116 villages in Bago, Kayah, Kayin selected based on Myanmar NMCP data
- Total population ~28,000 people
Malaria testing results

• **Primary outcome (RDT)**
  • n=32,194 RDT tests
  • average 2146 tests per month
  • average 14 months of observations per village
  • On average per village:
    - 282 total tests
    - 20 tests per month
  • n=50 *Plasmodium* spp. infections (.16%).

• **Secondary outcome (PCR)**
  • n=13,157 dried blood spot PCR tests
  • n=419 *Plasmodium* spp. infections (3%)
  • n=20 RDT
  ➢ PCR detected 21x the infection

*Villages withdrawn for security reasons*
Does repellent protect against malaria?
Does repellent protect against both species equally?

Repellent protects against malaria
Repellent does not protect

**Odds Ratio**

- **RDT**
  - ALL species
- **PCR**
  - ALL species
  - *P. falciparum*
  - *P. vivax*

**A** Repellent protected against
- 75% of RDT-detectable infections
- 18% of PCR-detectable infections
- 33% of *P. falciparum* infections
- 0% of *P. vivax* infections

- Repellent distribution significantly reduced *P. falciparum* but not *P. vivax* infections (which can also be caused by relapses)
- Indicates that repellent can protect against new *Plasmodium* spp. infections

GLMM model fixed part: Repellent distribution (dummy indicator, monotonic time-varying), Time (continuous linear), Season (dummy indicators, time-varying, ‘cool’, ‘hot’ and ‘rainy’)
Random part: Village (intercept), Month (intercept), Repellent distribution (slope)
Is repellent similarly effective across villages of varying malaria prevalence?

Malaria prevalence varies according to village and decreases over time

- Repellent reduced PCR-detectable *Pf* infection by 33% regardless of prevalence of malaria in a village
- Indicates that repellent will be effective at reducing the malaria infectious reservoir regardless of the prevalence of malaria at baseline and across time

**Figure 1: Marginal and village specific probabilities (PCR) by month, season and repellent status from GLMM**
Is repellent similarly effective across risk groups (forest dwellers/migrants)?

<table>
<thead>
<tr>
<th></th>
<th>PCR (AOR) (95%CI)</th>
<th>P</th>
<th>P. falciparum (ARRR) (95%CI)</th>
<th>P. Vivax (ARRR) (95%CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Resident</td>
<td>0.65 (0.44-0.96)</td>
<td>0.18</td>
<td>0.58 (0.38-0.88)</td>
<td>1.17 (0.58-2.36)</td>
<td>0.73</td>
</tr>
<tr>
<td>Forest Dweller</td>
<td>0.90 (0.63-1.29)</td>
<td>0.74</td>
<td>(0.45-1.22)</td>
<td>1.49 (0.79-2.82)</td>
<td></td>
</tr>
<tr>
<td>Migrant</td>
<td>1.13 (0.62-2.06)</td>
<td>0.77</td>
<td>(0.35-1.72)</td>
<td>2.05 (0.70-5.95)</td>
<td></td>
</tr>
</tbody>
</table>

AOR = Adjusted Odds Ratio; ARRR = Adjusted Relative Risk Ratio

Was repellent more effective against malaria when it was used more?
• Trend for increasing protection with increasing repellent use
• Caveat: Reported by VHV, large 95%CI

<table>
<thead>
<tr>
<th>Factors</th>
<th>Adj Odds Ratio</th>
<th>95% CI</th>
<th>p-value</th>
<th>% Reduction in malaria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intervention</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No repellent</td>
<td>ref.</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Repellent – monthly</td>
<td>1.54</td>
<td>0.14,16.7</td>
<td>0.722</td>
<td>0%</td>
</tr>
<tr>
<td>Repellent – weekly</td>
<td>0.33</td>
<td>0.01,22.2</td>
<td>0.604</td>
<td>66%</td>
</tr>
<tr>
<td>Repellent – daily</td>
<td>0.05</td>
<td>0.00002,10.3</td>
<td>0.272</td>
<td>95%</td>
</tr>
</tbody>
</table>

GLMM model fixed part: Repellent distribution (dummy indicator, monotonic time-varying), Time (continuous linear), Season (dummy indicators, time-varying, ‘cool’, ‘hot’ and ‘rainy’), Repellent use as shown
Random part: Village (intercept), Month (intercept), Repellent distribution (slope)
Summary

- Repellent distributed by VHV reduces the odds of
  - Routinely detected RDT infections by 75%
  - PCR-detectable infections (by 33%) which contribute to ongoing malaria transmission
- Repellent specifically protected against new *P. falciparum* infections
- For PCR infections - low heterogeneity of the effect of repellent across villages
- Repellent as an intervention to reduce malaria is applicable across a range of transmission settings, and populations


https://journals.plos.org/plosmedicine/article?id=10.1371/journal.pmed.1003177
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