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**consortium**  
*disease control, better health*

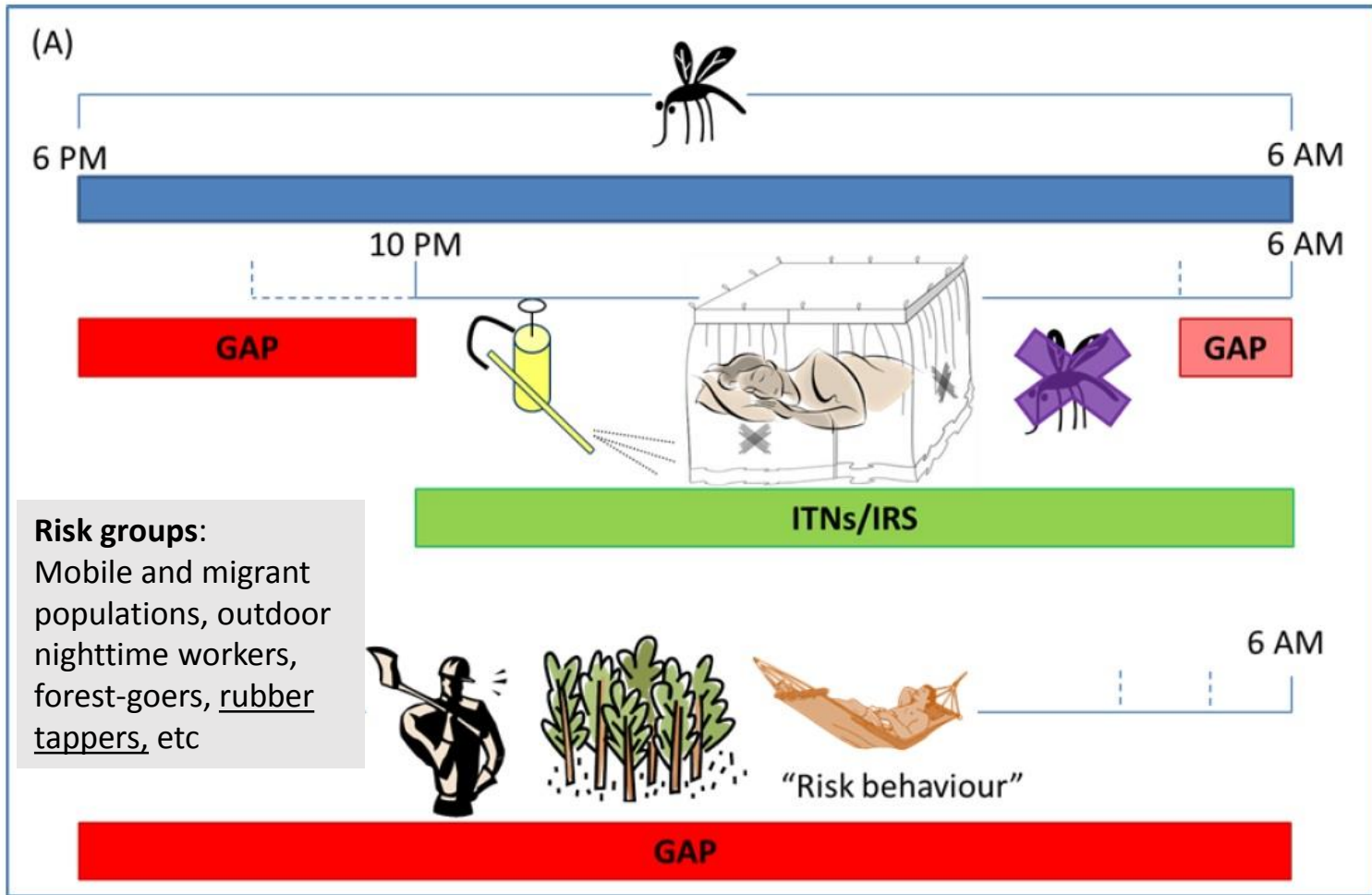
# Acceptability and protective efficacy of insecticide-treated clothing for outdoor malaria prevention among rubber tappers in Myanmar

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# Background I

- Insecticide-treated nets (ITNs)/long lasting insecticidal nets (LLINs) and indoor residual spraying (IRS) have been shown to be highly effective against malaria infection and disease and are a key component of the national malaria control programme in Myanmar
- However, even with high coverage of core interventions, a ‘protection gap’ can exist and lead to residual transmission of malaria:



**Figure 1.** Protection gap when only indoor insecticide-based vector control methods applied. *Adapted from Durnez, L. & Coosemans, M. (2013).*

# Background II

- Rubber tapping takes place throughout the night, coinciding with low and peak biting times of *Anopheles dirus* and *An. minimus*<sup>2,3</sup>. Wearing some form of protective clothing for rubber tapping is already an occupational norm (Shafique, 2013) and therefore may not require as much behavioural change as other interventions
- Wearing permethrin insecticide-treated clothing (ITC) has been shown to reduce *Aedes* biting rates by >90%<sup>4</sup> and impact malaria transmission<sup>5</sup>. However, only limited application so far, by military and recreational markets<sup>6,7</sup>
- More information needed to ensure success of ITC as a strategy, specifically on user perception, acceptability for personal protection and how acceptability affects use and adherence to the clothing
- This will help inform policymakers on targeted distribution to mobile and migrant populations (MMPs)



A rubber tapper wearing typical clothing stained from rubber latex (Source: Shafique, 2013)

# Operational research objectives

- **Primary objective:** To determine preference and acceptability of ITC by rubber plantation workers for night-time work
- **Secondary objectives:**
  - Investigate user perceptions related to ITC use to inform future social marketing or ITC distribution programmes
  - Investigate whether preference and acceptability of ITC change over a short and medium-term period
  - To assess bio-efficacy of ITC [versus non-treated clothing (NTC) control] worn by rubber tappers  
[note: study is on-going]

# Study design

# Study area

- Thanbyuzayat has an estimated population of 145,586 (IOM, 2012), of which 18,291 (12.6%) are migrants and approximately 33% are involved in a high risk work environment for malaria (forest-related, plantation and hillside farming, mining, hydropower plants, etc)
- All 10 townships in Mon State are classified as Tier 1\* under the MARC framework
- Malaria morbidity rate of 18.4 per 1000 population in Thanbyuzayat (IOM, 2012)
- Annual parasite incidence of 13.68 per 1000 population in Wae Kha Mi catchment area (WHO, 2012)
- Targeting these high risk populations is essential to the effectiveness of vector control measures (MDG6 & Objective 3 of MARC 2011-2015)



Source: [myanmar.threeland.com](http://myanmar.threeland.com)

\*Tier 1: Credible evidence of artemisinin resistance, where an immediate, multifaceted response recommended to contain or eliminate resistant parasites as quickly as possible (MOH & WHO, 2011)

# Study design

- Two arm, cluster-randomised non-inferiority crossover trial to investigate **acceptability and preference** of insecticide-treated clothing (ITC) versus non-treated clothing (NTC) in Wae Kha Mi catchment area, Thanbyuzayat, Mon State
- Cluster = rubber plantation with at least 8 HHs
- Sample size powered to allow a pairwise comparison between ITC and NTC
- Crossover design randomises each cluster to the sequence in which the two types of clothing (ITC/NTC) would be tested, allowing each participant to act as their own control and eliminating confounding from the comparison, provided no carry-over effect, which is unlikely
- Assuming acceptability of NTC is 95% and a maximum difference in acceptability between the groups is 10%,  $H_0 =$  the acceptability ratio is less than 0.89 (equivalent to difference of greater than 10%), while  $H_1 =$  that the acceptability ratio is greater than or equal to 0.89 (difference is less than or equal to 10%)
- Sample recruited such that in each ARM there was a minimum of 8 clusters x 12 individuals per cluster = 96 individuals, in order to have >80% power to reject the null hypothesis, assuming intraclass correlation coefficient due to clustering of individuals = 0.002 and alpha = of 0.05



# Intervention: ITC, NTC

Type	Material and size	Insecticide treatment
ITC	Long sleeve cotton shirt (dark blue) Cotton trousers (black) Myanmar-made 3-4 sizes for males and females	Treated in Insect Shield factory, 0.52% w/w $\pm$ 10% permethrin and a polymer (EPA-registered and WHO-approved)
NTC	Long sleeve cotton shirt (dark blue) Cotton trousers (black) Myanmar-made 3-4 sizes for males and females	Untreated regular garment



A proportion of ITC and NTC sets had stitched-on patches that were systematically removed at each follow-up round and sent for protective efficacy bioassays in Mahidol and arctec labs

**Social  
mapping,  
screening,  
randomisation**

Assessed for eligibility (n=811)  
Baseline survey  
Screening

**Inclusion criteria:**

- Adult (greater than or equal to 18 years of age)
- Head of household and/or fulltime rubber tapper
- Capable of giving informed consent to participate
- Intend to stay in study area for at least 5 months from enrollment

**Exclusion criteria:**

- History of skin allergy or eczema or previous adverse reaction to ITN/LLIN
- Pregnant or breastfeeding
- Likely to be absent from study area during study period
- Unable or unwilling to comply with study protocol



Excluded (n=577)

**Baseline**  
Jan 2015

Eligible participants (n=234)  
Pre-distribution survey; FGDs



16 clusters



Feb 2015

Cluster randomisation to study arms  
Distribution of clothing (ITC/NTC) - double-blind

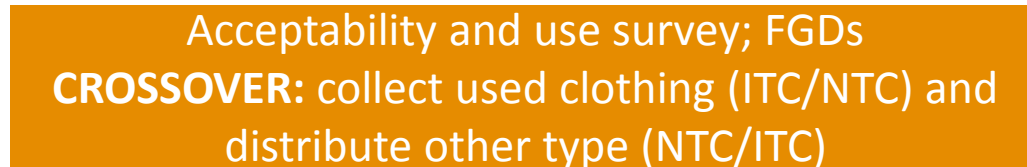
Participants instructed not to use bleach or dry clothing in direct sunlight as can reduce potency of insecticide



14 days

Supervisory visit

**First follow-up (FU1)**  
Feb-Mar 2015



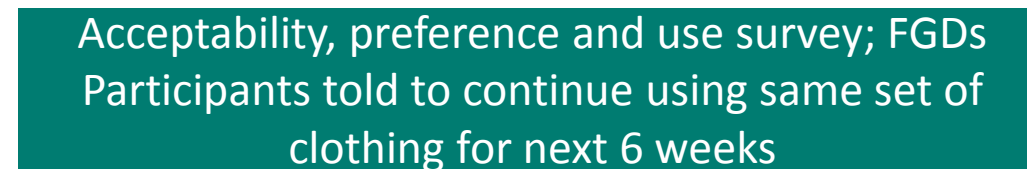
*First sets of patched clothing distributed*



14 days\*

Supervisory visit

**Second follow-up (FU2)**  
Mar 2015



*First set of patches removed; sent for bioassays*



6 weeks

Supervisory visit

**Third  
follow-up  
(FU3)**

May 2015

Acceptability, preference and use survey  
FGDs; IDIs

*Second set of patches  
removed and sent for  
bioassays*

Arm 1 participants  
remaining (n=79)

Arm 2 participants  
remaining (n=78)

END

Loss to follow up: n= 77 (Arm 1, n = 37; Arm 2, n = 40)

*Within acceptable attrition limits of the sampling  
framework*

**Analysis**

Quantitative:

Non-inferiority analysis performed on survey data from FU1 and FU2 using ordinary least squares (OLS) regression;

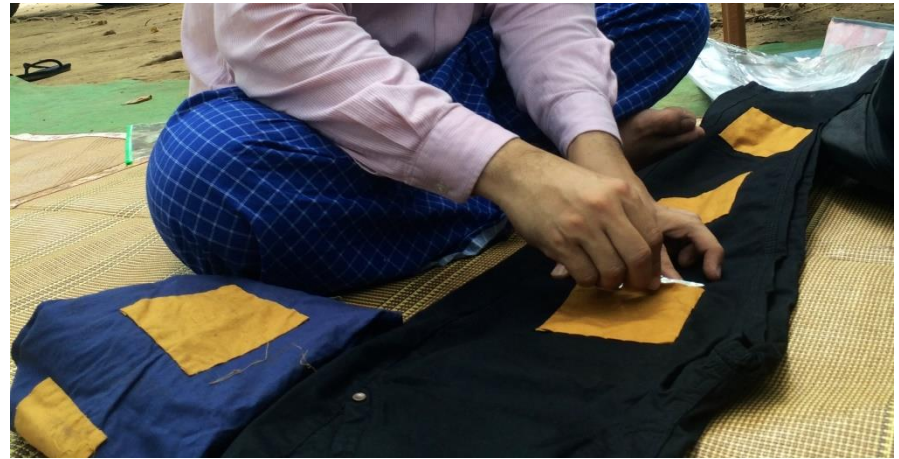
Chi-squared and Spearman rank correlation analysis performed on bioefficacy data

Qualitative:

Thematic analysis and hand-coding of qualitative transcripts.

# Ethics approval

- Ethical clearance for the 'Preference and Acceptability of ITC' study was obtained from Ethics Review Committee on Medical Research Involving Human Subjects, Department of Medical Research (Lower Myanmar) and Ministry of Health, Government of the Republic of the Union of Myanmar (Letter No. 54/Ethics 2014)
- Ethical clearance for the 'Evaluation of the protective efficacy of permethrin-treated clothing in the laboratory' was obtained from the Ethics Committee of the Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand (MUTM 2015-027-01)



*Removing test patches of ITC/NTC from the worn clothing in the field*



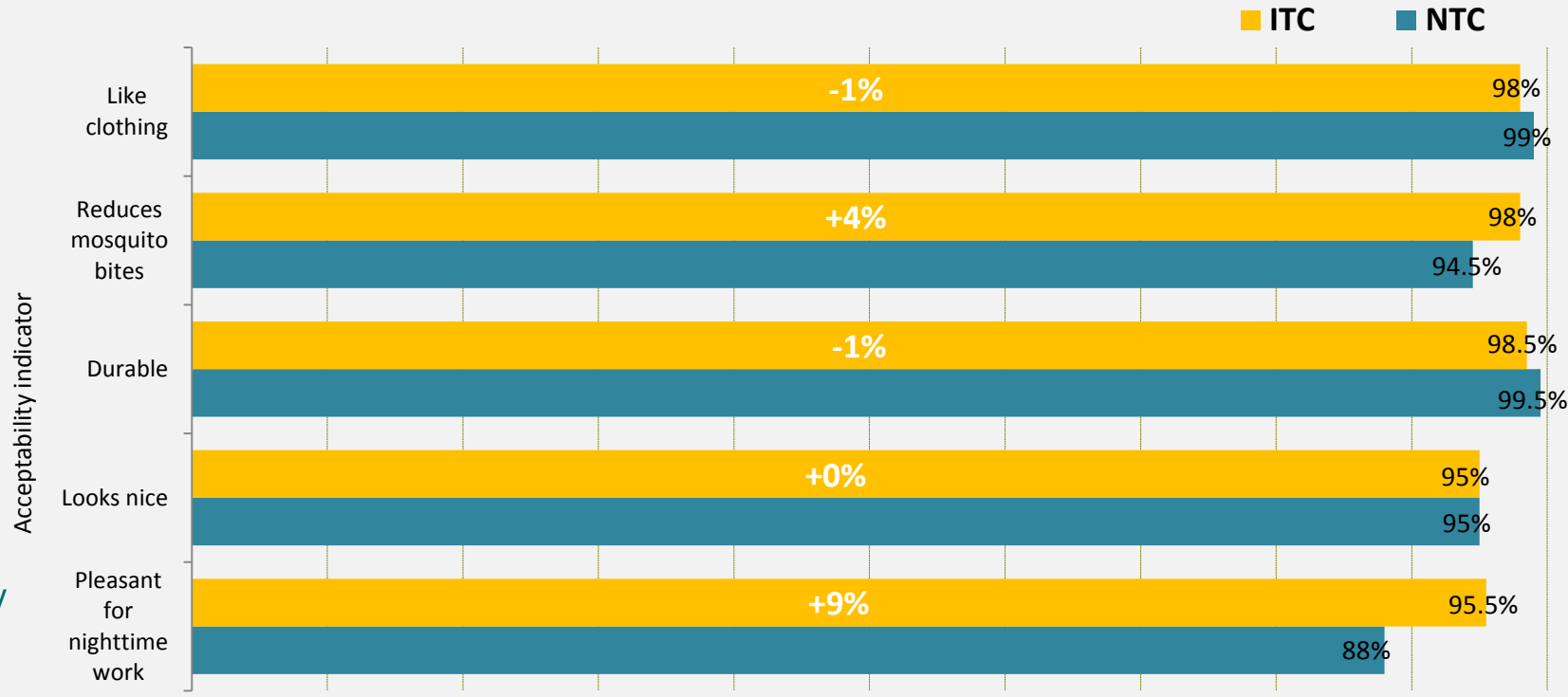
*Left: Test patch of worn clothing*



*Right: Performing WHO cone tests on patches of worn ITC/NTC*

# Results

# Acceptability of ITC versus NTC



Mean absolute difference, 95% CI for indicators: Like clothing: 0.0 [-3.3, 3.1]; Reduces mosquito bites: 0.0 [-7.6, 7.4]; Durable: 1.0 [-1.9, 3.8]; Looks nice: -1.2 [-7.0, 4.7]; Pleasant to wear for night-time work: 4.7 [-2.8, 12.2]

Figure 2. Non-inferiority analysis and mean percentage reporting “yes” across clothing distribution rounds 1 & 2: acceptability indicators. Non-inferiority shown for all displayed indicators.

Approximately 75% of respondents said they wore the distributed clothing (ITC or NTC) every night for work in the rubber plantation (across FU1 and FU2) [NB non-inferiority not shown].

$MAD = \frac{1}{n} \sum_{i=1}^n |x_i - \bar{x}|$  Mean absolute difference, where n = number of observed values, x-bar = mean of the observed values, and x<sub>i</sub> = individual values. ITC was non-inferior to NTC for: Like the clothing, Reduces mosquito bites, Reduces amount of mosquitoes indoors, Provides warmth, Looks nice, Keeps other clothing clean, Durable, Pleasant to wear for nighttime work. ITC was not non-inferior to NTC for: Reduces amount of mosquitoes outdoors, Easy to keep clean. Note: indicators reflect participants’ perceptions in response to structured questions.

# Acceptability: Qualitative findings

## Overall acceptability

*“After wearing the [ITC], no other measures are needed. It is perfect.”*

- Female rubber tappers, 25, 46

## Perceived reduction in mosquito bites

*“Before distribution of clothing, a lot of mosquitoes are over my head. They bite my ears and legs. Now, no mosquitoes are here. It is due to the insecticide treated clothing.”*

- Female rubber tapper, 46

*“We were moving and working while wearing those sets [of clothing]. The mosquitoes were crying and flying around us but didn’t bite us.”*

- Male rubber tapper, 27

## Pleasant to wear for night-time work

*“The texture of the distributed clothing is good. I can sit and stand freely.”*

- Male rubber tapper, 27

## Durability

*“Sewing lines are strong and good.”*

- Male rubber tapper, 33



# Protective efficacy of ITC

- WHO cone tests performed to assess % knockdown and % mortality of *An. dirus* on ITC and NTC patches
- Data on number of washes was collected in follow-up surveys
- No correlation between number of washes and % KD or % mortality
- 17.3% KD of *An. dirus* on worn ITC compared to 0% KD on worn NTC over 28 days of high usage and washing ( $p < 0.01$ )
- 1.27% mortality of *An. dirus* for worn ITC, compared to 0% mortality for worn NTC ( $p < 0.95$ )

Table 1. Spearman Rank correlation analysis between number of washes<sup>†</sup>, % KD at 60 minutes and % mortality at 24 hours after a 3 minute exposure of lab-reared *An. dirus* on worn ITC (n=43) for shirts and pants using WHO cone tests.

	No. of washes*	% KD	% mortality
No. of washes*	1		
% KD	0.10	1	
% mortality	-0.06	0.52*	1

\*Statistically significant; Spearman rank correlation

<sup>†</sup>Assumes shirt and pants in a set were washed the same number of times. Clothing was worn by participants over a period of 28 days. Clothing was washed by study participants using water + either soap or detergent.



# Conclusions and recommendations

# Conclusions and recommendations

- The four-week interval of ITC use demonstrated in this study  $\approx$  14-28 washes (assuming washing daily or every other day); percent mortality was well below the  $\geq 80\%$  mortality bioassay criterion set by WHO for LLINs<sup>5</sup>
- Given that Insect Shield technology is EPA-registered to last through 70 launderings, separate validation of our results are needed [and ongoing]. A reassessment of the maximum number of launderings clothing used for intensive occupational purposes can withstand is recommended.
- Retreatment of clothing is not a viable option for rubber tappers when durability of the clothing wanes rapidly in the short-term (damage from rubber latex stains); another long-lasting method, e.g. micro-encapsulation technique, may be needed (right, Yao et al. 2015)

<sup>5</sup> WHO (2013). Guidelines for laboratory and field-testing of long-lasting insecticidal nets.

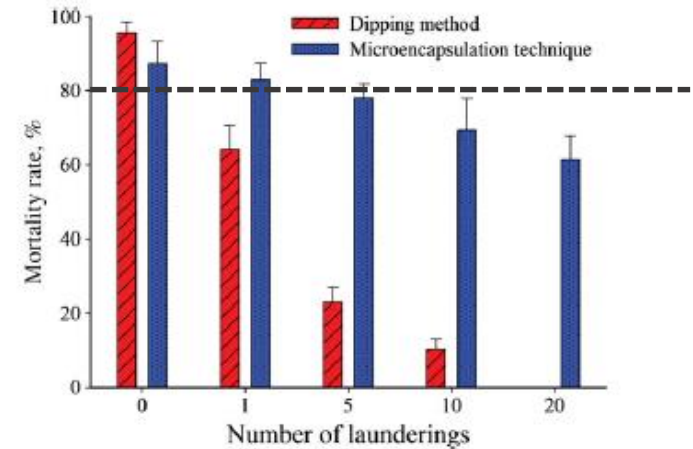


Fig. 4. Laundering-related insecticidal activity against *Stegomyia albopicta* of fabrics impregnated by the dipping or microencapsulation technique, respectively.

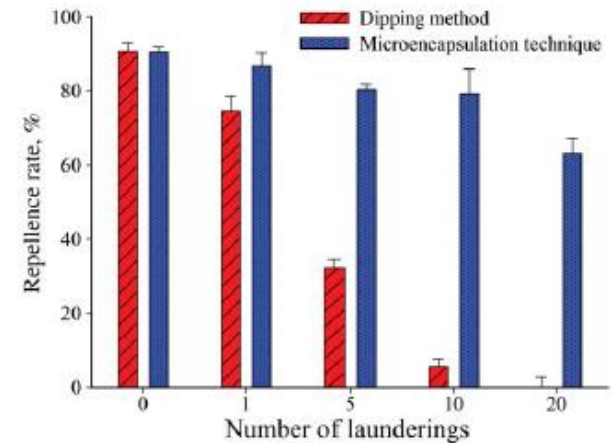


Fig. 5. Laundering-related repellent efficacy against *Stegomyia albopicta* of fabrics impregnated by the dipping or microencapsulation technique, respectively.

# Conclusions and recommendations

- Adherence: Improve clothing comfort and fit (temperature, thickness, size) to ensure routine wearing of clothing
- Adherence: May increase if participants given two sets of clothing to wear and different, season-appropriate sets of clothing (thick for winter, thin for summer)
- Protective efficacy: Validation of bioassay tests on clothing patches are on-going in Mahidol University and *arctec* labs. May need to control for other factors such as water source, washing technique, soap/detergent type, drying technique, extended daytime use of clothing, which may explain large variability in results
- Create demand for the clothing through BCC and appropriate media/channels
- Future longitudinal studies should account for potentially large loss to follow-up if population is mobile and migrant
- Conduct a costing, demand and supply analysis of ITC to guide implementation and feasibility of scale-up of ITC for MMPs [currently on-going by Malaria Consortium]

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