To screen or not to screen: An interactive tool that integrates costs and spatial heterogeneity to determine when mass-screen-and-treat is an effective malaria control strategy

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Background

Mass drug administration (MDA) vs. mass-screen-and-treat (MSAT):

- MDA is a malaria control strategy which involves presumptively treating an entire population or subpopulation with antimalarial drugs regardless of symptoms and without a confirmed diagnosis.
- MSAT is a related malaria intervention strategy involving a mass distribution of antimalarial drugs regardless of symptoms, but on the basis of a confirmed diagnosis from a rapid diagnostic test (RDT).
- Each intervention option contains meaningful tradeoffs (Table 1).

From a cost perspective, the factors that contribute to cost-effectiveness of MDA versus MSAT include:

- Baseline malaria prevalence.
- RDT performance (Sensitivity and Specificity).
- Likelihood of false positive.
- Likelihood of false negative.
- Additional cost/storage of RDT.

Table 1. Comparisons of mass intervention policy options.

<table>
<thead>
<tr>
<th>Intervention</th>
<th>MDA (MDA)</th>
<th>MSAT (MSAT)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All infected</td>
<td>Resource waste</td>
<td>Reduced waste of costly treatments</td>
</tr>
<tr>
<td>individuals receive treatment</td>
<td>Increased risk of drug resistance</td>
<td>Decreased risk of drug resistance</td>
</tr>
<tr>
<td>Only requires stock of treatments</td>
<td></td>
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Table 2. Cost equation parameters and associated likelihoods.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Equation</th>
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<tbody>
<tr>
<td>Costtreatment</td>
<td>[ \text{Cost}<em>{\text{treatment}} = \text{Cost}</em>{\text{treatment (e.g., antimalarial drugs)}} ]</td>
</tr>
<tr>
<td>Costrapiddiagnostic</td>
<td>[ \text{Cost}_{\text{rapid diagnostic test (RDT)}} ]</td>
</tr>
<tr>
<td>Costfalsepositive</td>
<td>[ \text{Cost}_{\text{associated with false positive outcome}} ]</td>
</tr>
<tr>
<td>Costfalsenegative</td>
<td>[ \text{Cost}_{\text{associated with false negative outcome}} ]</td>
</tr>
<tr>
<td>pR = (0.1)</td>
<td>[ \text{Likelihood of RDT outcome; (1 = positive, 0 = negative)} ]</td>
</tr>
<tr>
<td>pR = (0.1)</td>
<td>[ \text{Likelihood of false positive} ]</td>
</tr>
<tr>
<td>pR = (0.1)</td>
<td>[ \text{Likelihood of false negative} ]</td>
</tr>
</tbody>
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Methods

Data Collection:
- Data sourced from Demographic Health Surveys (DHS) and Malaria Indicators Surveys (MIS) from six western African countries (Burkina Faso, Cote d’Ivoire, Ghana, Guinea, Nigeria, and Togo).
- Contain malaria status for young children (age 6 to 59 months) based on microscopy and RDT, as well as relevant demographic information, for each region in each country (Table 3).

Modelling Prevalence, Sensitivity, and Specificity:
- Malaria status as a binary response variable based on individual-level covariates (X) using a mixed regression model with a binomial link function.
- Intercepts and covariates were modelled as level-random effects.
- Demographic covariates were gender, age (in months), and urban/rural community.
- Microscopy (M) was considered the "gold standard" for malaria diagnosis.
- RDT (R) was the screening diagnostic.
- Malaria prevalence was modelled as \[ (1 - (R \cdot M)) \] screening sensitivity was modelled as \[ (R \cdot M) \], and one minus screening specificity was modelled as \[ (1 - R \cdot M) \].
- All models were fitted using the ‘glmer’ package in the R statistical software.

Cost Equations:

\[ \text{Cost}_{\text{MDA}} = \text{Cost}_{\text{treatment}} + \text{Cost}_{\text{error}} + p(0) \]
\[ \text{Cost}_{\text{MSAT}} = \text{Cost}_{\text{treatment}} + \text{Cost}_{\text{falsepositive}} + \text{Cost}_{\text{falsenegative}} + p(0) \cdot \text{pR (0.1)} \cdot \text{pR (0.1)} \]

Results

Model Outcomes:
- Gender was found to be not significant for modelling malaria prevalence, sensitivity, and specificity, and was removed from each model. The fixed effects age and urban/rural environment were significant (p < 0.001) and positive, which suggests that older children in rural communities across the six observed countries. The regional random slopes for age were less variable than urban/rural environment, and both were much less variable than the regional random intercepts (Fig. 6).
- Malaria prevalence was higher in rural communities than in urban communities in each region. Overall, variations in malaria prevalence were greater in rural communities than in urban communities and differed between countries (Fig. 5).
- RDT sensitivity (true positive rate) was higher in rural communities than in urban communities. There was considerable overlap between countries in sensitivity and specific rates, once accounting urban and rural differences (Fig. 2).

Interactive Application:
- The interactive mapping application is available at https://jjmillar.shinyapps.io/msat-cost-map/ (Fig. 9). This application reveals that the substantial degree of spatial heterogeneity in malaria prevalence and RDT performance can undermine large-scale (e.g., country-wide) approaches to guiding malaria intervention strategies.
- Assuming a standard price for RDT of $0.60 and ignoring the cost of false positives and false negatives, in rural communities in Guinea a standard, country-wide cost of antimalarial treatment below $1.94 would favor presumptive treatment (MDA) in all regions, whereas standard cost above $7.55 would favor screening (MSAT) in all regions. Any treatment cost between these ranges would result in a mix cost-effective strategies depending on the region.
- This can be exacerbated by the effect of urban/rural differences within country. For example, in Ghana under the same assumptions as above, the minimum cost of antimalarial treatment required for MSAT to be cost-effective in all regions is $4.95 for rural communities and $6.41 for the urban communities.
- Incorporating indirect costs associated with misdiagnoses can further complicate the cost-effectiveness comparisons. If the cost of false positive is set to $0.00, then only the expected cost of MSAT is a function of prevalence (not RDT performance). However, when the cost of false positives is included, then expected cost of MDA also changes as a function of prevalence (increasing the expected cost of MDA at lower prevalence rates). This pattern can be readily observed in the given application available at https://jjmillar.shinyapps.io/msat-cost-graph/ (Fig. 4).

Discussion

The World Health Organization broadly recommends each distribution of antimalarial treatment be based on a confirmed diagnostic result, typically from an RDT. While RDT can substantially reduce waste of increasingly expensive antimalarial treatment, the potential high costs associated with false-negative results and the high degree of spatial heterogeneity in malaria prevalence and RDT performance can undermine the economic benefit of screening. Ultimately these patterns indicate that large-scale, country-wide policies are unlikely to be the most cost-effective approach for malaria control. Therefore, economic efficiency can be optimized by fitting intervention policy to the local conditions relevant to intervention success.

This project demonstrates a proof-of-concept for the use of interactive applications to connect modelling and data analysis to accountable decision-making tools. These applications can be fitted to varying contexts with different data sources, and can be further specified to address some of the notable limitations of this project. Ultimately we believe that interactive applications can be a useful tool for bridging the gap between statistical models and policy design, and supporting evidence-based and data-driven decision making.

Figure 1. Potential outcomes from mass drug administration (MDA) based on presumptive treatment, and mass-screen and treat (MSAT), based on rapid diagnostic tests (RDT).

Figure 2. Regional RDT performance rates. The true positive rate is plotted on the X-axis and the false positive rate (1 - specificity) is plotted on the y-axis. Each point represents an individual region, and each bubble encapsulates all regions for a particular country.