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Cost of the national malaria control program and cost-effectiveness of indoor residual spraying and insecticide-treated bed net interventions in two districts of Madagascar

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Abstract

Background Madagascar has made significant progress in the fight against malaria. However, the number of malaria cases yearly increased since 2012. ITNs and IRS are key interventions for reducing malaria in Madagascar. Given the increasing number of cases and limited resources, understanding the cost-effectiveness of these strategies is essential for policy development and resource allocation.

Methods Using a societal perspective, this study aims to estimate the cost of the National Malaria Control Program (NMCP) through the first national malaria strategic plan (implemented over the period 2009–2013) and to assess the cost-effectiveness of two individually implemented malaria control interventions (ITNs and IRS) in two districts, Ankazobe and Brickaville. The cost-effectiveness ratio (CER) of ITN intervention was then compared to the CER of IRS intervention to identify the most cost-effective intervention. The cost of the NMCP and the costs incurred in the implementation of each intervention at the district level were initially estimated. On the basis of two results, the CERs of ITN or IRS correspond to the total cost of ITN or IRS divided by the number of people protected or the number of disability-adjusted life years (DALYs) averted. A deterministic univariate sensitivity analysis was conducted to assess the robustness of the results with a discount rate of 2.5% (0–5%) (costs and DALYs) and a 95% CI (person protected).

Results From 2009 to 2013, the NMCP cost USD 45.4 million (USD 43.5–47.5, $r=0-5\%$) per year, equivalent to USD 2.0 per capita per year. IRS implementation costs were four times higher than those of ITNs. The CER of IRS per case protected (USD 295.1 [285.1–306.1], $r=0-5\%$) was higher than the CER of ITNs (USD 48.6 [USD 46.0–51.5, $r=0-5\%$] in Ankazobe and USD 26.5 [USD 24.8–28.4, $r=0-5\%$] in Brickaville). The CERs per DALY averted of IRS was USD 427.6 [USD 413.0–546.3, $r=0-5\%$] in Ankazobe and, for ITNs, it was USD 85.4 [USD 80.8–90.5, $r=0-5\%$] in Ankazobe and USD 45.3 [USD 42.2–48.4, $r=0-5\%$] in Brickaville. Compared to the country GDP per capita (USD PPP 1494.6 in 2013), ITN intervention was “highly cost-effective” while the CER for IRS interventions was sensitive to parameter variation (CI, 95% of persons protected), which ranges from highly cost-effective to only cost-effective (USD 291.5–2004, $r=2.5\%$).

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Conclusion In the Malagasy context, IRS intervention cost more and was less effective than ITN intervention. Willingness to pay for IRS is questioned. A relevant budget impact analysis should be conducted before a potential extension of this intervention.

Keywords Malaria control program, Cost-effectiveness analysis, Indoor residual spraying, Insecticide-treated nets, Madagascar

Introduction

The creation of the Global Fund (GF) in 2002 has reinvigorated the fight against malaria worldwide by providing new and important financial resources [1]. In addition, malaria research has helped WHO to define new regional and international strategies (such as the use of preventive tools in pregnant women and children under five, the use of malaria vaccines in selected areas, etc.) or to update strategies (distribution of impregnated bed nets and indoor residual spraying). These strategies have contributed to a significant reduction in malaria incidence and deaths worldwide [1]. Between 2000 and 2019, malaria incidence (cases per 1,000 population at risk) decreased from 80 to 57 cases per 1,000 population at risk, and malaria deaths decreased from 897,000 to 568,000 [1, 2]. Despite these successes, malaria remains the leading cause of morbidity and mortality, with 249 million cases and 608,000 deaths in 85 malaria-endemic countries and regions in 2022, particularly in the WHO African Region, where 94% of cases occur. Malaria also has an important economic burden. Countries with high malaria transmission experience an estimated 1.3% lower gross domestic product (GDP) growth per person per year (due to loss of life and productivity), while a 10% reduction in malaria incidence results in 0.11% faster per capita growth per year [3, 4]. Moreover, only 23 of the malaria endemic countries are on track to meet the 2025 global technical strategy (GTS) milestone i.e., malaria elimination [2]. Reaching this milestone in Africa could be hampered by two major factors in the coming years. First, insufficient funding has reduced the efforts made. For example, global malaria funding in 2017 and 2019 was USD 3.2 billion and USD 3.0 billion, respectively. This is far below the estimated USD 5.6 billion per year needed to stay on track toward the WHO GTS (USD 6.8 billion in 2020, rising to USD 9.3 billion in 2025 and 10.3 billion in 2030) [2, 5]. The second is related to emerging malaria parasite resistance to artemisinin-based combination therapy (ACT), coupled with increasing vector resistance to pyrethroids, the primary insecticide currently used in insecticide-treated nets (ITNs) [6–10]. Furthermore, some countries making progress towards malaria control, like Madagascar, are experiencing large increases of malaria cases over the past few years [2, 5].

Madagascar is a tropical island located in the Indian Ocean off of southern Africa. In 2022, GDP per capita was USD 1,781.8 in purchasing power parity (PPP) terms,

and 75.2% of people lived below the poverty line [11, 12]. Malaria remains a major public health concern in Madagascar, with total malaria cases increasing from 293,910 in 2010 to 1,366,205 in 2015 and 1,693,321 in 2022 [2]. Madagascar presents a large range in malaria transmission across the country: high transmission in the equatorial coastal zone (the East); seasonal transmission in the tropical coastal zone (the West); low, short and unstable transmission in the sub-desert area (the South) and an elimination phase in the central highlands and its fringes [13, 14]. The current National Malaria Control Program (NMCP) was established in 1998 and has resulted in three National Malaria Strategic Plans (NMSPs) over the past decade (2008–2012, 2013–2017 and 2018–2022).

ITNs and indoor residual spraying (IRS) are the most widely used malaria vector control interventions and recommended by the WHO. However, the spread of pyrethroid resistance in malaria vectors is recognized as the major threat to the effectiveness of ITN interventions. The results of studies on this issue are not always consistent, with some concluding that ITNs remain protective against malaria and others finding a significant reduction in efficacy. With regard to IRS, the trial evidence on their effectiveness has been very limited [2]. Therefore, the poorest countries, especially those on the path to malaria elimination, need more convincing elements not only to ensure the efficacy of the control strategies implemented, but also to assess their efficiency, especially in the context of constrained resources. Although a large number of studies carried out in endemic countries have already analyzed the costs and cost-effectiveness of these two types of interventions [15–22], the results have not always impacted the local policy. In fact, the heterogeneity of epidemiology (high or low malaria prevalence) and health care contexts, as well as the different analytical approaches (provider or community perspective), make it difficult to compare results, as the methods used vary (in terms of study design, type of data used (primary, secondary, simulation), cost and cost-effectiveness analyses, selection of health outcomes, etc.). Furthermore, most studies focused on a single intervention (ITNs or IRSs) rather than combined interventions (ITN+IRSs vs. ITNs or IRSs only) and took a provider perspective rather than a community perspective [21]. Finally, the results are not always consistent: some studies have concluded that ITNs are more effective and less expensive than IRS, while other studies have found that IRS, although

more expensive, appear to be more effective than ITNs [15, 18, 19]. Two systematic reviews of cost and cost-effectiveness analyses of malaria strategies, conducted 10 years apart, concluded for IRS and ITNs/LLINs that it is not possible to generalize about whether ITNs/LLINs or IRS are more cost-effective [16, 21]. To summarize, there is considerable heterogeneity in the methodological approaches used; studies on the cost-effectiveness of IRS are recent; most of the cost-effectiveness studies are from East Africa (Kenya and Tanzania); and the few studies on Madagascar have focused on treatment strategy.

As a low-income country with four epidemiological patterns of malaria and a recent but steady increase in malaria incidence, Madagascar is in need of more cost-effectiveness studies on the two strategies implemented (ITNs and IRS) in order to improve decision making and resource allocation. The objective of this paper was to estimate the total cost of the national malaria control program and evaluate the cost-effectiveness of two individual preventive strategies (ITNs and IRS) of the incidence of clinical malaria, to compare them, and to identify the most cost-effective approach. This analysis was conducted using a reference scenario that assumes no vector control interventions specifically, no consistent use of ITNs every night and no IRS application at the primary residence within the past 12 months. A case study was carried out in two districts (Brickaville and Ankazobe) following the standard methodology of the PALEV-ALUT research toolbox."

This paper contributes to the literature by combining primary and secondary cost data with field epidemiological data, by adopting a societal perspective, and by providing results in two different settings (high endemic transmission and pre-elimination) for a resources-limited country with low malaria incidence.

Materials and methods

This study was part of an operational study named "PALEVALUT," which aimed to develop a standardized multidisciplinary method (toolbox) for proposing an integrated operational evaluation of malaria control [23]. This study included, among others, a standardized method for the cost (economic tool) and for measuring the protective effectiveness of interventions against the occurrence of acute clinical episodes (epidemiological tool).

In this study, the economic tool was used to assess the costs of the NMCP and the cost-effectiveness of two malaria control strategies (IRS and ITNs) implemented in the districts of Ankazobe and Brickaville. The first step was to evaluate the overall financial expenditures associated with NMCP at the national level. Subsequently, at the district level, the cost associated with malaria control programs supported by the NMCP was estimated. Third,

an estimation was made of the cost of malaria treatment borne by households (HHs) and health facilities (HFs). Fourth, we employed the protective effectiveness of ITN and IRS interventions by using the data obtained from a case-control study (epidemiological tool of the PALEV-ALUT toolbox).

The Madagascar Ministry of Health (MOH) (approval no. 247/MNSANP/SG on 26/03/2013) and the National Ethics Committee of the Madagascar MoH (approval no. 12/MNSANP/EC on 03/12/2014) approved this study.

Data collection

Economic data at the national level

Although the NMCP has published annual reports since 2010, the data available were incomplete, as they excluded information regarding malaria activities conducted by partners. Consequently, the financial outlay of the NMCP was derived from the World Malaria Reports (WMRs). This encompassed the expenditure of the Madagascar government and its partners. The cost of the NMCP were drawn from the WMRs 2009–2013. This period corresponds with the implementation of the first NMSP (2008–2012) and aligns with the epidemiological, entomological, and health surveys that were conducted in 2014 to assess the efficacy of ITNs and IRS interventions [24, 25].

Economic data at the district level

The cost of the malaria program, as borne by both HFs and HHs, was determined through surveys conducted in 2014 in two distinct districts: Brickaville, situated in the eastern transmission zone (control phase), and Ankazobe, located in the fringe transmission zone (elimination phase). Brickaville exhibited perennial transmission patterns and benefited from multiple rounds of mass ITNs distribution campaigns. From 2009 to 2013, the most recent distribution in this district occurred in November 2013. In contrast, Ankazobe exhibited seasonal transmission patterns and benefited from multiple mass campaigns of pyrethroid-based ITNs (provided by the NMCP) and one IRS with bendiocarb per year (funded by USAID). The latest campaign of these two interventions in Brickaville took place in November and December 2013.

Cost of malaria prevention and cost of providing malaria treatment at HFs

The survey encompassed the public district hospital and public primary HFs, of which there were four in Ankazobe and five in Brickaville. The private sector was either nonexistent or limited to the district's chief town. The sector is represented only by two private centers, which collectively serve a mere fraction (less than 1.5%) of the district's population [26]. The two private centers were

not surveyed, as the cost of their services was borne by HHs and were included in HH surveys. For public HFs, data related to the treatment protocol and direct and indirect costs associated with the management of uncomplicated and complicated malaria were collected. Direct costs included the salaries of human resources engaged in managing malaria cases, based on the time devoted by medical and non-medical staff and the monthly salary per socio-professional category. Direct costs also encompassed antimalarial medicines and rapid diagnostic test (mRDTs), as well as other products employed for malaria treatment. Indirect costs were associated with other HF expenditures, encompassing management, equipment and other operational costs. Data collection covered a period of 12 months preceding the survey. In addition to the costs, the number of consultations and hospitalizations caused by malaria were collected.

Cost of malaria prevention and treatment borne by HHs

In each district, the survey included a total of nine fokontany (basic administrative subunits at the local level) randomly selected in the two communes. In Ankazobe and Brickaville, 405 HHs with 2,165 individuals and 398 HHs with 2,093 individuals, respectively, were investigated. The collected data dealt with expenditures for malaria prevention (nets, insecticide, mosquito coils, etc.) and out-of-pocket made in treatment of malaria (consultation fees, hospitalization costs, antimalarial medicines, transport costs, etc.). The HH survey was complemented by street vendors and private pharmacies surveys, which provided households with antimalarial drugs when health facilities were out of stock or for the purpose of self-medication. The costs derived from the HF and HH surveys were collected in Malagasy currency (Ariary).

Epidemiological data at the district level and the protective effectiveness of the two vector control interventions

As previously described [24], the protective effectiveness of vector control interventions (ITNs and IRS) against the occurrence of clinical malaria was determined from a case-control study conducted in HFs (further details can be found in Appendix 2). In summary, patients and controls were recruited between May and September 2014 in four HFs. The health outcome used to measure effectiveness is the occurrence of a clinical malaria episode. Cases were defined as individuals aged ≥ 6 months who resided within the study area, presenting at the HF with a fever or a history of fever, and malaria infection confirmed by mRDT detecting panLDH and pFHRP2 (mRDT, CareStart™, Access Bion Inc., Somerset NJ, USA) or by microscopy, as per NMCP protocol. Controls were defined as individuals aged ≥ 6 months who presented at the HF for any reason other than fever, with the exception of vaccination or antenatal care, and who resided in

the study area. Additionally, controls were required to have neither a recent history of fever nor hyperthermia as measured by axillary temperature. “Exposure to ITNs” was defined as having slept under an ITN every night for the preceding month. This criterion was selected because clinical malaria typically occurs within a month after infective mosquito bites in the absence of chemoprophylaxis, and intermittent use of ITNs significantly reduces their effectiveness. “Exposure to IRS” was defined as having received IRS treatments at one’s primary residence within the past 12 months. This criterion was chosen because IRS is typically applied once per year, usually just before the high transmission season, during which this study was conducted, and its protective effects last for up to six months. A multivariate logistic regression model using generalized linear models was established to estimate the association between the outcome (case versus control status) and the exposure to control interventions. The model was controlled for age, sex, socio-economic status, and commune. The study included 33 clinical malaria cases and 331 controls (no malaria cases) in Ankazobe and 180 cases and 601 controls in Brickaville. The protective effectiveness of each malaria control intervention was calculated independently for each district.

Cost estimation

The costs were estimated from a societal perspective. A three-step procedure was used to estimate the cost of the IRS and ITN interventions. This involved estimating the cost of the NMCP at the national and district levels, as well as the costs borne by HFs and households HHs.

The first step was to assess the total cost of the malaria control program at the national level (C_{Ti} , C_{ni}). The costs collected dealt with paid expenditures. All cost estimates are referenced to the year 2013, which marked the conclusion of the five-year malaria program. To account for the effects of inflation, a consumer price index (base 100 in 2010) was used, while the average exchange rate for 2013 (1 USD=2,207 MGA) [27, 28] was employed for conversion purposes. We also conducted a deterministic univariate sensitivity analysis to assess the robustness of the results with a discount rate of 2.5% (0–5%) applied, as recommended by the “Haute Autorité de Santé” (HAS) [29]. Given that the total cost at the district level is calculated for one year, the total cost of the NMCP at the national level is reported on an annual basis by dividing the total cost by the NMSP duration, which is five years.

The second step was to allocate a part of the average annual total cost of the national program to Brickaville and Ankazobe proportionally for the population of each district (C_{1d}). The last step was to assess the total cost (C_d) of malaria prevention strategies (ITNs and IRS)

borne by the NMCP (C_{1d}), HFs (C_{2d}) and HHs (C_{3d}) at the district level.

As previously mentioned, the total cost of the NMCP was computed from WMRs from 2009 to 2013 and was calculated per strategy and per intervention. The WMR expenditure breakdown included common expenditures (administrative management, planning and overhead, HR and training, supply management, infrastructure and equipment, monitoring and evaluation, and other expenditures (A. Table 1) and specific expenditures for preventive strategies such as nets and insecticides and communication and advocacy (B. Table 1) and for treatment strategies (mRDTs, antimalarial medicines (C. Table 1).

Common expenditures were allocated to each intervention (ITNs, IRS, IEC, diagnosis and antimalaria medicines) on a pro rata basis. The total cost was estimated for each component of the B and C strategies (C_{Ti}).

We calculated an average annual cost (C_{ni})

$$C_{ni} = \frac{C_{Ti}}{5}$$

The total cost of the malaria program at the district level (C_d) was the sum of three components:

$$C_d = C_{1d} + C_{2d} + C_{3d}$$

where.

- C_{1d} is the average annual cost of the NMCP borne by the government and its partners attributable to the district. It is calculated as the district population weighted sum of the annual cost of ITNs (C_{nITN}) and IRS (C_{nIRS}).

$$C_{1d} = (C_{nITN} + C_{nIRS}) \times \frac{\text{district target population}}{\text{national target population}}$$

- - C_{2d} is the total cost of malaria prevention borne by HFs and includes the financial resources spent by public HFs to provide a malaria prevention strategy (ITNs or IRS).
- - C_{3d} is the total cost of malaria prevention borne by HHs, including the financial or nonfinancial resources (valued in monetary terms) spent by HHs to acquire nets or to benefit from IRS.

$$C_{3d} = C_{HHIRS} + C_{HHITN}$$

where.

C_{HHIRS} = the average cost of IRS* the number of HHs that received IRS.

C_{HHITN} = the average cost of ITNs* the average number of ITNs purchased by HHs* the number of HHs in the district.

The MOH protocol for malaria treatment indicated that complicated cases should be referred and treated at the hospital. All malaria cases for which no hospitalization was required were considered uncomplicated malaria and were treated at PHFs. For the cost analysis, only cases confirmed by mRDT or microscopy were included (i.e., unconfirmed cases were excluded). The cost was calculated for complicated cases and for uncomplicated cases over one year (2013). For HFs, the cost attributable to malaria treatment included direct costs (as HR, medicines, consumables, etc.) and indirect costs attributed to the management of malaria. The cost was estimated by applying a standard costing procedure. Capital and recurrent expenditures were estimated using an ingredient approach combined with a top-down methodology [32, 33].

For HHs, the related costs to an episode of malaria included medical costs (drugs, mRDTs, hospitalization, etc.) and nonmedical costs (transport, food, or other informal expenses) for individuals who had an episode of fever in the three months preceding the cross-sectional survey.

Cost-effectiveness estimation

Preliminary data found that the implementation of IRS and ITN in combination was ineffective. The OR of exposure to ITNs only was lower (OR 0.14, 95% CI [0.01–0.98]), although not significantly, than exposure to both ITNs and IRS (OR 0.26, 95% CI [0.08–0.87]). We then estimated the cost-effectiveness of each strategy individually to assist the Malagasy government in selecting the most efficient strategy [21].

The cost-effectiveness ratios (CERs) of ITN and IRS interventions were computed separately and were performed using two outcomes, the number of persons protected and DALYs averted. In order to avoid double counting the effect of the strategy on health (in the numerator for costs and in the denominator for health outcomes), we calculate the CER on a net cost (NC) basis, i.e., the total cost at the district level (C_d) minus the cost of persons protected (C_{pp}).

$$NC = C_d - C_{pp}$$

C_d : the total annual cost of the national program at the district level.

C_{pp} : the total cost of persons protected at the district level

The CER per person protected was obtained by dividing the total annual net cost (NC) by the number of persons protected (N_{pp}).

Table 1 Cost components of the malaria control program at the national and district levels

Items	Components	Sources
I-Total cost of the NMCP from 2009 to 2013	Expenditure breakdown	WMR: 2009–2013 [30]
A-Common costs reallocated proportionately to B and C activities	Planning, management, overhead Human resources and training Supply management Infrastructure and equipment Monitoring and evaluation Other	
B- Preventive strategy	ITNs (nets) IRS (insecticides and spray equipment) Communication and advocacy	
C- Treatment strategy	Diagnostic tests: mRDTs and microscopy Antimalarial medicines	
II- Total cost of the malaria prevention program at the district level	Average annual cost of ITNs for the NMCP	Authors' estimation: Annual cost of ITNs from WMR 2009 to 2013 WMR 2013: Targeted population at the national and district levels
D- ITN intervention	Total annual cost of ITNs for HFs Management and overhead Human resources Supply management Infrastructure and recurrent expenditures Total annual cost of ITNs for HHs Cost of nets Other attributable costs to acquire nets	Authors' HF survey 2014: Brickaville: 1 hospital and 5 PHFs Ankazobe: 1 hospital and 4 PHFs District data: Number of HFs in the district Authors' HH survey 2014 Brickaville: 405 HHs (2,165 individuals) Ankazobe: 398 HHs (2,093 individuals) District data: Number of HHs in the district
E- IRS intervention	Average annual cost of IRS for the NMCP Total annual cost of IRS for HFs Management and overhead Human resources Supply management Infrastructure and recurrent expenditures Total annual cost of IRS for HHs Attributable cost to benefit from IRS	Authors' estimation: Annual cost of IRS from 2009 to 2013 WMR 2013: Targeted population at national and district levels Authors' HF survey 2014: Brickaville: 1 hospital and 5 PHFs Ankazobe: 1 hospital and 4 PHFs District data: Number of HFs in the district Authors' HH survey 2014 Brickaville: 405 HHs (2,165 individuals) Ankazobe: 398 HHs (2,093 individuals) District data: Number of HHs in the district
III-Cost of persons protected and DALYs averted at the district level		
F-Number of persons protect- ed at the district level	Npp through ITNs Npp through IRS	Case-control study 2014 Brickaville: 33 cases/331 controls Ankazobe: 180 cases/601 controls [30]
G- Number of malaria cases at the district level	Number of uncomplicated cases Number of complicated cases	
H- DALYs averted	Number of deaths averted Number of mild, moderate and severe malaria cases averted	Case-control study 2014 Brickaville: 33 cases/331 controls Ankazobe: 180 cases/601 controls [24, 31]
I-Mean treatment cost of uncomplicated cases at HFs	Direct cost Health care personnel Consumables Medicines Indirect cost: Capital and recurrent expenditures	Authors' HF survey, 2014 Brickaville: 5 PHFs Ankazobe: 4 PHFs Using ingredient approach with top-down methodology

Table 1 (continued)

Items	Components	Sources
J-Mean treatment cost of complicated cases at HF	Direct cost Health care personnel Consumables Medicines Indirect cost Capital and recurrent expenditures	Authors' HF survey, 2014 Brickaville: 1 hospital Ankazobe: 1 hospital Using ingredient approach with top-down methodology
K-Mean treatment cost of uncomplicated cases for HHs	Direct cost Consultation fees Drugs Indirect cost: Transport, meals, other	Authors' HH survey, 2014 Brickaville: 405 HHs (2,165 individuals) Ankazobe: 398 HHs (2,093 individuals)
L-Mean treatment cost of complicated cases for HHs	Direct cost Hospitalization Consumables Drugs Indirect cost Transport, meals, other	Authors' HH survey, 2014 Brickaville: 405 HHs (2,165 individuals) Ankazobe: 398 HHs (2,093 individuals)

Sources: [24, 30, 31, authors' HF and HH survey]

$$CER = \frac{NC}{N_{pp}}$$

$$C_{pp} = C_{ppHF} + C_{ppHH} = (Cucc * N_{ppuc} + Ccc * N_{ppcc})_{HF} + Cucc * N_{ppuc} + Ccc * N_{ppcc})_{HH}$$

C_{ppHF}: The Total cost of persons protected for the health facilities, **C_{ppHH}**: the total cost of persons protected for households.

Cucc: average treatment cost of an uncomplicated case. **Nppucc**: number of persons protected against uncomplicated cases. **Ccc**: average treatment cost of a complicated case. **Nppcc**: number of persons protected against complicated cases.

The estimation of the number of persons protected was based on the case-control study. Case-control studies estimate the proportion of exposure to a factor, such as a malaria control intervention, among malaria cases and non-malaria controls. This approach enables the estimation of odds ratios (ORs) and the assessment of the significance of the association between exposure to a factor and the occurrence of malaria cases. (see more details in Appendix 2).

$$N_{pp} = E_{INCM} * P_{pp} / (1 - P_{pp})$$

EINCM: is the estimated incidence of uncomplicated clinical malaria episodes in the general population; **Ppp**: is the proportion of persons protected against uncomplicated cases in the general population. Ppp is an adjusted estimate and was obtained as follows:

$$P_{pp} = CMCI * (1 - OR)$$

CMCI: is the prevalence rate of exposure to the intervention in the sample of controls, considered an estimate of the prevalence rate of exposure to the intervention in the general population (coverage of the malaria control intervention); odds ratio (OR) of the exposure to the intervention against uncomplicated malaria.

The CER per DALY averted equals

$$CER = \frac{NC}{DALYs\ averted}$$

NC=annual total net cost of the national program at the district level.

DALYs are the sum of the years of life lost (YLL) due to premature mortality and the years of healthy life lost due to disability (YLD).

$$DALYs = YLL + YLD$$

$$YLL = Nad * Le$$

Nad: number of deaths averted: **Le**=life expectancy at average age of death

$$YLD = NaMild * d1 * coef1 + NaMod * d1 * coef2 + Nacc * d2 * coef3$$

NaMild: number of mild malaria cases averted; **d1**: average duration of mild malaria; **coef1**: disability weight for mild malaria.

NaMod: number of moderate malaria cases averted; **coef2**: disability weight for moderate malaria.

Nacc: number of complicated malaria cases averted; **d2**: average duration of complicated malaria; **coef3**: disability weight for complicated malaria.

Table 2 Parameters for DALY estimation

Parameters	Value	Sources
Duration of moderate and mild malaria (days)	7	[34]
Duration of severe malaria (days)	14	[34]
Age at death (years)	2	[35]
Life expectancy at the age of death 62.7		[36]
Disease weight coefficient		[34]
Mild malaria [CI-95%]	0.006 (0.002–0.012)	
Moderate malaria [CI-95%]	0.051 (0.032–0.074)	
Complicated malaria [CI-95%]	0.133 (0.88–0.19)	
Disease weight proportion		[37, 38]
Mild malaria	24.8%	
Moderate malaria	66%	
Complicated malaria	9.2%	

Table 2 presents the parameters used for DALY estimation.

As DALYs lost are no longer discounted (since 2010 [39]), we chose to do so in this study. However, an univariate deterministic sensitivity analysis using confidence intervals (CIs) was performed to quantify the effect of uncertainty and a discount rate of 2.5% (0–5%) was

applied (costs of the program and DALYs) and a 95% CI (person protected) was computed.

For the Cost effectiveness analysis threshold, the intervention was considered as cost-effective or highly cost-effective if the cost per DALYs averted was lower than three times or one time the GDP per capita in PPP, respectively [40, 41].

Results

Organization of the NMCP in Madagascar

Since 2002, the NMCP has worked with the Roll Back Malaria partnership (RBM) to develop NMSPs. The implementation of the NMSPs program is coordinated by the MOH through the NMCP and was financed by donors and technical partners such as the Global Fund, PMI, UNICEF, and WHO (Fig. 1).

The NMSP is implemented over a five years period. Each year, the NMCP defines a malaria action plan that describes the input requirements, for instance, the quantity of ACT, ITNs, etc. The Global Fund allocates funding to entities named principal recipients (PRs) and orders these inputs from the PRs. Each PR worked with organizations called subrecipients (SRs) to carry out the activities (distribution of supplies, IEC, etc.) and once they are available, the NMCP carries out training, distribution,

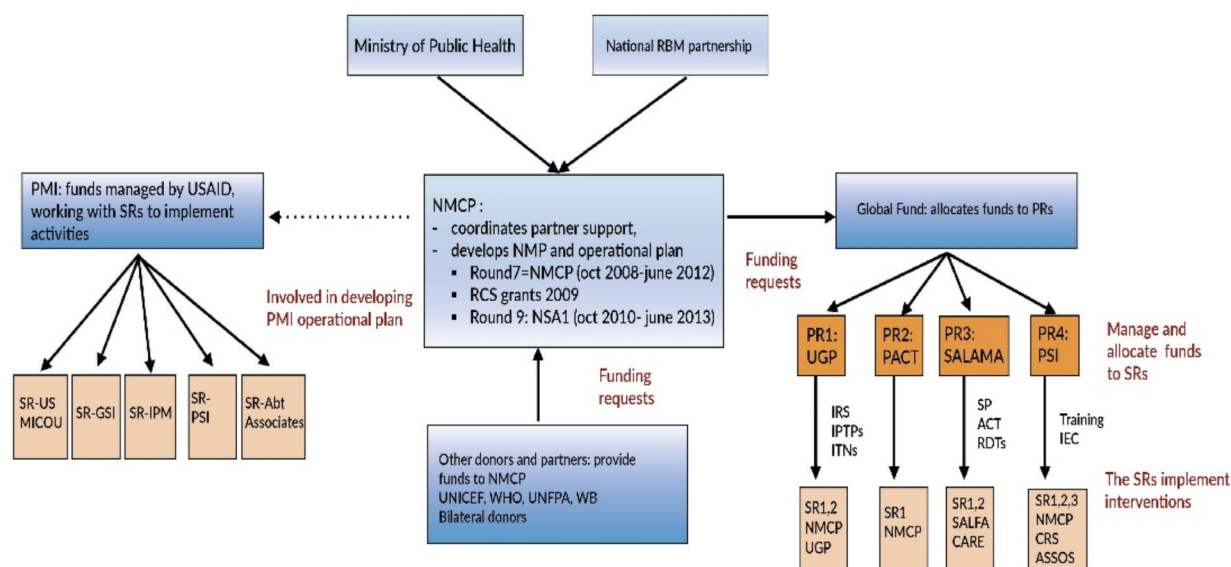


Fig. 1 Fight against malaria in Madagascar: partners and funding from 2009 to 2013. Source: Authors from interviews of different entities

and supervision activities, in collaboration with the SRs. In some cases, the NMCP becomes an SR and manages a few parts of the funding; in other cases, for targeted activities, the NMCP receives directly the funding from donors (Fig. 1).

NMCP: The National Malaria Control Program, **RBM:** Roll Back Malaria, **NGO:** nongovernmental organization, **PMI:** President's Malaria Initiative, **PR:** principal-recipient, **SR:** sub-recipient, **ACT:** Artemisinin-based combination therapy, **IPTp:** intermittent preventive treatment for pregnant women, **IRS:** indoor spraying of insecticide, **ITN:** insecticide-treated net.

From 2009 to 2013, the NMCP was composed of general management, project, financial and administrative units and five technical divisions associated with the strategies implemented: vector control, case management, epidemiological surveillance, monitoring and evaluation, and information, education and communication (IEC). During this period, the Global Fund financed 55.9% and the PMI 41.7% of the budget. The other funds came from the Malagasy government (less than 1%), UNICEF, the WHO and the Principality of Monaco. Since 2008, the PMI has supported IRS campaigns. However, between 2009 and 2013, due to the 2009 Malagasy political crisis, PMI did not work directly with the government but supported activities and interventions at the community level. Consequently, NMCP external core funding was withdrawn, and the implementation of the program was insufficiently coordinated during this period.

Malaria morbidity and mortality and universal coverage

From 2003 to 2011, the country registered progress in the fight against malaria. According to the MOH, malaria morbidity decreased from 13 to 1% and from 22 to 5% among children under five. During the same period, the malaria mortality rate fell from 26 to 8% among children under five and from 13 to 2% for those over five years of age [42]. However, this downward trend has been

reversed since 2012. Compared to 2010, the number of confirmed cases increased by approximately 2.3 in 2014, 4.6 in 2015 and 5.8 in 2022 (Fig. 2). An increase of more than 40% in mortality rate is observed between 2015 and 2021 [2].

The national malaria indicator surveys in 2013 [13] indicated that households obtained their ITNs mainly from mass campaigns (77% in rural areas and 63% in urban areas). Considering indicators of universal coverage, 79% of HHs owned at least one ITN, and 57% owned at least one ITN for every three people. In 2021, these proportions have fallen to 69.1% of HH with at least one ITN and 30.1% of HH with at least one ITN for every two persons [43]. ITN coverage has remained high since 2012 thanks to regular mass distribution of ITNs (2009–10, 2012–13, 2015, 2018–19, 2021) and community-based distribution [44].

Between 2010 and 2013, the IRS intervention was generalized in 21 districts and targeted in 32 districts. In 2012, the strategy was shifted to 'focus' on spraying in the central highlands (elimination phase). From 2014, the country shifted to a strategy of targeting regions with high levels of transmission and deployed IRS in the eastern and southeastern coastal districts [45]. This strategy, which is supported by the U.S. President's Malaria Initiative (PMI), has been implemented to date [46].

Cost estimation

The total cost of the NMCP from 2009 to 2013 was estimated to be about USD 227.6 (USD 237.6, 217.7; $r=0-5\%$) million. The inputs represented 55.3% of the expenditures: 46.8% for the preventive strategy (ITNs and IRS) and 8.5% for the curative strategy (ACT, mRDTs and microscopy). The management of the program accounted for 9.9% of the expenditures, and monitoring and evaluation accounted for 5.6%. The remaining cost was shared between human resources and training (18.2%), communication and advocacy (3.1%), supply, infrastructure and

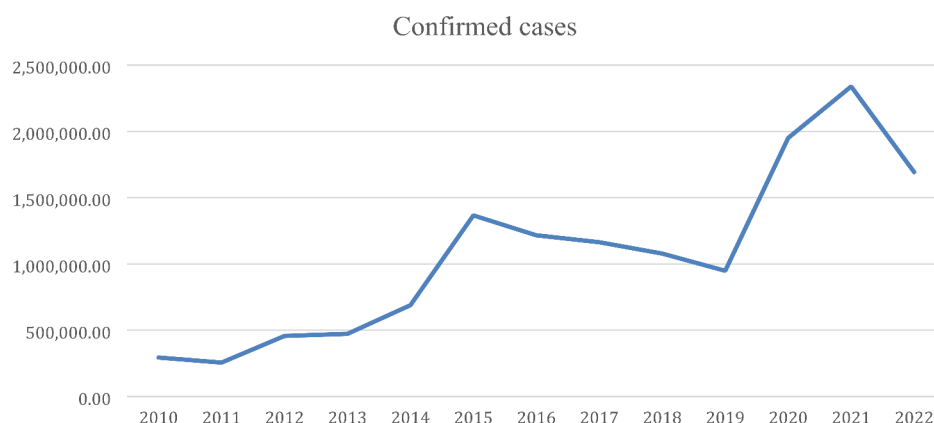


Fig. 2 Evolution of confirmed malaria cases between 2010 and 2022. Source [2]

Table 3 Cost of every NMCP activity from 2009 to 2013 (in 2013 USD)

Expenditure breakdown	<i>r</i> = 0%	<i>r</i> = 2.5%	<i>r</i> = 5%
Expenditures to allocate per activity			
Planning, management, overhead	23,344,310.3 (9.9%)	22,354,500.5 (9.9%)	21,452,393.7 (9.9%)
Human resources	18,832,191.0 (7.9%)	17,908,566.6 (7.9%)	17,073,288.8 (7.9%)
Training	24,079,991.4 (10.2%)	23,069,448.3 (10.2%)	22,140,357.8 (10.2%)
Monitoring and evaluation	13,200,902.1 (5.6%)	12,564,534.9 (5.6%)	11,986,597.2 (5.6%)
Supply management	7,680,371.2 (3.2%)	7,199,310.1 (3.2%)	6,762,849.9 (3.2%)
Infrastructure and equipment	12,228,240.7 (5.2%)	11,796,917.8 (5.2%)	11,397,866.8 (5.2%)
Other	6,756,056.6 (2.9%)	6,448,811.4 (2.9%)	6,170,403.7 (2.9%)
Total of common costs*	106,119,063.4 (44.6%)	101,342,089.6 (44.6%)	96,983,757.8 (44.6%)
Preventive strategies			
ITNs (nets)	63,687,643.1 (27.0%)	60,885,897.8 (27.0%)	58,345,090.2 (27.0%)
IRS (insecticides and spray equipment)	40,026,935.9 (17.1%)	38,696,527.1 (17.1%)	37,470,203.6 (17.1%)
Communication and advocacy	7,429,787.7 (3.1%)	7,077,639.1 (3.1%)	6,755,555.9 (3.1%)
Total	111,144,366.7 (46.8%)	106,660,064.0 (46.9%)	102,570,849.7 (46.9%)
Treatment strategy			
Diagnostic tests: mRDTs, microscopy	10,318,495.8 (4.4%)	9,638,662.99 (4.3%)	9,026,723.9 (4.3%)
Antimalarial medicines	9,991,983.0 (4.2%)	9,514,573.83 (4.2%)	9,076,804.4 (4.2%)
Total	20,310,478.8 (8.5%)	19,153,236.8 (8.5%)	18,103,528.3 (8.5%)
Total cost	237,573,908.8 (100%)	227,155,390.4 (100%)	217,658,135.9 (100%)

Source: [29]. * Further details on how common costs are allocated are given in Appendix 1

equipment (8.5%) and others (2.9%) (Table 3). On average, the NMCP spent USD 45.4 million (USD 43.5–47.5, *r* = 0–5%) per year over this period.

Cost of the malaria prevention program at the district level

The annual cost of ITNs was estimated to be USD 229,975 (USD 240,793–240,793, *r* = 0–5%) for Ankazobe and USD 312,066 for Brickaville (USD 326,746–298,743, *r* = 0–5%). In Ankazobe, the cost of the implementation of IRS was four times higher (USD 948,041) than the implementation of ITNs (Table 4). From a provider perspective, the mean cost of protecting one person from malaria ranged from USD 1.66 (USD 1.59–1.74, *r* = 0–5%) for ITNs interventions to USD 6.85 (USD 6.63–7.09) for IRS interventions.

Table 4 Average annual cost of ITN and IRS interventions at the district level from 2009 to 2013 (in 2013 USD)

National target population (1)	District target population (2)	Annual cost of the strategy at the national level (C _n) (3)	Annual cost of the strategy at the district level (C _d) (2)*(3)/(1) (<i>r</i> = 0%)	Annual cost of the strategy at the national level (C _n) (4)	Annual cost of the strategy at the district level (C _d) (2)*(4)/(1) (<i>r</i> = 2.5%)	Annual cost of the strategy at the national level (C _n) (5)	Annual cost of the strategy at the district level (C _d) (2)*(5)/(1) (<i>r</i> = 5%)
Ankazobe							
ITNs	13,218,942	23,020,105.9	240,793.6	21,985,847.0	229,975.1	21,047,191.2	220,156.6
IRS	2,038,005	14,467,866.3	981,597.6	13,973,283.7	948,041.8	13,516,862.1	917,075.1
Brickaville							
ITNs	13,218,942	23,020,105.9	326,746.2	21,985,847.0	312,066.0	21,047,191.2	298,742.8

Source: Authors' calculations from [30]

Table 5 Cost of malaria treatment for HFs at the district level in 2013 (in 2013 USD)

	Total cost for HFs surveyed (1)	Number of cases for HFs surveyed (2)	Mean cost (1)/(2)
Ankazobe			
Uncomplicated cases	2,715.3	1,007	2.7
Complicated cases	2,914.2	32	91.1
Brickaville			
Uncomplicated cases	3,288.0	968	3.4
Complicated cases	3,612.0	46	78.5

Source: Authors' calculations from the HF survey, 2014

Table 6 Cost of malaria treatment for HHs at the district level in 2013 (in 2013 USD)

	Total cost across all HHs surveyed (1)	Number of cases across all HHs surveyed (2)	Mean cost per case (1)/(2)
Ankazobe			
Uncomplicated cases	182.9	112	1.6
Complicated cases	-	-	9.3*
Brickaville			
Uncomplicated cases	1,271.8	380	3.3
Complicated cases	46.5	5.0	9.3

* No HH surveyed in Ankazobe presented a complicated case. The average cost of complicated malaria treatment was considered the same as that in Brickaville

Source: Authors' calculations from the HF survey, 2014

Cost of malaria prevention for HFs and HHs

According to the HF survey, activities related to malaria prevention delivered by HFs were free of charge for HF. Indeed, the district health office was responsible for the implementation of the IRS intervention, and the distribution of nets during prenatal visits by PHFs did not generate any additional management costs.

Regarding HHs, in the two districts, 97% had nets, received as endowments. In Ankazobe, the proportion of HHs that benefited from IRS was 80%. Non-spraying in the other households was due to the absence of family members during the IRS campaign. Almost all HHs spent no financial resources on IRS. Therefore, the cost of preventing malaria could be considered null for HFs (C_{2d}) and HHs (C_{3d}).

Cost of malaria treatment for HFs

The average cost of uncomplicated malaria treatment was relatively comparable for the two districts (USD 2.7 in Ankazobe and USD 3.4 in Brickaville). The treatment of a complicated case was estimated between 23 (USD 78.5 in Brickaville) and 33 times (USD 91.1 in Ankazobe) more than the treatment of a simple case (Table 5).

Cost of malaria treatment for HHs

Ankazobe and Brickaville have four and three legal drug depots, respectively, all of which are located in urban areas. Although antimalarial medicines are sold there, HH surveys showed that HHs use these depots or turn to street vendors when antimalarial medicines are out of stock in public HFs [47].

In Brickaville and Ankazobe, 35% and 17% of the HHs, respectively, reported having at least one member with signs of malaria in the last three months preceding the survey (Table 6). The average cost for an uncomplicated case was two times higher in Brickaville (USD 3.3) than in Ankazobe (USD 1.6).

Effectiveness of IRS and ITN interventions

The case-control study showed that the OR of the use of ITNs against the occurrence of uncomplicated malaria, was lower than one (thus protective), low (<0.50) and statistically significant in both Ankazobe (0.23, 95% CI 0.08–0.68) and Brickaville (0.43, 95% CI 0.20–0.86, Table 7), demonstrating that ITNs were an effective intervention in preventing uncomplicated malaria. The protective effectiveness of ITNs was lower in Brickaville than in Ankazobe, but this difference was not statistically significant. The point estimates of the preventive effectiveness (77% in Ankazobe and 57% in Brickaville) were used for subsequent calculations.

Regarding IRS, the OR was lower than one, relatively low, but not statistically significant (0.50, 95% CI 0.13–2.03, Table 7). Therefore, the protective effectiveness of IRS could not be demonstrated in this study, but the point estimate (50% protective effectiveness) was kept for further calculations, as it was in line with previous findings [24].

Cost-effectiveness of IRS and ITN interventions

The CER per person protected from ITNs was higher in Ankazobe than in Brickaville (Table 8), which corresponds to the difference in the incidence between the two districts. More importantly, the CER of IRS was higher, USD 295.1 (USD 285.1–306.1, $r=0-5\%$), than the CER of ITN in the two districts, USD 48.6 (USD 46.0–51.5, $r=0-5\%$) in Ankazobe and USD 26.5 (USD 28.4–28.4, $r=0-5\%$) in Brickaville.

The CERs per DALY averted (Table 9) were USD 526.8 (USD 508.8–546.3, $r=0-5\%$) for IRS and, for ITNs, USD 45.3 (USD 42.2–48.4, $r=0-5\%$) in Brickaville and USD 85.4 (80.8–90.5) in Ankazobe. Based on Madagascar's GDP (PPP) per capita in 2013 (USD 1494.6 [5]), ITNs and IRS interventions would be considered cost-effective. IRS was less cost-effective than ITNs, which were considered "highly cost-effective", i.e. the CER per DALY was lower than approximately thirty-two times the Madagascar GDP per capita. Moreover, the CER for IRS interventions

Table 7 Protective effectiveness and number of persons protected per year, 2013

Intervention	Population of district	EINCM	OR intervention [95%CI]	Protective effectiveness	Coverage (CMCI)	Ppp	Nppuc
Ankazobe	ITNs	138,272					
	IRS	138,272	0.23 [0.08–0.68] 0.50 [0.13–2.03]	77% 50%	65% 45%	50% 3,070	3,725
Brickaville	ITNs	187,629	0.43 [0.20–0.86]	57%	92%	53%	7,785

EINCM: estimated incidence of uncomplicated malaria cases; **OR** of the exposure to the intervention against uncomplicated malaria [95% confidence intervals]; **CMCI:** coverage of malaria control intervention; **Pppuc:** proportion of persons protected against uncomplicated malaria in the general population; **Nppuc:** total number of persons protected against uncomplicated malaria

Source: Ravolanjarasoa et al. Case-control studies for the evaluation of the protective effectiveness of malaria control interventions: How are they influenced by definitions of cases or controls? (Unpublished observations)

Source: Authors' calculations from the 2014 survey

was sensitive to parameter variation (CI, 95% of persons protected), which ranges from highly cost-effective to only cost-effective (USD 291.5–2004, $r=2.5\%$, Table 9).

Discussion

This study found that the NMCP spent USD 45.4 ($r=2.5\%$) million per year on malaria control, or USD 2 per capita [12], from 2009 to 2013. A sensitivity analysis indicates that the intervention using insecticide-treated nets (ITNs) is still considered highly cost-effective, as the CER per DALY averted is below the GDP (PPP) per capita. In contrast, the sensitivity analysis for IRS intervention indicates that the CER is sensitive to parameter variation, with the CER per DALY averted ranging between highly cost-effective to only cost-effective. The two interventions, when considered individually, are both efficient, but the ITN intervention was found to be more efficient and less costly than the IRS intervention. The NMCP has implemented universal ITN distribution in the two districts, but has also introduced IRS in Ankazobe, a low-transmission district, with the objective of enhancing control measures. However, the results of an epidemiological study indicated that combining IRS and ITN did not result in greater protection for the population. A recent study on the effectiveness of IRS in Madagascar also concluded that the evidence for a joint effect of ITNs and IRS was not yet conclusive, as only a few studies had evaluated the combined effectiveness of these two strategies [48].

This study also found that the cost of implementing malaria control interventions at the district level remained largely supported by the NMCP and its partners. Indeed, HH and HF expenditures on malaria prevention were not significant. The NMCP was not uniform across the country; it was adapted to the epidemiological context of each region. In Brickaville, where transmission was high, ITNs were the only prevention strategy implemented. However, in Ankazobe, where transmission was low, generalized IRS was added as recommended in the NMSP, meaning close to 100% of eligible structures were sprayed. The fact that IRS was adopted in pre-elimination zones (where the incidence was low) explained why this intervention turned out to be less cost-effective than ITNs. In Ankazobe, ITNs showed a higher protective effectiveness than IRS (77% vs. 55%), and they were also less expensive (USD 1.66 per capita vs. USD 6.85 per capita); hence, the cost-effectiveness ratio was almost four times lower despite their lower coverage (65% vs. 92%). The same result was found in India, where IRS was carried out in a low transmission area [49]. In Thailand and Benin, where IRS was implemented in highly endemic areas, it proved to be less efficient than ITNs [50, 51] or it was only efficient in urban areas [52].

Table 8 Cost-effectiveness ratio per person protected in 2013 (in 2013 USD)

	Np- pucc (1)	Nppcc (2)	Npp (3)	Cucc	Ccc	C _{pp}	HF(4)	HF(5)	HH(6)	HF(7)	HH(8)	HF(9)	C _{dpp}	C _d r=0%	NC R=0%	C _d (r=2.5%)	NC (r=2.5%)	C _d (r=5%)	NC (r=5%)	CER r=0%	CER (r=2.5%)	CER (r=5%)
				HH(4)	HF(5)	HH(6)	HF(7)	HH(8)	HF(9)													

Nppuc: number of persons protected against uncomplicated malaria. **Nppcc:** number of persons protected against complicated cases. **Npp:** total number of persons protected. **HHs:** households. **HF:** health facilities
Cucc: average cost of uncomplicated cases. **CCC:** average cost of complicated cases. **C_{dpp}:** weighted average cost of persons protected. **C_d:** total cost of the program at the district level. **C_{dpp}:** total cost of persons protected at the district level. **NC:** annual total net cost of the national program at the district level. **CER:** cost-effectiveness ratio. **CI[95%]** for uncertainty regarding effects. **lb:** lower bound. **ub:** upper bound
Source: Authors' calculations from surveys

Malaria has remained an important public health concern for the Malagasy government, especially in the context of an increase in cases since 2012. Although this study showed that IRS was less cost-effective than ITNs, this intervention should not be completely discarded, as it still prevented thousands of cases each year. Indeed, in the district of Ankazobe, IRS prevented 3,000 cases of uncomplicated malaria each year, while ITNs prevented 3,700 cases. The performance of IRS was related to its large coverage (92% compared with ITNs (65%). In endemic areas, IRS was recommended as a powerful vector control strategy to reduce malaria transmission [20, 53]. In Madagascar, a recent study conducted in nine districts with heterogeneous malaria presents evidence of a benefit of continuing IRS interventions over three years [48]. However, others studies showed also resistance to pyrethroids [54–56] and has led the NMCP to recommend rotation of insecticides every 2–3 years to manage insecticide resistance [57] in the NMSP 2018–2022. For instance, since 2016, non-pyrethroid insecticide products were deployed for IRS.

The latest WHO guidelines for malaria control [52] indicated that using both IRS and ITNs is not always more effective than ITNs or IRS when used alone (as we found in our study). Therefore, the WHO does not recommend one intervention over another and considers that local evidence such as the financial aspect (cost), malaria endemicity and cost-effectiveness would be the major factors in decision-making in certain countries [52]. A study discussed the challenge of making decisions only upon a national income-based approach. Authors have argued that the CER should be placed in the context of other local policies (such as equity and ethics), program options or budgetary impacts [57]. The stakes of these results are high for Madagascar. We have seen that IRS is much more expensive but less effective than ITNs. In terms of effectiveness, ITNs appeared to be more protective than IRS, while the two strategies appeared to be working independently (although this was not directly estimated). One reason suggested (but not tested in this study) could be the resistance to the bendiocarb used in IRS [48, 54, 55].

Although the total cost of the program was USD 2 per capita, it represented 10% of the health expenditures. This proportion may seem high, especially since the overall incidence of malaria in the country is low, but on the rise (14 per 1000 in 2010 to 20 in 2016 and to 57 in 2022) [58, 59, 60] and ITNs dominate in terms of protection [61, 62]. The NMSP 2018–2022 strategies focused on control in higher-burden zones whereas in low-burden zones, the focus is on elimination activities. After a mid-term review of the NMSP in 2020, the NMCP prioritizes IRS for transmission reduction in high-burden areas [57], i.e. 42 of 124 districts in Madagascar with a population

of 7,173,284 considered at high-risk [57]. Then, authorities may question their willingness to pay for the IRS-based strategy when it is much more expensive than the ITN-based strategy. The decision to maintain IRS will therefore depend on the willingness of Malagasy decision-makers to pay. Indeed, the NMCP's budget remains limited and relies on donations from the GF and PMI (439.9 million in current USD 2021 and 428.1 million in current USD 2013). A relevant budget impact analysis should also be conducted before any expansion of IRS intervention. Furthermore, given the effectiveness of ITNs, it is imperative that more people have access to ITNs (47.4% in 2020 and 54.2% in 2022) [2]. This should be coupled with solutions to insecticide resistance. One such solution should be the introduction of pyrethroid-piperonyl butoxide (PBO) long-lasting ITNs, which incorporate a synergist, PBO, into the net with a pyrethroid insecticide [61, 62].

The question of discounting costs and health outcomes is discussed in the literature. First, DALYs lost are no longer discounted (since 2010) [39]. All costs and outcomes are usually discounted at a same rate, while a recent literature considers that costs and benefits can be discounted at a different rate with a lower rate for non-monetized health outcomes. However, the debate is still open insofar as efficiency results seem to be sensitive to the fact of using different discounting rates [63]. Second, with the environmental crisis, we could imagine that time preference (i.e. short effect vs. long-term orientation) would change so that what would happen in the future will be as important as what happens in the present. An article suggests, for example, a positive relationship between long-term orientation and environmental policy performance [64]. Third, national guidelines on discounting in health economic evaluations show that European countries adopted their own discounting rates (from 1.5 to 5%); for some with different rates between costs and benefits (Belgium, Germany, The Netherlands) and for others with the same rates (Estonia, Finland, Italy) [64]. Fourth, discounting raises the question of equity between short-term or long-term priorities [65]. In our study, the sensitivity analysis related to the discounting rate does not change the cost-effectiveness results.

This study presented some limitations. It was performed in only two districts out of 114 in Madagascar. Nevertheless, given that the protective effectiveness of malaria control interventions was very consistent with that in national studies in Madagascar [25] and elsewhere [66] and that the cost of these interventions was relatively uniform across the country, these results could be extrapolated to areas in Madagascar with similar malaria endemicity (fringe and equatorial transmission patterns). The second limitation was the absence of data from private HFs and self-medication information from HHs.

Table 9 Cost-effectiveness ratio per DALY averted (in 2013 USD)

	YLL Mild	YLL Mod	YLL Cc	YLL	YLD	DALYs	NC (r = 0%)	NC (r = 2.5%)	NC (r = 5%)	CER/ DALY averted (r = 0%)	CER/ DALY averted (r = 2.5%)	CER/ DALY averted (r = 5%)
ITN Ankazobe												
Value	388	877.7	638.1	1,554.6	564.3	2,118.9	191,813.8	180,995.3	171,176.8	90.5	85.4	80.8
95% CI lb	8.3	352.5	270.2	630.9	313.5	944.4	218,806.0	207,987.5	198,169.0	231.7	220.2	209.8
95% CI ul	97.8	1,604.6	1,148.6	2,851.0	877.8	3,728.8	179,094.2	168,275.7	158,457.2	48.0	45.1	42.5
ITN Brickaville												
Value	81.1	1,834.3	1,333.6	3,249.0	1,316.7	4,565.7	220,760.5	206,080.3	192,757.1	48.4	45.1	42.2
95% CI lb	17.8	760.1	582.7	1,360.6	627.0	1,987.6	256,742.0	242,061.8	228,738.6	129.2	121.8	115.1
95% CI ul	202.0	3,314.4	2,372.4	5,888.8	2,131.8	8,020.6	194,730.3	180,050.1	166,726.9	24.3	22.4	20.8
IRS (Ankazobe)												
Value	32.0	723.4	525.9	1,281.2	438.9	1,720.1	939,623.6	906,067.8	875,101.1	546.3	526.8	508.8
95% CI lb	2.8	121.0	92.8	216.7	250.8	467.5	970,426.9	936,871.1	905,904.4	2,075.8	2,004.0	1,937.8
95% CI ul	79.6	1,306.1	934.9	2,320.7	752.4	3,073.1	929,359.1	895,803.3	864,836.6	302.4	291.5	281.4

YLLmild: years of life lost averted due to mild malaria cases averted. YLLmod: years of life lost averted due to moderate malaria cases averted. YLLcc: years of life lost averted due to complicated malaria cases averted. YLL: years of life lost averted due to total cases averted (YLLmild + YLLmod + YLLcc). YLD: years of healthy life lost due to disability. NC: annual total net cost of the national program at the district level

According to the MOH, there is no system to collect the number of consultations and cases managed by private HFs [14]. However, this limitation had a low impact on cost estimation, as the use of private HFs in malaria cases was low and nevertheless caught by HH surveys. Finally, the evaluation of effectiveness relies on field epidemiological surveys, which are subject to biases and uncertainty. Specifically, IRS has an effect at the community level (herd effect) that this case-control study could not capture. The third limit concerns data. This limit is reduced for certain parameters used, such as ITN and IRS coverage. In fact, mass campaigns for ITN and targeted campaigns for IRS have continued from 2008 to the present day, helping to maintain regular and high coverage. The question arises as to how the cost might have changed. While the cost may have varied, recent studies show that IRS remains costly compared with ITN.

This study encountered several difficulties, including data collection. Existing data were scattered among different technical and financial partners who implemented malaria control activities. Moreover, without technical and financial reporting of all activities carried out by partners, the NMCP cannot establish the details of financial reports of the program per the implemented strategy.

Conclusion

This study confirmed that ITN interventions are less costly than IRS interventions. In areas with low malaria transmission, IRS appeared less cost-effective than ITNs. This suggested that the NMCP, which began to roll back IRS implementation, may want to consider prioritizing IRS on endemic areas over low-transmission areas. Compared to GDP per capita, ITN interventions appeared highly cost-effective, and IRS interventions were cost-effective. In the Malagasy context, the cost of IRS was high, and IRS was less effective, so a budgetary impact analysis should be conducted before a potential extension of this intervention. The resistance to bendiocarb has been suggested to explain the low level of effectiveness and thus the efficiency of IRS. Finally, future research in Madagascar should estimate the efficiency of IRS, but also ITNs (if pyrethroid resistance were to increase) in other districts in order to (i) verify the robustness at a larger scale of the results obtained in our two districts, (ii) confirm these results while the number of malaria cases continues to increase.

Abbreviations

ACT	Artemisinin-Based Combination Therapy
DALY	Disability-Adjusted Life Year
GF	Global Fund
GDP	Gross Domestic Product
GTS	Global Technical Strategy
HF	Health Facility
HH	Household
HR	Human Resource

IEC	Information, Education and Communication
IPTp	Intermittent Preventive Treatment for Pregnant Women
IRS	Indoor Residual Spraying ITN: Insecticide-Treated Net
MoH	Ministry of Health
NMCP	National Malaria Control Program
NMSP	National Malaria Strategic Plan
PMI	President's Malaria Initiative
PPP	Purchasing Power Parity
OR	Odds Ratio
PBO	Pyrethroid-piperonyl Butoxide
PR	Principal Recipient
RBM	Roll Back Malaria
mRDT	Rapid Diagnostic Test
SR	Sub Recipient
UNICEF	The United Nations' International Children's Emergency Fund
WHO	World Health Organization
WMR	World Malaria Report

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Author contributions

MA designed the economic data collection framework. TK, MR and CR designed the epidemiological data collection framework. MA, TK, LR and VTA conducted the cross-sectional survey and analyzed the data. VTA and MA conceived the paper and drafted the manuscript. All authors reviewed and approved the final manuscript.

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Data availability

The datasets used and analyzed during the current study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate

The Ministry of Public Health of Madagascar (approval no. 247/MNSANP/SG on 26/03/2013) and the National Ethics Committee of the Ministry of Public Health of Madagascar (approval no. 12/MNSANP/EC on 03/12/2014) approved this study. All surveys followed ethical principles according to the Helsinki Declaration. Written informed consent was obtained from all participants or the parents/tutors of the children before inclusion.

Consent for publication

Not Applicable.

Competing interests

The authors declare no competing interests.

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