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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 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)
- Direct costs of supplies (antimalarial treatments and RDT)
- Indirect cost associated with misdiagnoses (false positive/negative, Fig. 1)

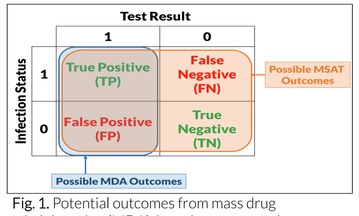

Fig. 1. Potential outcomes from mass drug administration (MDA), based on presumptive treatment, and mass-screen-and-treat (MSAT), based on rapid diagnostic tests (RDT).

Table 1. Comparisons of mass intervention policy options

Policy:	Pros:	Cons:
Mass drug administration (MDA)	- All infected individuals receive treatment - Only requires stock of treatments	- Resource waste - Increased risk of drug resistance
Mass-screen-and-treat (MSAT)	- Reduced waste of costly treatment - Decreased risk of drug resistance	- Potential for false negatives - Additional cost/storage of RDT

Table 2. Cost equation parameters and associated likelihoods

Equation Parameters	Description
$Cost_{Treatment}$	Cost of treatment (e.g. antimalarial drugs)
$Cost_{RDT}$	Cost of rapid diagnostic test (RDT)
$Cost_{FP}$	Cost associated with false positive outcome
$Cost_{FN}$	Cost associated with false negative outcome
$p(M=(0,1))$	Likelihood of microscopy outcome; (1 = infected, 0 = uninfected)
$p(R=(0,1))$	Likelihood of RDT outcome ;(1 = positive, 0 = negative)
$p(R=1\|M=0)$	Likelihood of false positive
$p(R=0\|M=1)$	Likelihood of false negative

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 covariate slopes were modelled as region-level random effects
  - Demographic covariates were gender, age (in months), and urban/rural community.
- Microscopy (M) was considered the "gold standard", RDT (R) was the screening diagnostic
- Malaria prevalence was modelled as $(M|X)$, screening sensitivity was modelled as $(R|M=1,X)$, and one minus screening specificity was modelled as $(R|M=0,X)$
- All models were fit using the 'glmer' package in the R statistical software

Cost Equations:

$$\boldsymbol{Cost_{MDA}} = Cost_{Treatment} + Cost_{FP} * p(M=0)$$

$$\boldsymbol{Cost_{MSAT}} = Cost_{RDT} + Cost_{Treatment} * \big(p(R=1|M=1) * p(M=1) + p(R=1|M=0) * p(M=0)\big) + Cost_{FP} * \big(p(R=1|M=0) * p(M=0)\big) + Cost_{FN} * \big(p(R=0|M=1) * p(M=1)\big)$$

Parameters are defined in Table 2.

Interactive Application:

- An interactive application for comparing MDA and MSAT using the `shiny` package in the R programming language.
  - Can create interactive webpages without internet programming (e.g. HTML, JavaScript)
- Uses the model parameters and cost-estimate equation to construct maps for each country which display the comparison of cost-effectiveness of MDA and MSAT based on the inputted cost values
- We also constructed a generic application that allows the user to set RDT sensitivity and specificity in addition the cost parameters, which can be used to test hypothetical conditions

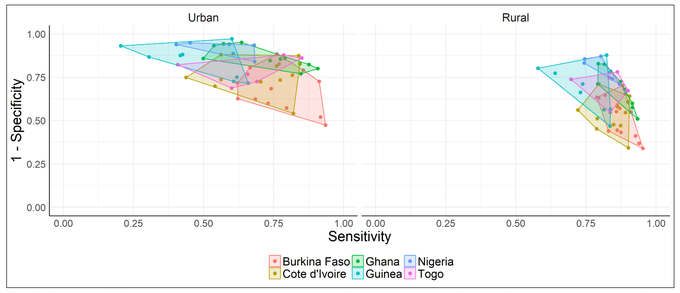

Fig. 2. Regional RDT performance rates. The true positive rate (sensitivity) is plotted on the x-axis and the false positive rate (1 – specificity) is plotted on the y-axis. Each point represents an individual region, and each polygon encapsulates all regions for a particular country.

Table 3. Data sources for malaria prevalence and RDT performance models

Country	Survey	Collection Period	No. of Children	No. of Regions
Burkina Faso	MIS	09/2014 – 11/2014	6112	13
Cote d'Ivoire	DHS	12/2011 – 05/2012	3344	11
Ghana	DHS	09/2014 – 12/2014	2713	10
Guinea	DHS	06/2012 – 10/2012	3198	7
Nigeria	MIS	10/2014 – 12/2014	5127	6
Togo	DHS	11/2013 – 04/2014	3215	6

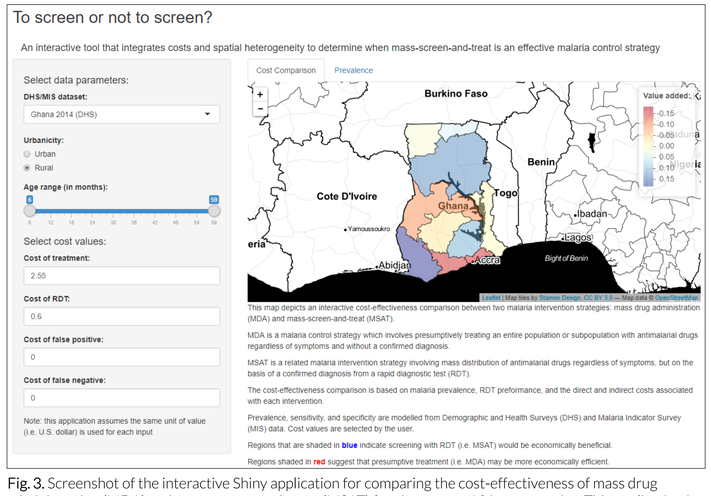

Fig. 3. Screenshot of the interactive Shiny application for comparing the cost-effectiveness of mass drug administration (MDA) and mass-screen-and-treat (MSAT) for six western African countries. This application is available at https://jjmillar.shinyapps.io/msat-cost-map/. Code is available upon request (please email jjmillar@ufl.edu).

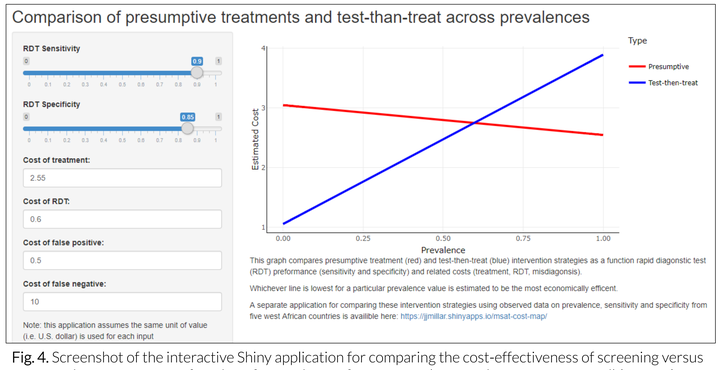

Fig. 4. Screenshot of the interactive Shiny application for comparing the cost-effectiveness of screening versus presumptive treatment as a function of screening performance and economic costs across possible prevalence rates. This application is available at https://jjmillar.shinyapps.io/msat-cost-graph/. Code is available upon request (please email jjmillar@ufl.edu).

Results

Model Outcomes:

- Gender was found to not be a significant covariate 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 communes in each region. Overall variability in malaria prevalence was 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. 3). 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 strategy.
- 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 this 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 $4.09 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 (which increases at higher prevalence rates). 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 generic application available https://jjmillar.shinyapps.io/msat-cost-graph/ (Fig. 4).

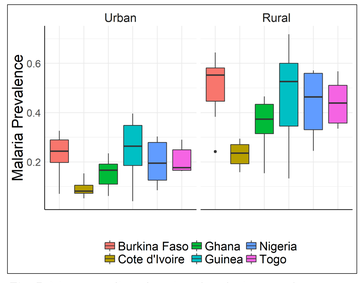

Fig. 5. Mean predicted regional malaria prevalence rates.

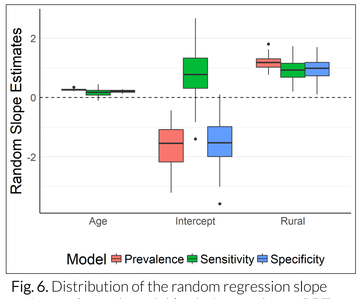

Fig. 6. Distribution of the random regression slope estimates for each model (malaria prevalence, RDT sensitivity, and RDT specificity).

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 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.