CONFIDENTIAL

Research proposal

Title: Discrete choice experiment for the identification of malaria intervention community preferences in southern Mozambique

Acronym: DCE

PI and co-PI: Elisa Sicuri and Joe Brew

Areas and/or Programs in which the proposal is framed: Malaria, elimination, CISM

Summary

Background (maximum 5 lines)

Human preference and choice determine the effectiveness of public health interventions. Malaria eradication will require that interventions be matched to the preferences of communities. Whereas studies of "revealed preference" (through observation of behavior) are useful, novel methods for malaria control (vaccination and mass drug administration) require an assessment of *hypothetical* preferences, which can be measured through discrete choice experimentation.

Objectives (maximum 15 lines)

Primary objective

This project has one primary objective: to elicit, quantify and rank community preferences, acceptance and aversion to two malaria control approaches (vaccination and mass drug administration) in the districts of Manhiça and Magude, Mozambique.

Secondary objectives

Secondary objectives include:

- Quantify and account for the social and demographic confounders to preferences.
- Estimate the role of hypothetical disease burden on preferences, thereby enabling the prediction the impact of the epidemiologic transition on malaria control preferences.
- Understand the effect of MALTEM's campaign, particularly the community experience of mass drug administration, on community preference regarding both drugs and vaccination.

Methods and Design (maximum 15 lines)

Briefly explain the study as you would to a reviewer who is not a specialist in your area of expertise

Discrete choice experiments consist of asking a participant to choose between two different "alternatives", repeatedly, with different "attributes" (ie, other factors). Here is an example of one choice-set:

Which of the following three choices do you prefer for you and your community?

Choice A	Choice B	Choice C
Mass drug administration	Vaccination	Neither
50% effectiveness	75% effectiveness	
No side effects	Severe side effects	
Anti-malarial effect of 1 month	Anti-malarial effect of 1 year	
$5	free	
30% incidence	60% incidence	

By keeping constant the "alternatives" (row 1) while varying the attributes (other rows), one can then model (a) which of the alternatives if preferred by the population, (b) which attributes affect that preference (ie, a cost-threshold at which preference changes, etc.), (c) which extra-survey

confounders affect preference (ie, sociodemographic's effect on preference).

Evaluation criteria

1. What are the ethical considerations that need to be addressed and how will they be addressed? (Maximum 10 lines)

This will be a survey-only experiment. It will deal with stated preferences, as reported by participants. Particpants will be randomly selected from existing CISM DSS (the census). Data collected from this project will be merged with census data, albeit anonymously.

2. **List the ethics committees (both human and/or animal) which either have reviewed or will review this proposal**

We are submitting the protocol to both the ISGlobal ISC, as well as the ISC of the CISM. In regards to ethical approval, we are not carrying out an intervention and would like to request exemption from review by an ethical board. However, on the matter of exemption, we see the ISC's input (whether we will be exempt, or whether we should submit to ethical boards).

3. Describe the expertise required for the project and which member(s) of the research team will provide each area of expertise (maximum 10 lines) [Example: Epidemiology , including study design and analysis: Wolfgang Mozart, Laboratory Analysis of Samples: Pablo Picasso, Field collection and identification of mosquitoes: Miguel de Cervantes Saavedra, Spatial modeling and mapping analysis: Juan Sebastian de Elcano, etc.]

Elisa Sicuri has experience in economic analyses pertaining to malaria in developing countries. Joe Brew will contribute with the data management and analysis, using multinomial models (an area in which he has a great deal of familiarity).

4. How does the proposal fit in with ISGlobal's scientific agenda? (Maximum 10 lines) [Select an established area or program of ISGlobal research and describe how the study fits in the selected area or program, or describe a new line of research]

This project fits in with ISGlobal's scientific agenda in the following ways:

- Strengthens collaborations with the CISM
- Increases international presence and clout
- Adds to research production and knowledge generation in a field in which ISGlobal is already a thought leader (malaria control / elimination), while supplementing with novel approaches (discrete choice experimentation)

Budget estimation and expected source of funding for this study (Maximum 3 lines)

$8,100 of already available funds. No new funding required from ISGlobal.

Other comments

- **Have all co-investigators read and approved this proposal? YES (Brew + Sicuri)**
- **Do you expect to handle samples of human origin in the study? NO**
- **Do you expect to handle personal information in the study? YES.**

PLEASE SEE FULL PROTOCOL (APPENDIX)

cism
centro de
investigação
em saúde de
manhiça

Discrete choice experiment for the identification of malaria intervention community preferences in southern Mozambique

Research Protocol

Principal Investigator: Elisa Sicuri
Co-investigators: Joe Brew, Laia Cirera, Sergio Alonso, Quique Bassat, Beatriz Galatas, Francisco Saute, Pedro Alonso, Pedro Aide

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Summary

Preference determines effectiveness

Human preference is the driver of human choice. And outside of the laboratory, human choice is what determines the success and failure of interventions, particularly those in public health. The difference between an intervention's efficacy (laboratory) and effectiveness (real-world) can often be explained in large part due to a community's aversion or receptiveness to the treatment being offered. When a community's preferences are in line with the intervention's assumptions, efficacy mirrors effectiveness; on the other hand, when a community's preferences go in contrary to the intervention, efficacy and effectiveness diverge, and resources go to waste.

Discrete choice experiments reveal preference

Discrete choice experiments, a methodology from the field of economics, presents participants with two discrete, hypothetical choices. For example, a participant might be asked if they would rather have (i) a bednet for every member of their household or (ii) a malaria vaccine. The choices are randomized and arranged in a way that allows for the analyst to later rank and quantify human preference at the population level, as well model factors which determine preference.

Future malaria interventions can be informed by discrete choice

In the struggle against malaria, a great deal of academic attention has focused on the *biological*, *medical*, and *logistical* feasibility of various vector control and malaria treatment approaches. Resources are directed towards assessing malaria vaccine effectiveness, mass drug administration's side effects, antimalarial resistance, etc. However, there is a lack of attention towards a corresponding *preference* for the respective approaches, particularly in regards to the relatively "untested" methods of mass drug administration and vaccination. To the extent that the elimination of malaria will be contingent on a massive "scaling up" of these interventions, understanding hypothetical preferences regarding novel methods is an essential piece of the eradication puzzle, and will enable a convergence of malaria control interventions' efficacy and effectiveness by matching intervention approaches with community preference.

Background and study rationale

Background

Malaria's burden in Mozambique

Understanding community preference can shed insight on numerous health interventions, but it is particularly relevant to the case of malaria in Mozambique. The burden of malaria is extremely high in Mozambique, even by regional standards ("WHO on Health and Economic Productivity" 1999). With a prevalence as high as 40%, malaria accounts for 29% of all deaths, and 42% of deaths among children under five (Hanlon and Joseph, n.d.; OECD 2011; Munguambe et al. 2011). In some areas, as many as 90% of children under the age of five years are infected with Malaria parasites. Nearly a quarter of maternal deaths are due to malaria (Singh et al. 2014). Along with HIV/AIDS (Berg et al. 2014), malaria is one of the greatest threats to public health in southern Mozambique.

In addition to malaria's impact on the health of its victims, the illness also has major economic consequences for the ill. Children who survive malaria face hurdles which can have lifelong economic repercussions, particularly those related to intellectual development (such as cerebral malaria) (Idro et al. 2010; Idro et al. 2016) and general growth anemia (Mabunda et al. 2008). Their families also pay economically - 32-34% of households incur malaria-related costs which rise to the level of "catastrophic" per the World Health Organization's standards (ie, 10% of household income or 40% of non-food income) (Castillo-Riquelme, McIntyre, and Barnes 2008). Though the burden of malaria is decreasing (GBD 2013 Risk Factors Collaborators et al. 2015), the costs of the disease at the individual level remain enormous, given that the disease affects primarily those with low socioeconomic status. Malaria control has been found to be associated with economic growth in multiple studies (Barofsky, Anekwe, and Chase 2015). By eliminating early-life blocks on the development of a population's human capital, the returns on a reduction in malaria's burden are long-term and exponential.

The global health community has been waging war against malaria for decades. Though the burden has decreased drastically in rapid years, elimination across endemic countries and - eventually - global eradication, will rely on a change in the interventions being employed.

Specifically, it is likely that either vaccination or mass drug administration (or both) will be scaled up and employed in new areas.

The need to understand preference

Unfortunately, there is no “silver bullet” for eliminating malaria. Vaccine development is promising, but not yet effective enough to be used solely. Vector control is the “tried and true” method, but portends ongoing costs as well as environmental side effects, and adherence can be troublingly low. Mass drug administration is potentially revolutionary, but it has not yet been evaluated comprehensively at a large scale.

Because of the multiple methods of malaria control and prevention available, it is vital that organizations and institutions seeking to eliminate malaria pick the right tool for(s) for their respective communities. Implementing a theoretically efficacious method in a community which widely distrusts or is otherwise averse to said method is both wasteful and potentially disastrous for public health. However, by matching methods to previously assessed community preferences, public health practitioners can ensure that the effectiveness of malaria control and prevention interventions in the real world will mirror that in the laboratory.

Measuring preference

Eliciting preference, particularly in the fast-changing world of malaria control and prevention methods, is not a straightforward task. Ideally, a simple observation of “revealed preference” (ie, how a community behaves) would be sufficient. In this perfect scenario, consumer choice - as revealed through practices and purchases - would directly mirror community preference, and interventions could be tailored from that revealed preference. There would be no need for surveys of hypothetical questions.

However, we do not live in an ideal world, thus the “revealed preference” of those targeted by malaria control and prevention interventions is biased by several factors. First, the predominant role of the public sector in the distribution of health services and management of campaigns creates a health economy driven by the supply-side. In other words, consumer choice is constrained by availability, and unlike in a true market, supply is more a reflection of policymakers’ - not community - preferences. Second, the relatively low purchasing power of those living in malaria endemic regions means that even where purchases *could* be revealing, they are constrained by competing non-malaria priorities (food, shelter, education,

etc.). Third, malaria control and prevention interventions have changed rapidly over recent years, making it impossible to construct a dataset of comparable “revealed” preferences. This is particularly the case with vaccination and mass drug administration, since the population in endemic countries generally has no or little experience with the interventions in question.

In other words, the choice between novel methods (such as vaccination and mass drug administration) is largely a *hypothetical* one, and therefore cannot be assessed through revealed preference. Thus, preference is best measured through discrete choice experimentation, a methodology with several advantages. By using hypothetical questions, it addresses numbers one and two of the above biases (public sector availability constraints and low purchasing power). And by including in the hypothetical choices only those methods currently being considered for scaling-up, no matter how new, one can assess preference in a manner that is wholly relevant to options for future interventions, rather than those of the past.

Study rationale

The Mozambican Alliance Towards the Elimination of Malaria (MALTEM) and the Manhiça Health Research Center (CISM) have positioned themselves as both thought and action leaders in the world of malaria elimination. Previous and current studies are assessing the health and economic effects of wide-scale malaria vaccination, mass drug administration, indoor residual spraying, bednet distribution, intermittent preventive treatment, as well as other less directly-related health interventions to control and prevent malaria. MALTEM and CISM’s coordinates and evidence-based research strategies will provide a template for elimination across other geographical areas, thereby leading to global malaria eradication.

Because of MALTEM and CISM’s position at the center of the malaria eradication movement, it is of vital importance that the knowledge products and practice recommendations generated through interventions be as generalizable as possible. Fortunately, producing research which will be applicable even vastly different geographical, cultural and social milieus is theoretically feasible, given the extremely detailed and high quality sociodemographic collected and stored by CISM.

This project aims to leverage two factors unique to MALTEM and CISM to generate high quality learnings related to the role of community preference in malaria elimination,

complementing MALTEM's general goals, and filling in research gaps. First, it will capitalize on the high familiarity of the population of southern Mozambique with different malaria control interventions, a result of years of studies, trials and health campaign implementations. Second, it will take advantage of the wealth of sociodemographic data in census (CISM DSS).

By quantifying community preference towards malaria control and prevention interventions, and by qualifying that preference through the analysis of related social and geographic factors, this project will assess those factors which could enable or harm interventions' effectiveness, as well as address interventions' generalizability, enabling the massive scaling-up of MALTEM's methods and the future success of elimination programs generally.

Objectives and impact

Primary objective

This project has one primary objective: to elicit, quantify and rank community preferences, acceptance and aversion to two malaria control approaches (vaccination and mass drug administration) in the districts of Manhiça and Magude, Mozambique.

Secondary objectives

Secondary objectives include:

- Quantify and account for the social and demographic confounders to preferences.
- Estimate the role of hypothetical disease burden on preferences, thereby enabling the prediction the impact of the epidemiologic transition on malaria control preferences.
- Understand the effect of MALTEM's campaign, particularly the community experience of mass drug administration, on community preference regarding both drugs and vaccination.

Impact

In addition to its specific scientific objectives and knowledge products (above), this project has the potential to have important implications for public health. These include:

- Improved targeting of public health interventions and government allocation of resources, as a result of a better understanding of the behavioral and social components of disease control campaigns.
- The establishment of historical "benchmarks" to gauge the effectiveness of public health education campaigns (ie, their effect on community preferences).
- Knowledge generated regarding how preference *changes* as a result of participation in novel elimination strategies (vaccination and mass drug administration), as well as how proximity to areas of elimination interventions may affect preference.
- Insight gained into the effect of the previous malaria vaccination trial in Manhiça on preferences.

Methods

Study design

This study's design will be consist of a standard discrete choice experiment, employing an attribute-based survey, administered at a cross-section in time, among quasi-randomized residents of Magude and Manhiça, in order to measure, rank, and quantify preferences in regards to the myriad of malaria control and prevention methods available. This design will facilitate the construction of a dataset which will facilitate the overall comparison of preferences pertaining to individual interventions' attributes, as well the association of social, demographic, and geographic factors with those preferences.

Study area

The study area is comprised of the districts of Magude and Manhiça, in southern Mozambique. The selection of these areas is intentional, and meant to capitalize on their unique similarities and differences.

Magude, the district in which MALTEM's elimination plan is currently being implemented, is in the Northwestern part of the province of Maputo. It shares a border with Massingir, Cholkwe, and Bilene (Gaza province), Manhiça (Maputo province). It has a total area of 6,961 square kilometers and approximately 60,000 inhabitants. The incidence of malaria in 2012 was approximately 20,000 cases per 100,000 population at risk.

Manhiça, a district of 165,000 inhabitants, will be used as a comparison to Magude. Like Magude, the burden of malaria in Manhiça remains high. Though similar socially, geographically, and economically, Manhiça is not part of MALTEM's current elimination campaign. Because of this, the pairing of Magude and Manhiça offers the unique opportunity of a natural experiment, enabling researchers to assess whether and how MALTEM may have affected community preference.

Because Magude is the location of a recent mass drug administration, we anticipate that residents selected from Magude are more likely than their Manhiça counterparts to have experience (both direct and indirect) with MDA. This creates an ideal comparison, to assess how the MDA has changed preferences not only regarding the MDA, but also the hypothetical implementation of a malaria vaccine.

Timeline

Specifically, the study will be carried out in the following order.

- Systematic selection of study participants from the DSS, using quasi-random methodology (see "Study population" section); June-July, 2016.
- Administration of fieldworkers in order to provide information on study and collect informed consent; August, 2016.
- Administration of discrete choice experimentation survey (see "Survey content" section); September-October, 2016.
- Analysis, manuscript writing, dissemination, and publication; November-December, 2016.

Sample size

The survey will be administered to residents of both Magude and Manhiça districts. Our calculations for minimum sample size, which are based on the recommendations for best practice of Bekker-Grob (de Bekker-Grob et al. 2015), employ the following parameters and assumptions:

- Significance level (α): 0.05
- Statistical power level ($1-\beta$): 0.80
- Statistical model used in the analysis: generalized multinomial logit (GMNL)

- Prior estimation of parameter values (γ): (currently set conservatively)
- Discrete choice design: see "Survey content" in the appendix

With these assumptions, we construct an asymptotic variance-covariance matrix (AVCM) ($\Sigma\gamma$), extract the diagonal of each attribute we are testing ($\Sigma\gamma\kappa$), which in turn enables us to employee the following formula for the calculation of minimal sample size:

$$N>((z_{1-\beta}+z_{1-\alpha})\sum\gamma k\sqrt{}/\delta)2$$

Where the effect size (δ) is inversely correlated with the sample size (N), and the size of the AVCM yields exponential growth in the necessary sample size. At our parameters, a total sample size of 190 participants is required. However, we double this in order to perform independent analyses for each of the two study locations (380), and add 1000% to account for the possibility of either (a) inaccurately low prior estimation of parameter values or (b) attrition and nonresponse rates, for a total sample size of 760 (380 from Manhiça, 380 from Magude).

Discrete choices

Participants will be asked to choose between hypothetical (i) vaccination versus (ii) drug administration, with an additional option of (iii) "neither" for all comparisons. These 3 alternatives will be complemented by permutated variations of the following 4 attributes:

Attribute	Levels
Effectiveness	1. 25% 2. 50% 3. 75% 4. 100%
Side effects	1. None 2. Moderate 3. Severe
Duration of effect	1. 1 month 2. 1 year 3. 5 years
Cost	1. Free 2. $2 3. $5 4. $10
Annual	1. 0%

incidence of malaria	2. 30% 3. 60%

The permutation of the two main alternatives (vaccination versus drug) and the number of levels (17) results in 432 total possible discrete choice-sets, of which each participant will be randomly assigned to answer 16 discrete choice-sets. The below is an example of one choice-set:

Which of the following three choices do you prefer for you and your community?

Choice A	Choice B	Choice C
Mass drug administration	Vaccination	Neither
50% effectiveness	75% effectiveness	
No side effects	Severe side effects	
Anti-malarial effect: 1 month	Anti-malarial effect: 1 year	
$5	free	
30% incidence	60% incidence	

Inclusion and exclusion criteria

All censed adults (18+ years of age) living in the districts of Magude or Manhiça for at least two consecutive years at the time of study administration are eligible for participation. For optimum representativeness, households will be selected randomly from the census, as will household members. Exclusion criteria included (i) inability to understand Portuguese or Changana (the two questionnaire languages), and (ii) having moved from another district at any time over the previous two years.

Informed consent will be obtained from all potential participants prior to the administration of the questionnaire. Participants will have the option to complete the questionnaire on-site (at their home) or at the CISM. In both cases, there will be an option to complete the questionnaire in either written or oral format (the latter being for those who cannot or prefer not to write/read).

Data obtained from the questionnaire will be digitized and then destroyed. The only identifiers will be the household and person numbers (which are linkable via the census). These data will only be available to the researchers named in this study.

Data collection and management

The data used from this project are both primary and secondary.

Primary data to be collected

From each of those households, all adults will (18+ years of age) will be invited (in-person) to participate in the questionnaire (quantitative) portion of the study. The questionnaire will be entirely in the form of discrete choices, a methodology which has the advantage of parsing ranked preference and explicitly quantifying preference through implicit trade-offs. The World Bank has suggested that discrete choice experiments are "extremely useful for policymakers", which is of particular relevance to the malaria eradication campaign.

In addition to those data generated from the questionnaire, participants will also be asked the following:

- Who from their household has ever participated in the MDA.
- If the participant personally participated in the MDA.
- Who from their household has ever been vaccinated against malaria.
- If the participant personally was ever vaccinated against malaria.
- Which malaria prevention methods they currently employ:
    - Indoor residual spraying (and time since last spray)
    - Bednets
        - Impregnation status
        - How many members of household sleep under net every night
        - If participant him/herself sleeps under net every night

Secondary data

In order to complement the analysis of the primary data, two secondary datasets are required for the carrying out of this project.

(1) The most recent Manhiça health district census data (DSS) will be used in order to both to (a) enumerate participating households and household members as well as (b) join relevant sociodemographic variables (sex, age, occupation, socioeconomic status, years in district, etc.) to the final dataset so as to estimate the effect of sociodemographic factors as

well as control for their influence in the estimation of the effect of the elimination campaign on preferences.

(2) Data from MALTEM's mass drug administration will be used to examine which participants partook in the MDA and which did not.

(3) Data from the previous malaria vaccination trial in Manhiça will be used to examine which participants partook in the vaccination trial and which did not.

Data analysis

The discrete choice survey will be analyzed using generalized multinomial regression. The GMNL model will (a) provide a ranked order of community preferences regarding malaria control and prevention interventions, (b) generate estimates for the parameter-specific impact on preferences (for example, at what price threshold an otherwise preferred method becomes less preferred), and (c) allow for the integration of parameter-specific estimates into economic and simulation models, which in turn can be generalized to other areas with different sociodemographic or health conditions (ie, a region with higher prevalence, greater wealth, etc.).

Importantly, the regression model can be used to estimate both the overall and adjusted effect of MALTEM's malaria elimination campaign. Put simply, the model-generated parameter estimate associated with geography, as well as the estimate associated with malaria elimination campaign participation, can shed light on the effect the MALTEM elimination campaign on community preference. Though indirect, this will allow us to address the question of whether exposure to elimination activities (such as the mass administration of drugs) has an effect on the preference for that activity.

All data analysis will be carried out in R. Though all data will be privately housed on CISM servers, all code for analysis will be hosted publicly on Github.

Ethical clearance

The protocol, consent forms and questionnaires will be approved by the CISM Institutional Ethics Review Board, National Ethics Committee of Mozambique and the Ethics Committee of the Hospital Clínic of Barcelona before its implementation.

Confidentiality

All information on individuals will remain confidential and be shared only by the study team. Unique identifiers will be used for computer-based data entry. In all cases, the principal investigator will ensure that the completed identification code list are kept in locked and encrypted files.

Appendix

Budget

This study requires no funding from MALTEM. It will be managed by Joe Brew, who is funded by the Transdisciplinary Global Health programme. Mr. Brew's grant will provide the funding for the design, data cleaning, and analysis portions of this study, as well as his travel and lodging to and from Manhiça.

Mr. Brew will rely on CISM personnel to administer the 760 surveys. We estimate a total cost (transportation + wages) of approximately $10 per survey administered (760 * $10 = $7,600).

Mr. Brew will require assistance in translation of questionnaires from English to Portuguese and Changana. The estimated cost for this is $500.

The total breakdown for funding, along with accompanying sources, is below:

Category	Source	Amount
Study design, data management, analysis	Mr. Brew's PhD grant from the Transdisciplinary Global Health programme	0
Transportation and local survey administrators	MALTEM Economics fund	$7,600
Translation of questionnaires	Mr. Brew's PhD grant	$500
Total Budget		$8,100
Amount already covered		$8,100 (100%)
Additional amount needed		$0 (0%)

Survey content

To the extent that the survey questionnaire will consist of 16 randomly selected discrete choices from a possible combination of 432, it is impractical to print all permutations here. That said, the below is a sample of 4 of the 432 permutations.

Choice set	Alternative	Effectiveness (%)	Side effects	Duration	Costs	Incidence (%)
25	vaccine	50	none	1 month	5	30
25	mda	75	moderate	1 year	10	30
81	vaccine	100	moderate	1 year	2	0
81	mda	75	moderate	1 month	0	30
215	vaccine	50	severe	1 year	5	30
215	mda	100	moderate	5 years	5	60
402	vaccine	25	severe	1 month	5	60
402	mda	25	severe	5 years	0	30

The entire table of permuted choice-sets is viewable at https://goo.gl/M1b7xO.

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