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
Does repellent protect against malaria?
Does repellent protect against both species equally?

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
Is repellent similarly effective across risk groups (forest dwellers/migrants)?

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

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

| Factors     | Adj Odds Ratio | 95% CI   | p-value | % Reduction in malaria |
|-------------|----------------|----------|---------|------------------------|
| Intervention|                |          |         |                        |
| No repellent| ref.           | -        | -       |                        |
| Repellent – monthly | 1.54 | 0.14,16.7 | 0.722 | 0%                     |
| Repellent – weekly   | 0.33 | 0.01,22.2 | 0.604 | 66%                    |
| Repellent – daily    | 0.05 | 0.0002,10.3| 0.272 | 95%                    |

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

**Effectiveness of repellent delivered through village health volunteers on malaria incidence in villages in South-East Myanmar: a stepped-wedge cluster-randomised controlled trial protocol**

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