Protocol for the Economic Benefits of MALTEM in Magude District, Mozambique

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ABREVIATIONS

ANC ï antenatal care

BMGF - Bill & Melinda Gates Foundation

CISM- Manhiça Health Research Centre

DHS ï Demographic and Health Survey

DSS ï Demographic Surveillance System

GDP - Gross Domestic Product

IPTp - Intermittent Preventive Treatment for Pregnant women

IRS - Indoor Residual Spraying

ITNs - insecticide treated nets

MALTEM- Mozambican Alliance Towards the Elimination of Malaria

MCA ï Multiple Correspondence Analysis

MDA- Mass Drug Administration

MISAU - Mozambican Ministry of Health

MOH ï Ministry of Health

NMCP ï National Malaria Control Program

OR - Operational Research

RDT- Rapid Diagnostic Test

SEP - Socio Economic Position

SUMMARY

Malaria elimination brings benefits to societies that go far beyond the impact on populationôs health. Further benefits of moving from high malaria burden to low burden include productivity gains such as increased human capital and increased productivity of production factors. In addition to measuring direct benefits and cost-effectiveness analysis, in the context of the malaria elimination program that will be implemented in the district of Magude, this project aims to provide primordial information on the economic gains associated with malaria elimination, by estimating the burden of malaria among workers and its impact on productivity (working absenteeism), as well as scholar attendance as proxies for economic growth. The study will also explore the relationship between householdsô socio-economic position (SEP) and malaria incidence over time.

Data on school attendance of 7.158 students from 6 to 12 years old in Magude district (intervention group) and 20.670 students from 6 to 12 years old in Manhiça district (control group) will be collected over the period of study. Working absenteeism data will also be collected from the main industries in the region, namely the Açucareira de Xinavane, based in Magude, and the Açucareira de Maragra, in Manhiça. Finally, SEP data will be collected through the demographic census from Magude and Manhiça, which collect data from 51.454 and 165.497 individuals, respectively.

The information from this study will be crucial to inform policymakers as well as the international community on magnitude of the economic gains as well as the efficacy of investing resources in moving from a state of controlled malaria to malaria elimination.

BACKGROUND/STUDY RATIONALE

Mozambique is one of the endemic countries with the highest-malaria burden in the world. Malaria accounts for over 40% of all outpatient consultations, for 56% of in-patients in paediatric wards and for almost 30% of all hospital deaths. In some areas, more than 90% of children under the age of five years are infected with Malaria parasites (DHS, 2011).

Within this context, the Manhiça Health Research Center (CISM), through the project MALTEM, is supporting the Mozambican NMCP to adopt coordinated, evidence-based plans, secure adequate capacity and resources to scale up elimination-tailored strategies, and execute programs that will dramatically accelerate progress towards elimination in Maputo and significantly decrease malaria transmission rates in Gaza and Inhambane provinces by 2020.

In such a high burden country, malaria elimination is likely to generate conspicuous economic benefits, both direct and indirect, where the former (direct) are the savings associated with fewer (or no) malaria cases to treat. Because of the expected high health impact, malaria is likely to be more cost-effective compared with malaria control. However, costs associated with malaria elimination are also expected to be high, especially during the first phases. In this respect, Sabot et al (2010), presented the first attempt to model costs and benefits of elimination campaigns versus control campaigns using data from eight case studies.

Other broad economic benefits have been postulated, such us the impact of elimination on economic growth through the effects on human capital accumulation, which can be considered as the main indirect benefits. Specifically, in the few studies conducted, elimination programmes are retrospectively used as quasi-natural experiments with the aim of identifying the causal relationship between health improvements and economic growth (Bleakely H, 2010; Barofsky J et al, 2011). Where studies looked at the impact of past malaria campaigns on the incomes of individuals or households, the results were conflicting, sometimes suggesting higher earnings and literacy rates or years of schooling in adults born after malaria elimination campaigns and sometimes results show no significant effects (Bleakely H, 2010; Barofsky J et al, 2011).

Some studies suggest a possible dilemma resulting from eradication/elimination. If life expectancy increases, GDP per capita could fall unless the increase in GDP was sufficient to offset the increase in population (Lucas, 2013). However, focusing on life expectancy for evaluating the economic impacts of disease elimination may not be always appropriate (The Economist, 2008). Some health improvements may not lead to a longer life but may improve quality of life and hence productivity (Sicuri et al, 2015). When studying the impact of a malaria eradication campaign in Colombia, Bleakely noted that the elimination of *Plasmodium vivax* malaria led to more significant gains in human capital and income than the elimination of *Plasmodium falciparum,* even though *falciparum* causes more deaths than *vivax*.

Other arguments suggests that the sustained gains in human capital may alter the trajectory of investment decisions of the individuals, foreign investors and local firms, which all together change the productivity of the country after elimination (Sabot et al, 2010; Gallup et al, 2001). Overall, macroeconomic assessments of the effects of malaria on long-term incomes quantified the impact of malaria on growth (Gallup et al, 2001), but failed to identify the pathways concerned (Sicuri et al, 2015).

The evaluation of the indirect benefits consequent to malaria elimination as part of the MALTEM project will help to better understand the relationship between malaria elimination and economic growth from a microeconomic foundation. It has been proved (Cutler et al, 2010) that absenteeism on the job is a good measure for labour productivity and human capital accumulation, and that capital accumulation increases the growth of national income.

However, not only the impact on labour absenteeism is a good proxy for economic growth but also on scholar absenteeism, as higher levels of education increase the growth of national income (Jamison et al, 2007). Other evidence shows that early test scores are correlated with education, earnings and future labor participation (Leibowitz, 1974).

Following these arguments, the economic analysis within MALTEM will estimate the burden of malaria among workers and its impact on productivity (working absenteeism), as well as scholar attendance as proxies for economic growth. Finally, socio economic data at the household level will also be analyzed to measure householdsôsocio-economic position (SEP) over time.

OBJECTIVES

General objective

To generate information on the economic benefits associated with malaria elimination in Mozambique that could be used by policymakers in taking decisions as well as assess the cost-effectiveness of malaria elimination strategies

Specific objectives

1. To estimate the **direct economic benefits** from the government in implementing malaria elimination strategies (i.e. cost savings that will accrue from not treating cases after elimination or after burden reduction)
2. To estimate the **indirect economic benefits associated with malaria elimination** in Mozambique (i.e. benefits obtained on non-health indicators, such as reduced school and work absenteeism and that serve as proxies for economic growth).
3. To assess the **cost-effectiveness of malaria elimination compared with malaria control** through the strategies tested in MALTEM program.
4. To assess the **cost-effectiveness of achieving malaria elimination beyond the district** of Magude

METHODS

Study Area:

The malaria elimination plan will take place in Magude District, on the North-Western area of Maputo Province, Southern Mozambique. Magude District borders with the district of Massingir (Gaza Province), in the North, Manhiça District and the province of Gaza (Chokwe and Bilene Districts) on the East, Moamba District in the South, and the South African Kruger National Park on the West. It has an area of 6,961 km2, with approximately 60,000 individuals and 11,408 family compounds. The district has seven health facilities with a total of 43 beds (1.65 beds per 1,000 inhabitants) and reported 20,000 malaria cases per 100,000 population at risk in 2012.

Manhiça district will be used as a comparator area for the analysis of the interventions and variables of interest. Manhiça, located 80km north of the capital, Maputo, is a semi-rural area, with a population of 165.497 habitants. As of 2013, malaria remains one of the main causes of under-five morbidity and mortality in the district.

Study Design:

In order to capture the economic benefits of MALTEM interventions beyond the health impact, observational studies will be conducted in a sample of children between 6 and 12 years old, working adults and households, and indicators such as scholar absenteeism, working absenteeism and householdsô Socio Economic Position will be monitored before and after elimination activities will be conducted in Magude district. Such indicators will be monitored both in the intervention area (Magude district) and the control area (Manhiça).

The estimate of direct benefits and the cost-effectiveness analysis will imply comparing costs of malaria elimination activities with costs of malaria control malaria control. Again, observational studies (although not individual level studies) will be carried out.

Study Population: The economic observational studies involve different study populations:

- In order to capture changes in scholar absenteeism, data at the school level and from students between 6 to 12 years old will be collected.
- Working absenteeism will include workers from Xinavane and Maragra cane sugar companies

Socio Economic Position measures are obtained from all households within the districts of interest (Manhiça and Magude). For the cost-effectiveness analyses, data from the population of the district of Magude is used (all the population, including children and adults). The extrapolation of the estimates to the national level will use data from the whole countryøs population.

Timing and duration of the study:

The economic studies will be conducted between the months of June and December 2015, a period of time that allows capturing data from before, during and after MALTEMøs interventions.

Data Collection and Management:

The information on school absenteeism will be collected using smart phones and it will be downloaded directly into data bases at CISM. The information on workersô absenteeism and SEP will be both self-reported and collected during the demographic census in Manhiça and Magude. Workersôabsenteeism will be also derived from the archives of the two main sugar cane factories of the districts. These data will be entered into electronic data bases from the paper files available in the firms. Information on direct benefits will be derived from the difference between costs of control and costs of elimination and managed through Excel software.

The principal investigator will ensure that the study protocol is strictly adhered to and that all data are collected and recorded correctly on the case report form. Data derived from source documents should be consistent with the source documents, or the discrepancies should be explained. Any change or correction to a case report form should be dated and explained and should not obscure the original entry.

Data analysis:

For the indirect benefits Data analysis will be performed using STATA software and a pre-defined data analysis plan will be followed. For the direct benefits and cost-effectiveness analysis, data analysis will be performed in Excel.

Ethics 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 files.

Methodology specifications by objective:

Objective 1: Direct economic benefits

The estimated direct economic benefits (or cost-savings) of the elimination plan are computed as the cost difference between the malaria control strategy and the malaria elimination strategy.

Costs associated with malaria elimination have been explained and methodology detailed in the "Protocol for the Costing of MALTEM in Magude District". Costs associated with malaria control strategies will be estimated based on costs for malaria case treatment already estimated in the area (Sicuri E et al, 2010; Cohen L et al, 2010; Chase C et al, 2009) and on costs for prevention in control mode will be available from ministerial sources (ITNs, IRS, IPTp). The number of cases to treat in control mode will be modelled based on the study of the trend of the number of malaria cases detected in areas where no malaria elimination activities have been carried out and then those findings adjusted to the area of intervention sociodemographic and epidemiological characteristics. Cross-sectional studies to measure the prevalence of malaria in a district with no malaria elimination interventions are considered for this purpose (Manhiça district). Trend analysis will be applied to data collected during the last five years and future number of cases will be estimated under the assumption that it will follow similar trends as previously observed. Number of cases will be multiplied by the unit costs of treatment of one case. Prevention costs averted will be multiplied by the projected population at risk. Based on historic data to which a constant increase in population will be applied, Demographic data from the DSS of Manhiça during the last five years will allow to calculate the number of children and pregnant women who will require protection against malaria, as well as the overall size of the population at risk in the Manhiça study area for the next ten years. Unit costs will be applied to these figures.

Objective 2: Indirect economic benefits

Indirect economic benefits will be identified through three main indicators: 1) households' socio-economic position (SEP); 2) absenteeism from work; 3) and absenteeism from school. For the three indicators, it is hypothesized that a reduction will be observed after the implementation of a successful elimination campaign..

Each indicator will be computed for each individual/household; thus, the analysis will be performed at micro rather at macro level. In order to take into account potential confounding factors that may affect the observed changes, before and after information of the same indicators will be collected and compared across areas with and without elimination interventions.The identification of the impact of malaria elimination on these indicators will be carried out using a difference-in-difference analysis, which measures the difference between the intervention and control districts (Shahidur et al, 2010).

Therefore, for each indicator, the measure of the impact will be given by:

(Ia-Ib)-(Ca-Cb)

Where **Ia** is the value of the indicator in the intervention area after the elimination campaign; **Ib** is the value of the same indicator in the intervention area before the elimination campaign; **Ca** is the value of the indicator in the control area after the elimination campaign and **Cb** is the value of the indicator before the elimination campaign.

Difference-in-difference analysis will be performed as regression analysis, which will allow to control for potential confounding factors, such as the demographic, socio-economic, morbidity and mobility status of the population.

a) HouseholdsôSEP (Socio Economic Position):

Measurement of SEP is widely used within health research studies and has different definitions. The most commonly SEP indicators used have been monetary measures such us income or consumption expenditure. However, it is argued that income might come from different sources and might vary a lot depending on the time of the year (Friedman, 1957). On the other side, consumption relies a lot on prices fluctuation and might be difficult to capture. Within this context, collection of householdsôasset data has been identified as a better measure of SEP than income or consumption expenditure, as it can be directly observed and requires very simple questions.

In consequence, within this analysis, The SEP for each household will be measured by applying multiple correspondence analysis (MCA) on the set of assets owned by the households.

Data on assets owned, collected through the demographic census in Magude (intervention group) and Manhiça (control group) before and after the intervention, will be used for this analysis. 18 variables regarding householdsôassets are captured and included within the index: construction material, kitchen, bath, fuel, water, waterloc (location of nearest water source) electric (electricity), phone, radio, video, freezer, car, moto, television, computer, stove, swine, bicycle.

From this set of asset variables, MCA will extract a common ĥbackgroundò factor that will indicate wealth. This technique has recently been used to construct the SEP of subgroups of the population in Manhiça by using data from the demographic surveillance system (Alonso et al, Clara Pons et al).

Differently from what expected for the other indicators analysed (absenteeism from work and school) no relevant changes are expected of the SEP as a consequence of malaria elimination activities in the short term. However, changes may be identified in the medium/long term and it is important to monitor this indicator in relation with the changes, either increase or decrease, or the burden of malaria, in the past, currently and in the future.

Difference in difference analysis will be performed to identify and measure the potential impact of malaria elimination activities in the medium/long term and, in parallel, trend analysis will be performed to study the time dimension of this indicator. The time series of the SEP variable will be regressed against a time trend and against the time series of a malaria indictor (data either from community cross-sectional studies or from Outpatient and Inpatient data from the Hospital of Manhiça). This analysis will be mainly done by using data from Manhiça, where longer series of data are available.

b) **Work Absenteeism:**

Work absenteeism is defined as the number of working days lost in the adult population during the previous month due to illness.

These data will be collected through two different strategies:

- Through the cross sectional studies conducted in Manhiça and Magude before and after the elimination campaigns take place. In this case information on absenteeism will be self-reported;
- Through information collected from the main Sugar Cane companies in the respective areas (control vs. treatment group): Illovo (Maragra) and Xinavane. In Xinavane, although the sugar case factory is in the Manhiça district, a relevant number of workers are from the district of Magude.

c) **School Absenteeism:**

School absenteeism is defined as the number of days of school lost in the previous month among primary school students (6 to 12 years old).

These data will be captured through primary data collection at schools, both in Manhiça and Magude during a period of 6 months to capture data before and after the intervention. More specifically, in Manhiça, from 96 schools existent in the district, data will be collected from 15 of them, and in terms of students, data on 20.670 students over 46.773 students existent in the district will be analysed. In Magude, data from 15 out of the 63 existent schools will be collected, which will comprise a sample of 7.158 students, which represent 53% of all students in the district (table 1). More details on the data collection plan can be found in the annex.

	Manhiça	Magude
Nº schools selected	15	15
Nº schools district	96	63
% schools covered	16%	**24%**
Nº students selected	20.670	7.158
Nº students district	46.773	13.460
% students covered	**44%**	**53%**

Source: ñ3 de março 2015ò, Ministério de Educaçao

The analysis of both work absenteeism and school attendance will be performed by merging, where feasible, data from the schools and for the workplaces with individual level data of children and workers from the DSS. This merge will be done through the *permanent identification number (Perm_ID)* provided by the DSS (children at school/their parents and workers will be asked to provide this information). A tentative merge by using a combination of names/date of birth/sex will be done if information on *Perm-ID* is not available. This will allow, in the difference in difference analysis, to control with the main personal and familiar factors of every child/worker, particularly the socio-economic condition.

Objective 3: Cost-effectiveness analysis in Magude

This will imply to estimate and compare the strategy that provides the greatest impact at the lowest cost, or the one with greatest ñvalue for moneyò (control vs. elimination strategies). This will be done through **cost-effectiveness analysis,** this means, comparing the relative costs and outcomes (effects) of two or more courses of action (control vs. Elimination strategies). The CEA will expressed in terms of a ratio where the denominator is a gain in health from a measure (years of life, malaria cases averted, malaria related deaths averted) and the numerator is the cost associated with the health gain.[2] Disability-adjusted life years (DALY)[1] will be used to express the health impact of both interventions. The numerator of the cost effectiveness ratio will be given by the direct benefits (savings) of malaria elimination compared with control. That is, the costs of malaria elimination will be subtracted from the cost of malaria control. The estimate of costs of malaria elimination, control and case management is explained in the costing protocol. In brief, the costs of malaria control, in terms of prevention (bed nets distribution, indoor residual spraying, etc) will be taken from Ministry of Health documents and the costs of malaria case management will be taken from previous estimates. The costs of malaria elimination will be estimated within the MALTEM context.

The health impact of malaria elimination will be provided within the framework of MALTEM study; the health impact of malaria control will be provided by the malaria studies conducted up to now by the CISM.

Objective 4: Cost-effectiveness analysis beyond Magude

The cost effectiveness analyses will be defined as net costs per disability-adjusted life years (DALYs) averted. Net costs are given by the difference between intervention costs (costs of malaria elimination estimated both for the district of Magude and scaled up either to the South of the country or to the whole country. These costs are defined in the costing protocol). In terms of health impact, the cost effectiveness analysis beyond Magude will be based on different potential scenarios of reduction of malaria cases due to elimination strategies:

- No malaria cases;
- Low prevalence of malaria (1%);
- Medium prevalence of malaria (5%).

[1] DALYs: The disability-adjusted life year (DALY) is a measure of overall disease burden, expressed as the number of years lost due to ill-health, disability or early death.

The burden of malaria for the whole country associated with the current malaria control mode will be taken from national reports.

DALYs averted will be calculated by multiplying the number of DALYs due to the disease by the reduction in morbidity and mortality resulting from the interventions. DALYs will be discounted but not age-weighted (Fox-Rushby, 2001).

The cost-effectiveness analysis will be performed according to the time frame defined for the costing. Importantly, the cost-effectiveness analysis will be only contingent in this study as there may not be the need to undertake such an analysis. This will happen if the strategy ‟malaria control" will be dominated by the strategy ‟malaria elimination" which may happen if the health impact of the latter is higher compared with the former strategy and the net costs of the latter are lower than those of the former strategy.

As for costing, the CEA will be both deterministic and probabilistic. All model inputs will be expressed in as probability distributions (Briggs et al). Probabilistic sensitivity analysis will be performed through Monte Carlo simulations using Microsoft Excel©. The cumulative average net monetary benefits (threshold level*incremental effects - incremental costs) will be depicted in graphs to evaluate the number of iterations needed to produce stable results. A threshold analysis will performed to estimate cut-off points beyond which the elimination is no longer cost-effective compared with control. Threshold analysis will be mainly performed on the MDA drug price and malaria incidence.

Incremental cost-effectiveness ratios will presented graphically in the cost-effectiveness plane (Black et al, 1990) and as acceptability curves (Fenwick et al, 2004).

JUSTIFICATION OF THE CHOICE OF THE CONTROL AREA

The study we propose is not not a randomized one. Malaria elimination activities will be carried out in Magude and not in a randomized way (it is not possible to randomize malaria elimination). In order to identify the impact of malaria elimination activities on indicators of economic development (workers and children absenteism) and in order to perform the general cost-effectiveness analyses a comparator is needed. Manhiça may be not ideal but all the information on costs we available are from that district and it is from that district that we can rely on good quality of data from the DSS. Also, The sugar cane factories from which data will be extracted for workersô absenteeism are in the Manhiça district.

In the estimates we will control for potential confounders, exactly because good data are available from both districts. It is possible to control, for instance, for the socio-economic status of people living in the two districts. Features of the health systems of the two districts are also known.

WORKPLAN (2015- 2016)

	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec	Jan
Development of protocols												
Preparation and data collection												
Data management and analysis												
Study completed												
Results dissemination												

BUDGET (FEBRUARY 2015- JANUARY 2016)

Item	Total (in USD)
Field data supervisor cost	**3.000**
Office Material	**1.500**
Transport and fuel (field work activities)	**2.500**
Publication costs	**5.000**
Communications	**500**
Data entry and analysis	**5.000**
Total direct costs	**17.500**

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APPENDIX

District	Posto Adm.	School name	Nº Stud.	% Stud.	Junho					Julho					Agosto					Setembro					Novembro					December				
					22	23	24	25	26	6	7	8	9	10	24	25	26	27	28	7	8	9	10	11	23	24	25	26	27	30	1	2	3	4
Magude	Posto Sede	Bobe	309	2%																														
Magude	Posto Sede	Maguiguana	834	6%																														
Magude	Posto Sede	Magude	721	5%																														
Magude	Posto Sede	Mawandla	984	7%																														
Magude	Posto Sede	Graça Machel	826	6%																														
Magude	Posto Sede	Matchabe	1.200	9%																														
Magude	Posto Sede	Simbe	131	1%																														
Magude	Posto Sede	Duco	158	1%																														
Magude	Posto Sede	Moine	228	2%																														
Magude	Posto Sede	Ungucha	170	1%																														
Magude	Motaze	Motaze	742	6%																														
Magude	Motaze	Pontia	166	1%																														
Magude	Motaze	Nwambyana	376	3%																														
Magude	Panjane	Panjane	233	2%																														
Magude	Panjane	Nhiuane	80	1%																														
TOTAL MAGUDE			7.158	53%																														
Manhiça	Manhiça Sede	EPC Manhiça Sede	1.295	3%																														
Manhiça	Manhiça Sede	Mulembja	1.843	4%																														
Manhiça	Manhiça Sede	7 de abril	3.000	6%																														
Manhiça	Manhiça Sede	Maciana	1.744	4%																														
Manhiça	Manhiça Sede	Eduardo Mondlane	946	2%																														
Manhiça	Manhiça Sede	Maragra	2.359	5%																														
Manhiça	3 de fevereiro	Palmeira	1.585	3%																														
Manhiça	3 de fevereiro	3 de fevereiro	1.734	4%																														
Manhiça	3 de fevereiro	Chicuachana	1.080	2%																														
Manhiça	Xinavane	EPC Xinavane	832	2%																														
Manhiça	Xinavane	Mepambe	1.641	4%																														
Manhiça	Xinavane	Aguiar	874	2%																														

Manhiça	Ilha Josinha Machel	Ilha Josina Machel	988	2%																														
Manhiça	Ilha Josinha Machel	Mampsana	403	1%																														
Manhiça	Ilha Josinha Machel	Dzonguene	346	1%																														
TOTAL MANHIÇA			20.670	44%																														