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INDOOR RESIDUAL SPRAYING: THE EFFECTS OF IMPLEMENTATION STRATEGIES AND RESIDUAL EFFICACY ON EFFECTIVE COVERAGE

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A research report submitted to the Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, in fulfilment of the requirements for the degree of MSc Infectious Disease and Epidemiology

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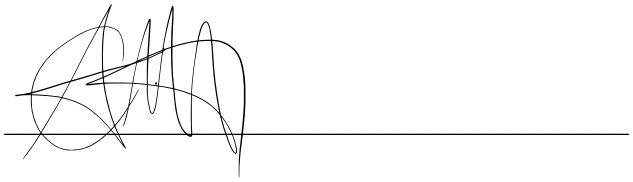
Johannesburg, April 2021

DECLARATION

I, Celso António Alafo declare that this research report is my own, unaided work. It is being submitted for the degree of Master of Science in Epidemiology in the field of Infectious Disease and Epidemiology at the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at any other University.



Celso António Alafo
05 April 2021

DEDICATION

To my son, Ciro Axl Alafo, may the force be with you.

ABSTRACT

Background: Malaria remains one of the major public health problems in Mozambique and it is estimated that nearly 26 million people are still at risk. To achieve malaria elimination in South Africa and Eswatini, and pre-elimination in Mozambique, indoor residual spraying (IRS) has been used as a core malaria vector control tool in the previous and current regional and cross-bordering initiatives between the governments of Mozambique, South Africa and Eswatini.

Methods: This is a secondary analysis of a Goodbye Malaria cross-sectional study data collected by indoor residual spraying operators. The analysis involved household location information and the date of spraying insecticides inside eligible structures in Magude district between 2016 to 2018, from a total of 7407 spray operator's records that translated to 8855 households in 2016 and 9130 households in 2017 in Magude district. A known residual efficacy of the insecticides of 6 months was combined with the actual dates of IRS implementation to assess the level of coverage over time, during each malaria season. Additionally, data from the Malaria Indicator Survey 2018 (MIS) from the Demographic Health Survey (DHS) was analyzed using a multilevel mixed-effects logistic regression model to better understand the sociodemographic characteristics of the households that are visited for IRS, for which a sample size of 1531households were used.

Results: The estimated 2016 IRS campaign coverage was 80.8% (of all eligible structures), while in 2017 the coverage increased to 83.26%. In both years, the implementation of IRS began in August, and more than half the households were visited and sprayed by the end of September, with peak spraying occurring in September. The campaign lasted until November 21st and December 16th for the 2016–2017 and 2017–2018 malaria season, respectively. Combining these data with the residual efficacy of the product sprayed, 67.51% of the households in the district may have lost their protection from IRS during 2016-2017 by March (malaria peak transmission period), whereas during the 2017 IRS campaign this values was 60.69% for the same period. Households owned by females were less likely to be sprayed when compared to those owned by males, and households in the rural areas were more likely to be sprayed when compared to those in the urban areas (OR 1.77, 95%CI 1.47 – 2.12).

Conclusions: These study findings suggest that the implementation of IRS in southern Mozambique should be done two months before the onset of the rainy season as compared to the current operational guidelines of 3-4 months prior to the rainy season. This change in the operational guideline will ensure that the IRS chemical has at least 80% efficacy to kill the

mosquitoes throughout the malaria season. This study also recommends future research on this topic, and that an in-country advisory group, including epidemiologists, entomologists, and modelers, work together to optimize the timing of spraying considering environmental events and work with local communities to increase acceptance rates, further increasing IRS coverage in those communities.

Keywords: Indoor residual spraying, implementation strategies, effective coverage, Mozambique.

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To my father and my family, thank you for believing in me – this is us achieving this. I would like to thank the community of Magude district and appreciate the hard work of spraying operators, supervisors and all other personnel from Good Bye Malaria. I'm also thankful to Dr Krijn Paaijmans for the mentorship and all the assistance provided throughout my professional carrier.

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LIST OF ABBREVIATIONS/NOMENCLATURE

ACT – Artemisinin based combination therapy

ANC – Antenatal care

CISM – Centro de Investigação em Saúde da Manhiça

EIR – Entomological inoculation rate

Endophagy – the ability of vectors to feed indoors of human habitations

Endophily – the ability of vectors to rest indoors of human habitations

Exophagy – the ability of vectors to feed outdoors of human habitations

Exophily – the ability of vectors to rest outdoors of human habitations

GBM – Good Bye Malaria, an indoor residual spraying implementation partner in southern Mozambique

LLINs – Long-lasting Insecticidal Nets

ITNs – Insecticide-treated nets

IRS – Indoor Residual Spraying

HBR – Human biting rate, defined as the average number of mosquito bites received by a host in a unit of time, specified according to mosquito species.

NMCP – National Malaria Control Program

PMI – US President Malaria Initiative

SP1 – Spray operators forms

Residual Efficacy – the duration of which the insecticide particles remain capable of killing susceptible vectors on sprayed surfaces

RDT – Rapid Diagnostic Test

WHO – World Health Organization

1. INTRODUCTION

Mozambique belongs to the top five tier countries with the highest malaria burden worldwide (1), as malaria remains one of the major public health problems in this country (2). It is estimated that nearly 26 million people are at risk of malaria (3). Malaria transmission is perennial in Mozambique, but the disease incidence varies across the country, being higher in the northern and lower in the southern provinces of the country (2,4).

History taught that in-country interventions alone cannot sustain the gains towards the malaria-free world (with an intermediate goal of 90% reduction of incidence and mortality by 2030 (5)) and that regional and cross-bordering collaborations are recommended (6–9). With this, an alliance between the governments of Mozambique, South Africa and eSwatini launched the Lubombo Spatial Development Initiative (LSDI) and significantly reduced the malaria burden in their bordering regions between 1999 and 2011 (8,10). The alliance relied mostly on scaling up indoor residual spraying (IRS) alongside with the implementation of effective diagnostics and treatment with rapid diagnostic tests (RDTs) and artemisinin-based combination therapy (ACT) in Maputo Province (Mozambique) (8,9).

Several years after ending the LSDI, the MOSASWA (Mozambique, South Africa and eSwatini) initiative was launched with a similar vision, but also aiming to move from (i) malaria pre-elimination to elimination in eSwatini and South Africa, and (ii) from control to pre-elimination in southern Mozambique (9). Meanwhile, the *Magude Project*, an in-country alliance between the Ministery of Health, academic and research institutions, aimed to evaluate the feasibility and impact of the broad range of tailored interventions towards malaria elimination that included: (i) usage of HRP2-based rapid diagnose testing and treatment with artemether-lumefantrine; (ii) enhanced entomological and epidemiological intelligence through improved surveillance; (iii) stronger community engagement; (iv) universal coverage with IRS on top of standard LLIN mass distribution by the NMCP and mass drug administration (MDA) with dihydroartemisinin-piperaquine (DHAp) (11).

The current mainstay tool for malaria vector control in Mozambique is universal coverage long-lasting insecticide-treated nets (LLINs), which are supplied through mass distribution campaigns every three years. These nets are also continuously supplied to all pregnant women attending antenatal care (2,12–14). IRS has been implemented as a supplementary tool in areas where (i) there is resistance to pyrethroids used in LLINs or (ii) areas that have to transition from malaria control to elimination (15).

1.1.1 Etiology of Malaria

Malaria is a mosquito-borne disease caused by protozoa of genus *Plasmodium spp.* which can be transmitted by the bite of infected female mosquitoes from genus *Anopheles spp.* (16). As for the parasites, there are known to be five species of *Plasmodium* species that can infect humans, namely *Plasmodium falciparum*, *P.ovale, P.vivax, P.malariae, P. knowlesi* (17), with *P.falciparum* and *P.vivax* counting for 99.7% and 0.3% of malaria cases in the Sub-Saharan Africa respectively (1). The life-cycle of the parasite takes places in two different hosts: (i) in *Anopheles* mosquitoes the final host and (ii) humans his intermediate host (18) (see figure 1 for more details).

As for the clinical signs and symptoms, it is mostly characterized by headaches, arthromyalgias, fevers or history of fevers, and pallor being the least occurring symptom(19). Other symptoms like convulsions can also occur (19).

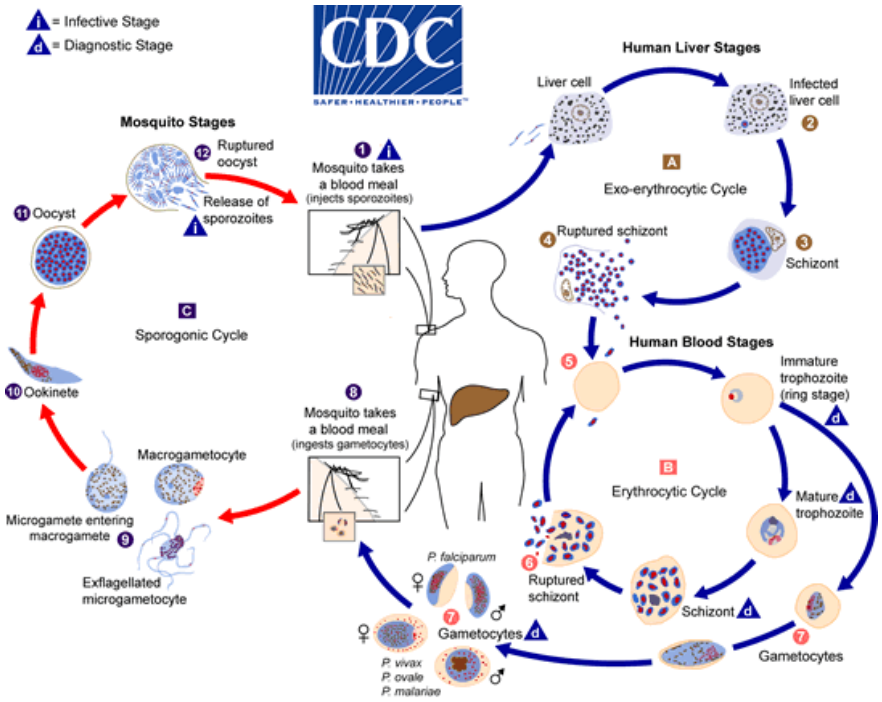

Figure 1| Life-cycle of the malaria parasite: Plasmodium spp. Source: CDC – Center for Disease Control and Prevention

1.1.2 Malaria vectors in Sub-Saharan Africa

Mosquitoes are holometabolous arthropods and their life-cycle occurs in two distinct environments: (i) aquatic habitats, where the egg, larvae and pupae stages develop and (ii) terrestrial habitats where the adults fly, feed and rest (20). There are approximately 430 species on the *Anopheles* genus, which only 30 – 40 species are known to be vectors of human malaria (18). Several members of the *Anopheles gambiae* species complex and *Anopheles funestus* group are considered to be the most efficient malaria vectors in Sub-Saharan Africa (20,21).

In Mozambique, the major malaria vectors are *Anopheles gambiae s.s.* which is predominant in the northern provinces*, An. arabiensis* which is predominant in the southern provinces, and *An. funestus s.s.,* which is widely distributed across the country (3,22,23). Other species such as *An. merus* (belonging to the *An. gambiae* complex) and *An. tenebrosus* have been found infected with *P. falciparum* (24,25, Alafo et al. unpublished data).

Other anophelines regularly found in Mozambique are *An. pharoensis* and *An. ziemanni,* which are known malaria vectors in other countries of Sub-Saharan Africa (26,27), however, they are not yet identified as vectors in Mozambique. *An. vaneedini*, a member of the *An. funestus* group was recently found to be secondary vectors of malaria transmission in Mpumalanga and KwaZulu Natal, South Africa (28), and is also present in Mozambique.

1.1.3 Malaria vector control

Malaria vector control interventions target biological traits of anopheline mosquitoes such as biting and resting behaviors, their need for aquatic breeding sites and their insecticide susceptibility. At the beginning of the nineteenth century, vector control activities were mostly based on larviciding through petroleum oil and environmental control (20,29), and nowadays the frontline interventions for malaria vector control are Insecticide Treated Nets and/or Long-lasting Insecticidal Nets and IRS (30).

1.1.3.1 Insecticide-treated nets and Long Lasting insecticidal treated nets

ITNs/LLINs are estimated to have contributed significantly to the reduction of malaria disease burden, followed by IRS and ACTs between 2000 and 2015 (31). The WHO current guidelines recommend replacing LLINs every 3 years through mass distribution campaigns as well as

periodic ‘top-ups’ during ANC visits and child immunization campaigns (30,32). However, reports of failure of this frontline tool are abundant, and reasons include : (i) early loss of physical barrier due to holes in the nets (33–35); (ii) rapid decrease of the insecticidal activity over time (36–38), (iii) the widely spreading of insecticide resistance to pyrethroids throughout Sub-Saharan Africa (39–42) and (iv) human behaviors that increase their exposure to malaria vectors before being protected under LLIN (43–47). Also, there have been reports of local malaria vectors changing their biting behaviors from indoors (endophagic) to outdoor biting (exophagic) after increased and continuous usage of this tool (48–50). All those together can increase the host (human) and the vector (mosquitoes) encounter, therefore increasing blood-feeding probabilities and malaria infection.

1.1.3.2 Indoor residual spraying

There are many different modes of actions for insecticides used in agriculture and crop science, but very few are currently being recommended for the use in public health: carbamates, organophosphates, organochlorines, pyrethroids and the recently added neonicotinoids and pyrroles (51–53). IRS has helped reducing malaria transmission in many countries (54–56), and South Africa has adopted this intervention as its mainstay for malaria vector control for over half a century (57,58). One of the key advantages of this tool is that it doesn’t solely rely on the user’s compliance to be effective, and secondly, the insecticide remains present on the sprayed surfaces for a certain period (the WHO requires it to be of at least 3 months after application)(30).

However, the effectiveness of this tool can be hampered by (i) insecticide resistance (59); (ii) recent discovery of new malaria vectors which may not be affected by it and sustain malaria transmission (28); (iii) changes in mosquito behavior post-vector control interventions (49,50); (iv) sub-optimal compliance on the communities (60) and (v) duration of residual efficacy and coverage (61–63). The latter, coverage, is related with the implementation strategy as implementation can take months depending on the area and number of structures that needs to be covered, and combined with the residual efficacy of the product can lead to a rapid changing in coverage over time and space.

1.2 Problem statement

In Mozambique, the implementation of IRS campaigns is not per se synchronized with malaria seasonality, but it starts well before the onset of the rainy season (August is the aim every year, while the rains normally start in October/November), intending to reduce malaria vector density throughout the beginning of malaria transmission season, which normally peaks between March and May in Mozambique (see figure 2).

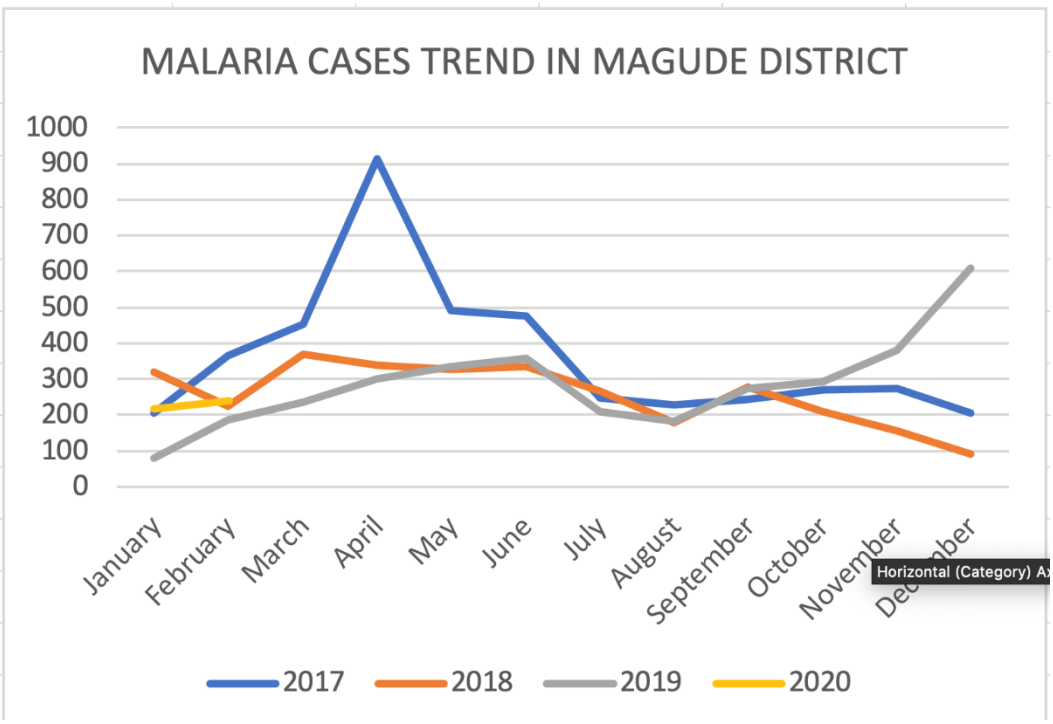

Figure 2| Epidemic curve of malaria cases in Magude district reported by the Health Facilities. Y-axis number of malaria cases; X-axis is the date. Data source: *Direção Provincial de Saúde de Maputo*, National Malaria Control Programme

The IRS campaigns usually last for 21 weeks (5 months) to be fully implemented in a given district, and if it follows a similar pattern as shown on Figure 3, this translates to 35% to 50% of the sprayed households losing the desired efficacy of the product kills less than 80% of susceptible mosquitoes as per the WHO's pre-determined threshold before the malaria transmission peaks in Mozambique (thus not killing the mosquitoes responsible for transmission during this peak malaria time).

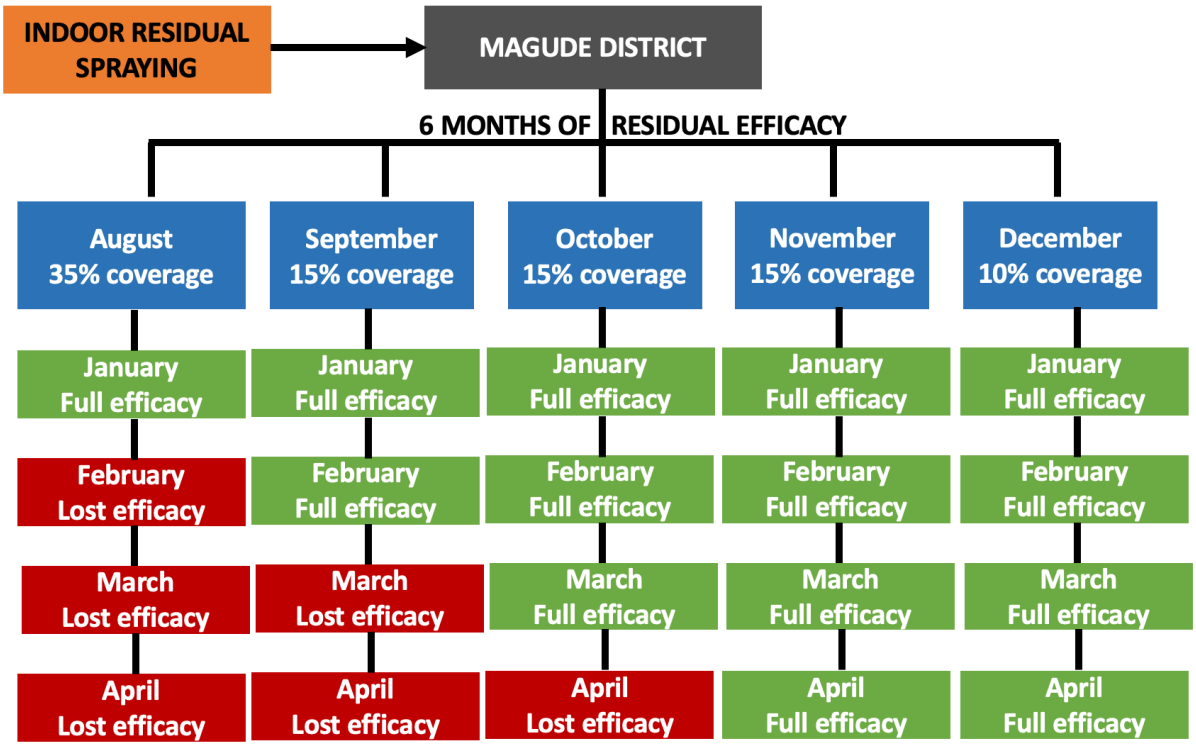

Figure 3| Hypothetical indoor residual spraying implementation strategy for malaria vector control: Conceptual framework

To achieve the best impact with limited resources, Mozambique's National Malaria Control Program (NMCP) and IRS implementation partners such as Good Bye Malaria (GBM) and US President's Malaria Initiative (PMI) may need to re-evaluate the timing of IRS implementation to ensure the most people are protected for every dollar spent.

1.3 Study Justification

The control of mosquito-borne illness relies heavily on the control of the mosquito vectors. Improvement of the current implementation strategies for indoor residual spraying will result in a more cost-effective vector control strategy and could lead to the protection of a larger population size against malaria throughout the transmission window.

1.4 Research Question

How is the current timing of IRS, combined with the product's residual efficacy and sociodemographic characteristics, impacting IRS coverage during the malaria transmission season?

1.5 Study Aim

To ultimate aim is to guide the Mozambican NMCP on when and how to best target districts with IRS, by informing the optimum spraying approach over space and time.

1.6 Objectives

1. To describe the spatial distribution and coverage of indoor residual spraying in Magude district from 2016 to 2018;
2. To overlay these data with recorded data on the residual efficacy of IRS products and describe its effects over space and time in Magude district;
3. To understand the sociodemographic characteristics of indoor residual spraying targeted dwellings in Mozambique in 2018.

2. METHODS

This is a secondary analysis of data analysis. The chapter describes the data used, the process of primary sample collection, the methods and the statistical analysis used in this study.

2.1 Primary study

Two different primary studies were used to address the different objectives of this study: Good Bye Malaria IRS implementation data and the 2018 Mozambique Demographic Health Survey Malaria Indicator Survey (DHS – MIS).

2.1.1 Good Bye Malaria IRS implementation data

Data from IRS campaigns between 2016 – 2018 in Magude district (Figure 4) was used to understand the implementation strategies and coverages. The study aimed to implement IRS in Magude district between 2015 and 2018 under the malaria elimination initiative in the district. All spraying was conducted using the Hudson X-Pert® spraying pumps (Hudson Manufacturing Co., Chicago, IL) with appropriate nozzles for pirimiphos-methyl (Actellic 300CS, Syngenta).

A household was defined as *"a person or group of people with or without kinship, who live together (s) in the same housing unit (s), who recognize an adult male or female as head of household, who share the same situations domestically and that a single unit is used"* (15). A house was defined as a building or dwelling capable of or intended for human habitation; while structures are the number of rooms or compartments inside a house or building. Data collected for this study include information on spraying dates, the number of households and structures sprayed as well as area.

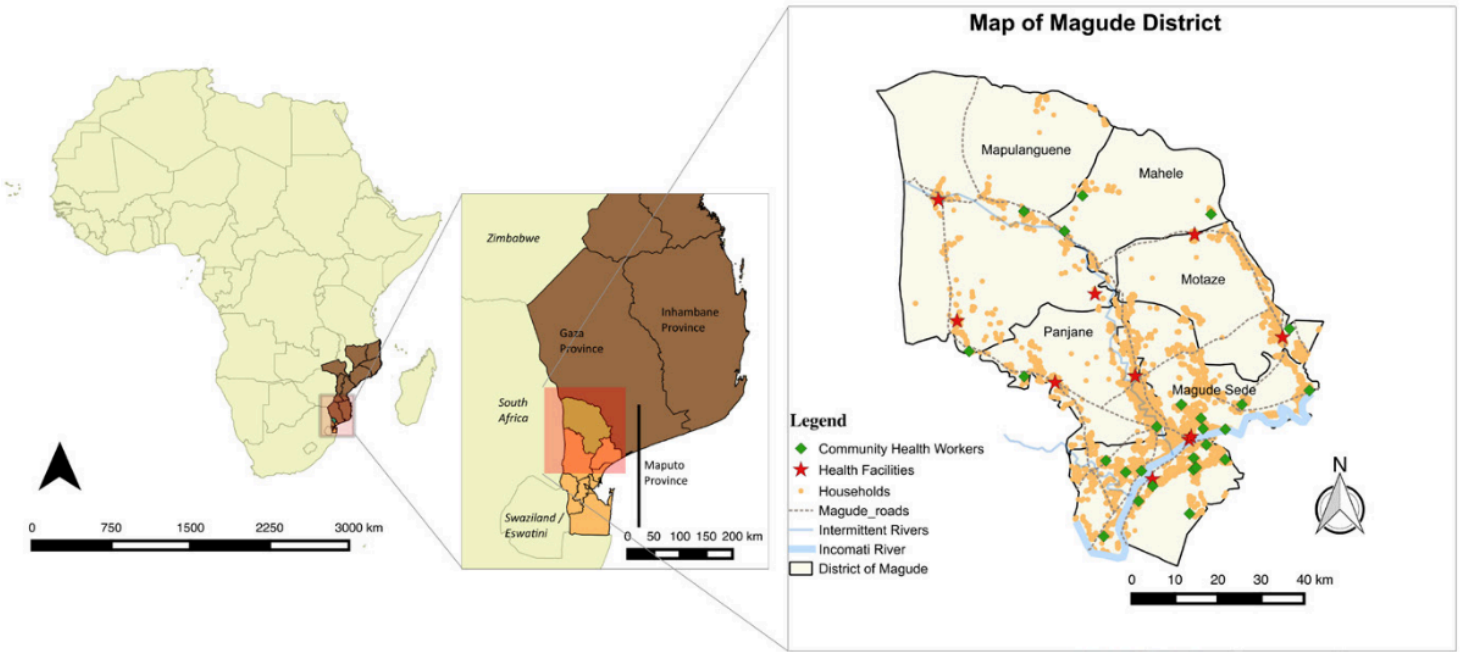

Figure 4| Map of Magude district, southern Mozambique, with rivers and roads. Source: Galatas & Nhacolo et al. 2020

2.1.2 DHS Malaria indicator survey

The 2018 Mozambique DHS Malaria Indicator Survey was a population-based survey that aimed to generate estimates of malaria indicators at the national, provincial, urban and rural context to complement routine data, which are used to guide Mozambique's NMCP and to influence policymakers (15). Data included in the analysis presented here include household spraying status, area, bed net ownership, wealth index, household wall material, age of head of household and malaria rapid diagnostic test result.

2.1.3 Primary study sampling method

The Good Bye Malaria IRS implementation aimed to cover the whole households of Magude district, and therefore no sample size nor sampling was to be done. Data collection of the 2018 DHS Malaria indicator survey cross-sectional study was carried out between March to June in 2018, and the primary sampling unit which was referred as the cluster for the 2018 DHS MIS was defined taking into consideration the enumeration areas (EAs) from the 2007 general population census and the general agricultural census of 2009 (15).

A two-stage cluster design sampling of the EAs covered by the 2007 general population census was performed, and a total of 224 EAs or clusters were selected, with probability proportional to the size, from this 92 were located on the urban areas and 132 in rural areas (15). The second stage of sampling comprehended the systematic selection of households from each of the EAs,

in which 28 households were selected totalling 6272 representative households to be visited without substitutions (15).

All 15-49-year-old women who were regular members of the selected households and those who had spent the night before the survey in the selected households were eligible to be interviewed, and all children aged 6-59 months of age residing in these households were eligible for testing for anemia and malaria (15).

2.2 Secondary analysis methods

2.2.1 Study design, population and participants

The study design used in the present research report was an observational cross-sectional secondary analysis of data of households sprayed in Magude district by Good Bye Malaria between 2016 and 2018.

2.2.2 Power calculation

There was no sample size calculation nor sampling for this study since this was a secondary analysis of data provided by the gatekeepers. Hence, all available data from the primary study were used in this study. Data provided by Good Bye Malaria covered the entire Magude district, offering direct population information. As for the data provided by the DHS, a power computation was performed using *clustersampsi ado file* (64). An IRS coverage of 16% was obtained from the 2018 DHS MIS (15). Assuming that 21% of the interviewed population were offered IRS intervention at an alpha level of 0.05, a design effect of 4.24, inter-cluster correlation (ICC) of 0.12, a total of 224 clusters and 28 households per cluster, a study power of 81% was estimated.

2.2.3 Inclusion criteria

For the Good Bye Malaria datasets, the inclusion criteria used were households belonging to Magude district and that was included in the 2015 census. The inclusion criteria for the 2018 DHS MIS were households who answered whether or not the IRS was implemented in their homes in the past 12 months.

2.2.4 Study participants

During the Good Bye Malaria IRS implementation, the baseline census in 2015 reported a total of 52,802 individuals to be living in Magude district and 10,965 households (65).Of whom 48,448 residents and 4,133 non-residents, corresponding to 91.8% and 7.8% respectively. There are five administrative posts in Magude district (Figure4), and the population is distributed as follows: Magude sede accounted for 73% of the total population and is also the district's capital; Motaze accounted for 14.1% of the total population; Panjane accounted for 5.9% of the total population; Mapulanguene accounted for 3.7% of the total population and Mahele accounted for 3.4% of the total population (65). The DHS MIS aimed to interview a total of 6272 households in 2018, and from that, 6196 households were successfully interviewed in 2018, of which 1543 households met the inclusion criteria.

2.3 Data management and analysis

2.3.1 Data management

Datasets obtained by Good Bye Malaria were in excel ".xlsx" format and were reshaped in excel so that the first row corresponded to the label variables and subsequently converted into ".csv" format. All datasets were merged using R version 3.3.2 (R Core Team: **A language and environment for statistical computing**. Vienna, Austria. R Foundation for Statistical Computing; 2020) and cleaned by cross-checking for duplicated observations and missing values. DHIS MIS datasets were downloaded from the DHS website on Stata (StataCorp. 2017. College Station, TX, USA) compatible format ".dta". Dataset was cleaned by checking for missing values and duplicated observations. Taking into account the survey design, the sample weight was calculated by dividing the household sample weight by 1000000.

2.3.2 Statistical analysis

2.3.2.1 Analysis of Objective 1: To describe the spatial distribution of indoor residual spraying in Magude district from 2016 to 2018

The coverage of IRS was calculated at the household level for each year (2016 and 2017) using the number of reported sprayed households divided by the number of households reported on the 2015 census. The results were also stratified by administrative posts in the district. MATLAB version 9.8.0.1417392 (R2020a. Natick, Massachusetts: The MathWorks Inc.) was

used to analyze the implementation strategy of IRS, and tridimensional "Z" graphs were created using the dates of spraying grouped into calendar months, the number of households sprayed and their location (administrative posts).

2.3.2.2 Analysis of Objective 2: To overlay these data with recorded data on the residual efficacy of IRS products and describe its effects over space and time in Magude district

With households spraying dates grouped in months for each spraying season, the dates were overlaid with an estimated residual effect of six months (66) to understand the different levels of protection of this tool on the community. The results were then tabulated in two-way frequency distribution table using the time (in months) of residual efficacy and the number of households with lost efficacy.

2.3.2.3 Analysis of Objective 3: To understand the sociodemographic characteristics of indoor residual spraying targeted dwellings in Mozambique in 2018.

Using the IRS status in households (sprayed vs non-sprayed) as the outcome variable, a two-way contingency and frequency table was created for the categorical (e.g.: gender of head of household, region, mosquito bed net ownership) and continuous (e.g.: age) variables. The results for the continuous variables were expressed in means and 95%CI. Appropriate statistical methods to measure the association between the different covariables and the outcome variable were used, being the Pearson's chi-square test and the clustered adjusted Pearson's chi-square test used for the categorical covariables and the outcome. After checking for normality using the histogram on the continuous covariables and the assumptions satisfied, Student's t-test and clustered t-test (*clttest ado*.) was used to measure the association between them and the outcome variable IRS status.

Univariate analysis using logistic regression was performed to evaluate the association between the IRS status in the dwellings and the independent variables. A stepwise using backward elimination selection (alpha level is ≤ 0.20) was used to select the variables to include on the multilevel mixed-effects logistic regression model. The multilevel mixed-effects model was built using the cluster number, and the motive to use the multilevel mixed-effects logistic regression was because the model can take into account random effects and the survey design:

individuals nested within households nested within clusters contained in the rural or urban areas.

2.4 Ethical considerations

Indoor residual spraying was carried out by the NMCP in collaboration with GBM, the latter being responsible for the day-to-day operations. Datasets obtained from Good Bye Malaria (IRS implementer) did not contain any personal information nor the household aggregate number from the census of 2015. Written approval was given by the DHS program to use the 2018 DHS MIS data. As these data are anonymized, and ethical waiver for the present research report was obtained by the University of Witwatersrand Human Research Ethics Committee, with approval reference number W-CBP-200622-01.

3. RESULTS

3.1 Data used in the analysis

A total of 3934 spraying operators' records from the 2016 IRS campaign and 3,473 from the 2017 campaign was used for the analysis (note that each record can contain IRS information from multiple households). From those records, 114 records corresponded to a second spraying round in 2016 to visit the houses again where the owner was not present the first round. This number was 307 records in 2017. 7,715 observations from the "people's records" and 1,654 observations from the "household records" both from DHS Malaria indicator survey of 2018 were used, corresponding to the three provinces where indoor residual spraying has been used and additional vector control tool: Maputo Province, Maputo City and Nampula province.

3.2 IRS coverage

During 2016, the IRS campaign started on 22 August and a total of 8,855 households were sprayed by November 21st during the primary round. This translated to an 80.8% coverage at the household level, whereas the 2017 IRS campaign implementation began on 21 August with a coverage of 83.26% by December 16th (n= 9,130). In total, 16,886 houses were sprayed in 2016 (one household can have multiple houses or structures), of which 16,572 during the primary cycle of spraying and 314 houses during the second round (mop-up). When the total houses sprayed were analyzed per administrative post, 11,407 houses (67.6%) were sprayed in Magude-sede, 2,688 (15.9%) in Motaze, 1,402 houses (8.3%) in Panjane, 582 (3.4%) in Mahele and 807 (4.8%) houses sprayed in Mapulanguene. Overall, 542 houses were not sprayed because they were locked when the spray operators visited their premises [Magude-sede (n= 464); Motaze (n= 46); Panjane (n= 13); Mahele (n= 17); Mapulanguene (n= 2)], and an additional 101 households [Magude-sede (n= 76); Motaze (n= 5); Panjane (n= 4); Mahele (n= 5); Mapulanguene (n= 11)] refused IRS.

During the 2017–2018 malaria season, 16,998 houses were sprayed throughout the campaign, of which 15,655 houses during the primary cycle and 1,343 houses to the second (mop-up) round. This translated to 11,194 houses (65.9%) that were sprayed in Magude-sede, 2,733 (16.1%) in Motaze, 1,569 houses (9.2%) in Panjane, 787 (4.6%) in Mahele and lastly 715 (4.2%) houses in Mapulanguene. However, 402 houses failed to be protected by IRS because they were locked during the visits [Magude-sede (n= 324); Motaze (n= 36); Panjane (n= 28);

Mahele (n= 8); Mapulanguene (n= 9)] and another 101 households refused IRS [Magude-sede (n= 64); Motaze (n= 15); Panjane (n= 14); Mahele (n= 4); Mapulanguene (n= 4)].

When analyzing the total households sprayed per month throughout the campaign in 2016 (note that one household can have multiple houses on the same compound), 2,640 (29.8%) households were sprayed in August, 3,338 (37.7%) households were sprayed in September, 2,249 (25.4%) in October and 628 (7.1%) in November. Whereas in 2017, 2,167 (23.73%) households were sprayed in August, 3,374 (36.96%) in September, 2,814 (30.82%) in October and 764 (8.37%) in November. Only 11 (0.12%) households were sprayed in December.

3.3 Implementation strategy, 2016 IRS campaign

Of the five administrative posts located in Magude district, Magude-sede had 79.38% coverage in 2016 (Table 1). As for the implementation strategy for this area, the peak of sprayed households over a month was registered in September [n= 2540, (39.94%)]; whereas 27.73% (n= 1763) and 23.43% (n= 1490) of the households were sprayed in August and October, respectively (Figure 5).

Motaze, the second most populated administrative post of Magude district, had an IRS coverage of 84.84% coverage, and the peak of households sprayed occurred in September during which approx. half of the households were sprayed [n= 622, (49.84%)].

In Panjane, a coverage of 85.65% was achieved during IRS campaign, in which more than half of the households were sprayed in October [n= 347, (64.62%)]; Mapulanguene had 78.48% (n= 312) of its households sprayed in August and overall coverage of 85.39% (Figure 5 and Table 1). Lastly, Mahele administrative post had 82.12% (n= 248) of its households sprayed in August with an overall coverage of 80.1%.

Table 1| Indoor residual spraying campaign coverages in Magude district

	Administrative post				
	Magude-sede [n= (%)]	**Motaze [n= (%)]**	**Panjane [n= (%)]**	**Mapulanguene [n= (%)]**	**Mahele [n= (%)]**
Households in 2015†	8011 (73.1)	1471 (13.4)	627 (5.7)	479 (4.4)	377 (3.4)
Households sprayed 2016	6359	1248	537	409	302
Households sprayed 2017	6087	1535	712	363	433
IRS coverage 2016	79.38	84.84	85.65	85.39	80.1
IRS coverage 2017	75.98	104.35	113.56	75.78	114.85

†Source: Galatas & Nhacolo et al. 2020 (65)

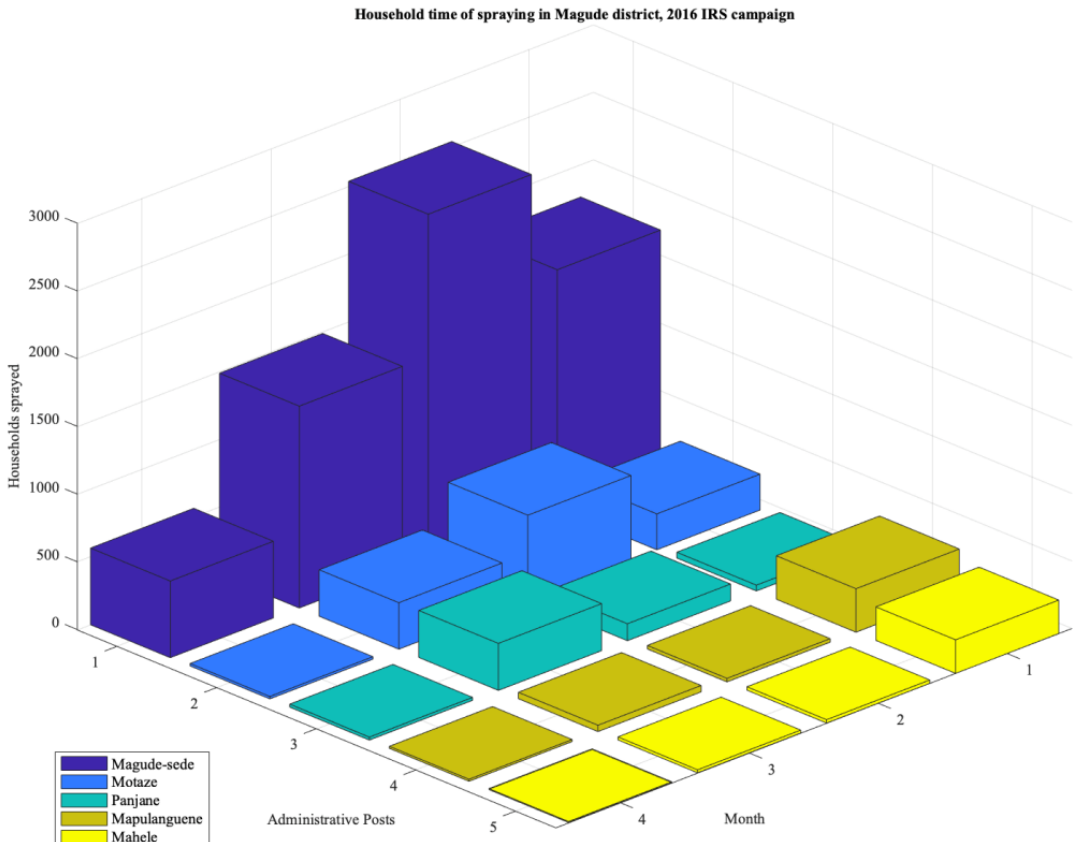

Figure 5| Household time of spraying in Magude district in 2016. Y-axis represents the number of households sprayed; X-axis are the administrative posts in the district; and Z-axis represents the month of spraying of which the numbers 1, 2, 3 and 4 it corresponds to August, September, October and November respectively.

3.4 Implementation strategy, 2017 IRS campaign

In 2017, the coverage for IRS was 75.98% in Magude-sede, and similarly to the previous year, the peak of spraying happened in September [n= 2427, (39.87%)] and October [n= 2322, (38.15%)] (Table 1 and Figure 6, respectively).

In Motaze, a 104.35% IRS coverage was achieved in 2017 (this is because more households were found during spraying than it was reported on the 2015 census for this area), with more than half of the households being sprayed in August [n= 632, (41.17)] and September [n= 759, (49.45%)]. The administrative post of Panjane registered coverage of 113.56% for IRS (due to the denominator and more households were found during spraying than it was reported on the 2015 census), where more than half of the households were sprayed on a single month, September [(n= 383, (53.79)]. In Mapulanguene, similarly to the previous year, more households were sprayed in August and September [n= 276, (76.03%); n= 80 (22.04%), respectively] when compared to rest of the months. A coverage of 114.85% of households was achieved in Mahele during the 2017 IRS campaign, of which the majority were sprayed in August [n= 372, (85.912)].

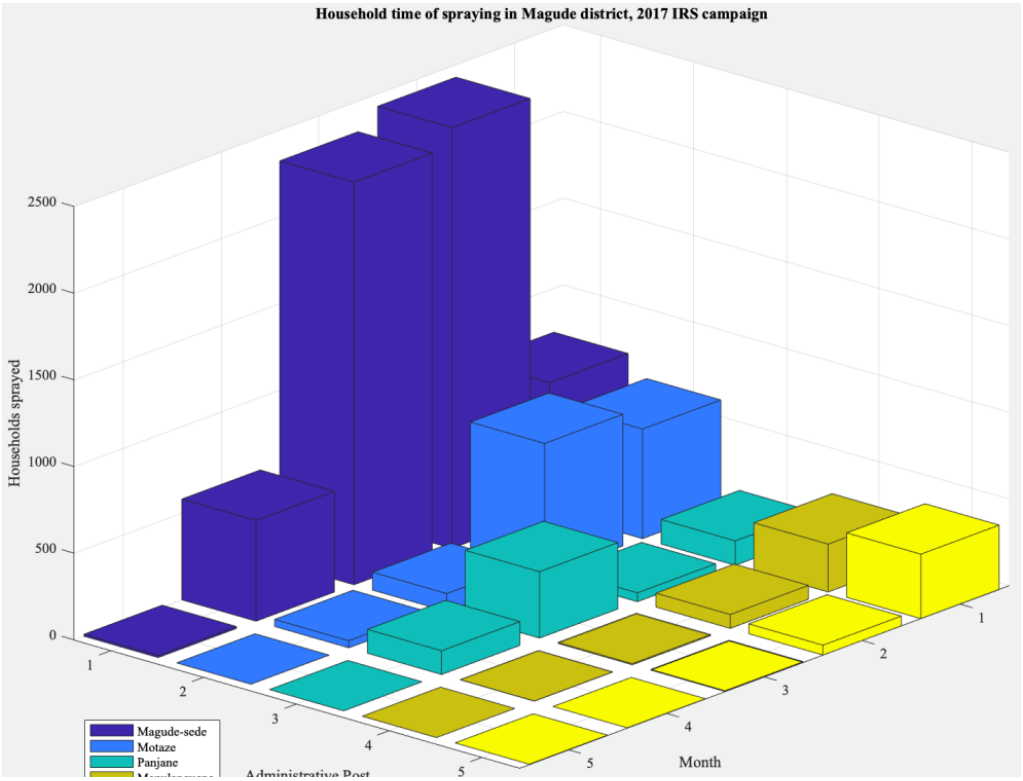

Figure 6| Household time of spraying in Magude district in 2016. Y-axis represents the number of households sprayed; X-axis are the administrative posts in the district; and Z-axis represents the month of spraying of which the numbers 1, 2, 3, 4 and 5 it corresponds to August, September, October, November and December respectively.

3.5 Combining IRS spray dates with the product's residual efficacy

Looking at the overall duration of the residual efficacy using the date of spraying and taking into count that most of the current residual insecticides used on malaria vector control fall below WHO's 80% mosquito mortality threshold (67) around 6 months (i.e. are not effectively killing mosquitoes any more), the results are shown in Table 2.

In 2016 – 2017 IRS campaign, 67.51% lost their protectiveness from this tool by March, and 92.91% by April, the months wherein malaria incidence normally increases. The loss of protectiveness in 2017 – 2018 was similar, with 60.69% of the households in the district losing their protection by March, and 91.51% by April.

Table 2| Duration of effectiveness of indoor residual spraying in Magude district

	2016 IRS campaign (SP1 forms)			**2017 IRS campaign (SP1 forms)**		
	Households (N)	**Percent (%)**	**Cumulative (%)**	**Households (N)**	**Percent (%)**	**Cumulative (%)**
January	2640	29.81	29.81	2167	23.73	23.73
February	3338	37.7	67.51	3374	36.96	60.69
March	2249	25.4	92.91	2814	30.82	91.51
April	628	7.09	100	764	8.37	99.88
May				11	0.12	100

3.6 Sociodemographic characteristics of IRS targeted dwellings

During the 2018 DHS malaria indicator survey in Mozambique, 1531 households responded whether or not the dwelling has been sprayed in the last 12 months, and from this, 1166 (76.2%) households had received IRS; and the population weight-adjusted results showed similar results (75.07%) as seen in Table 3. There was a no significant difference between the regions of the country, age and gender of the head of the households, and the wall materials and IRS status, however, there were significantly more sprayed households in the rural areas (41.3%) when compared to urban areas (Table 3). There was some of evidence of wealth index, household bed net ownership and age of head of household and IRS status.

The univariate analysis showed that the age of the head of the household had a significant statistical p-value, and there was some evidence that the number of children <5yrs who slept

under bed net were associated with IRS, whereas the gender, wall materials, region, gender of the head of the household, malaria rapid test result and the number of people who slept under bed net were not associated with IRS (Table 4). Households who had some children <5yrs sleeping under a mosquito bed net were 2 times more likely to be sprayed when compared to households who did not have any children <5yrs sleeping under a mosquito bed net (OR 2.8, 95%CI 0.87 – 9.07), whereas households who had females as the head of the households were less likely to be sprayed when compared to those owned by males (odds ratio (OR)= 0.78, 95%CI 0.41–1.47).

The households with zinc walls were less likely to be sprayed when compared to traditionally built households (OR= 0.91, 95%CI 0.19- 4.37) while households built with conventional walls were equally likely to be sprayed when compared to traditionally built households (OR= 1.1, 95%CI 0.59–2.05). Households in the rural areas were 1.58 times the odds of being sprayed when compared to those in the urban areas (95% CI 0.9 – 2.78).

After using the stepwise backward elimination selection approach of variables from the univariate analysis, five variables were included in the final multilevel mixed-effects logistic regression: age and gender of the head of household, region, place of residence and number of children <5yrs who slept under a bed net. Taking into account the intracluster correlation among sprayed households within the cluster, non-random effects, as well as random effects were fitted in the model (Table 5).

The age and gender of the head of household, the place of residence and number of children <5yrs who slept under bed net significantly increased the odds ratio. When taking into account the random effects, the odds ratio of spraying and the place of residence increased from 1.77 to 17.56; households in the southern region were 1.96 odds of being sprayed when compared to households in the northern region (OR 1.96, 95%CI 0.607 – 6.31) and households in the central region were less likely to be sprayed when compared to the same region (OR 0.303, 95%CI 0.015 – 6.24). As seen before, households owned by females were less likely to be sprayed when compared with those owned by males (OR 0.77, 95%CI 0.634 – 0.93).

Table 3| Bivariate analysis of IRS and sociodemographic characteristics of households in Mozambique, DHS Malaria Indicator Survey 2018

		IRS status in last 12 months					
		Un-weighted			Weighted		
Variables	**Category**	Not sprayed [n=365 (23.84%)]	Sprayed [n=1166 (76.16%)]	Test statistics (p-value [a])	Not sprayed [n=322 (24.93%)]	Sprayed [n=969 (75.07%)]	Test statistics (p-value [a])
Region	Northern	116 (31.78)	427 (36.62)	χ^2 = 7.29 (0.026)	172 (13.35)	526 (40.78)	F= 1.17 (0.3059)
	Central	87 (23.84)	207 (17.75)		57 (4.39)	132 (10.22)	
	Southern	162 (44.38)	532 (45.63)		93 (7.18)	311 (31.26)	
Place of residence	Urban	262 (71.78)	620 (53.17)	χ^2 =39.41 (<0.001)	193 (14.92)	436 (33.8)	F = 7.72 (0.0062)
	Rural	103 (28.22)	546 (46.83)		129 (10)	533 (41.28)	
Gender of the head of household	Male	236 (64.66)	793 (68.01)	χ^2 = 1.42 (0.234)	221 (17.15)	698 (54.1)	F= 0.6 (0.4414)
	Female	129 (35.34)	373 (31.99)		101 (7.78)	271 (20.97)	
Age of head of household	Mean [95% CI]	44.2 [42.54 – 45.93]	46.2 [45.32 – 47.05]	t= -2.1 (0.035)	44.83 [43.02 – 46.64]	45.92 [44.85 – 46.98]	t= -1.65 (0.0998)
Wall material	Traditional material	112 (30.85)	420 (36.36)	χ^2 = 7.3580 (0.061)	124 (9.9)	429 (34.32)	F = 1.7 (0.1772)
	Plywood and Cardboard	1 (0.28)	0 (0)		1 (0.055)	0 (0)	
	Zinc	8 (2.2)	17 (1.47)		7 (0.54)	10 (0.77)	
	Conventional material	242 (66.67)	718 (62.16)		184 (14.73)	496 (39.68)	
Has a mosquito bed net for sleeping	No	51 (13.97)	104 (8.92)	χ^2 = 7.8 (0.005)	41 (3.12)	81 (6.22)	F= 2.79 (0.0969)
	Yes	314 (86.03)	1062 (91.08)		281 (21.8)	888 (68.85)	
Wealth index	Poorest	40 (10.96)	125 (10.72)	χ^2 = 16.29 (0.003)	60 (4.63)	166 (12.86)	F= 2.18 (0.0878)
	Poorer	40 (10.96)	138 (11.84)		54 (4.2)	170 (13.15)	
	Middle	31 (8.49)	147 (12.61)		27 (2.1)	136 (10.52)	
	Richer	91 (24.93)	360 (30.87)		63 (4.8)	237 (18.4)	
	Richest	163 (44.66)	396 (33.96)		118 (9.2)	260 (20.15)	

Table 4| Univariate analysis of the explanatory variables adjusted for survey weights

Categories and Variables	OR* (95% CI)	P-value
Has a mosquito bed net for sleeping		
No	Ref	
Yes	1	N/S
Age of head of household	1.02 (1 – 1.04)	0.046
Gender of the head of household		
Male	Ref	
Female	0.78 (0.41 – 1.47)	0.436
Wall material		
Traditional material	Ref	
Plywood and Cardboard	1	N/S
Zinc	0.91 (0.19 – 4.37)	0.909
Conventional material	1.1 (0.59 – 2.05)	0.752
Place of residence		
Urban	Ref	
Rural	1.58 (0.9 – 2.78)	0.11
Region		
Northern	Ref	
Central	0.7 (0.4 – 1.24)	0.223
Southern	1.31 (0.67 – 2.59)	0.429
Malaria RDT result		
Negative	Ref	
Positive	1.16 (0.72 – 1.88)	0.534
Children <5yrs who slept under a bed net		
No children	Ref	
Some children	2.8 (0.87 – 9.07)	0.099
Number of persons who slept under a bed net		
0	Ref	
2	0.76 (0.3 – 1.96)	0.57
3	0.8 (0.29 – 2.17)	0.655
4	1.2 (0.35 – 4.12)	0.765

*OR: Odds ratio; Ref: Reference; N/S: not significant; CI: confidence intervals

Table 5| Multivariable analysis of determinants associated with IRS status in dwellings

Categories and Variables	**Multivariable (non-random effects)**	**Multivariable (random effects)**
	AOR** (95% CI) p-value	AOR** (95% CI) p-value
Age of head of household	1.02 (1.02 – 1.03) <0.0001	1.03 (0.998 – 1.07) 0.066
Gender of the head of household		
Male	Ref	Ref
Female	0.84 (0.7 – 1.02) 0.077	0.77 (0.634 – 0.93) 0.007
Children <5yrs who slept under bed net		
No children	Ref	Ref
All children	0.85 (0.66 – 1.09) 0.206	0.996 (0.38 – 2.63) 0.993
Some children	2.11 (1.42 – 3.14) <0.0001	2.24 (0.38 – 13.24) 0.375
No net in the household	0.92 (0.63 – 1.33) 0.648	1.07 (0.67 – 1.7) 0.767
Place of residence		
Urban	Ref	Ref
Rural	1.77 (1.47 – 2.12) <0.0001	17.56 (0.244 – 12615.5) 0.393
Region		
Northern	Ref	Ref
Central	0.95 (0.77 – 1.16) 0.602	0.303 (0.015 – 6.24) 0.439
Southern	1.12 (0.93 – 1.34) 0.243	1.96 (0.607 – 6.31) 0.261

**AOR: Adjusted odds-ratio; Ref: Reference; CI: confidence intervals
ICC=0.12

4. DISCUSSION

The niche of IRS as a malaria vector control tool shas been widely investigated with emphasis on insecticide resistance in mosquitoes, residual efficacy of the product on different surfaces, changing vector behaviours post-intervention and more recently the community compliance towards this tool.

The present study was designed in the hope to spark a new discussion on the complexity of IRS programs: how current IRS implementation strategies may fail to target malaria mosquitoes responsible for transmission during peak malaria season. Our results indicate that the implementation of IRS in southern Mozambique usually begins in August with most houses being sprayed by September, which means that more than half of the households may have lost their IRS protectiveness by the end of March – a month before malaria transmission peak; it also showed that the southern region of Mozambique is more likely to be sprayed when compared to other regions and households owned by females are more likely to refuse IRS.

4.1.1 Spatial distribution of IRS

Spraying operations in a given area usually take several months of planning and collaboration of a broad range of institutions and professionals. As an example, to identify a given area as suitable for IRS deployment, prior epidemiological profiling of malaria risk, entomological investigations of the local malaria vectors, an assessment of environmental and socio-demographic determinants are required. Besides, it also requires both financial and political commitment to make IRS possible, sustainable and effective (63,68).

Both financial and political commitment were achieved during the Lubombo Spatial Development Initiative (LSDI) between 1999 to 2011 and the MOSASWA initiative which is currently ongoing since 2015 (9), being able to sustain the gains despite the four-year gaps of action. Not all countries were able to achieve this, as seen in Malawi between 2007–2009, PMI funded a pilot programme for IRS implementation on a single district, which later led the government to scale up to additional seven highly endemic districts between 2010–2012, but reduced back to one by 2014 before achieving their goals, risking to jeopardizing the efforts made (69).

With indoor residual spraying operations usually beginning in August – the late dry season and its carried out until November and December – the onset of the rainy season in southern

Mozambique, it differs from the northern region: where IRS was implemented between October and November as seen on a randomized control trial (70). During the LSDI cross-bordering alliance between Mozambique, eSwatini and South Africa, indoor residual spraying interventions were implemented on the following schedule: (i) twice a year IRS implementation with Bendiocarb insecticide (Bayer CropScience, Mannheim, Germany) between November to February in Mozambique, which has an average of 3 months residual efficacy (55); (ii) once a year between September to December with DDT insecticide in eSwatini, which has an average of below 6 months residual efficacy (61,71); and (iii) from October onwards in both Mpumalanga and Kwazu-Natal provinces in South Africa (10).

The WHO states that spraying should be completed just before the onset of transmission which usually coincides with the rainy season, and should not be started too early as the residual life of the insecticide should cover the whole transmission season (63). In personal communication with Good Bye Malaria's Operations CEO – Francois Maartens, he identified a trade-off between stretching and shortening the IRS campaign: when stretching, less spray man operators are needed and logistics are easier to manage (e.g.: training and transport), whereas shortening the campaign requires more operators and is harder to manage. He also mentioned that the current strategy first focuses on targeting the highly populated areas and move out towards the more rural areas (additional roving teams are also deployed to the very remote villages), as this helps to build momentum.

Other countries have tied their IRS implementation closely to the WHO recommendations. In Benin, the indoor residual spray operations began before the onset of the rainy season with Actellic 50 EC and residual efficacy from cone bioassays showed that it lasted only for three months (62). In Mali, the rainy season usually takes place between late May until late September, and the IRS was implemented between July and September (55). In Tanzania, IRS operations began in March which is before the onset of the rainy season albeit having two rainy seasons: the first and long one between March and April, and short one which usually takes place between October and December (66).

However, with recent climate change, which are characterized by extreme/prolonged drought, increased heat or cold waves and floods in time and/or areas where they were not expected, synchronizing spraying operations to finish onset of the rainy season can be a huge challenge. This was seen in Mozambique in 2019, where it was devastated by two tropical cyclones: (i) cyclone Idai on March with a death toll of 603 people and cyclone Kenneth on April with 45 people dead, and both with subsequent outbreaks of infectious diseases like cholera and malaria (72).

4.1.2 IRS residual efficacy and effective coverage

We reported coverages of 80.8% (achieved in four months) and 83.26% (achieved in five months) to the 2016–2017 and 2017–2018 malaria season, respectively, however, our coverages were calculated taking into count total number of households sprayed during the campaigns rather than the total households reported on 2015 census. The WHO defines coverage as a percentage of a total number of structures or houses sprayed compared to the overall targeted, and it recommends a minimum of 80% coverage to be achieved (preferable in less than two months) (63). Albeit that definition and using households as a reference, our results showed that the minimum required percentage coverage was achieved on both.

A study report from KwaZulu-Natal province, South Africa, indicated that after almost a decade of more than 80% in IRS coverages for malaria vector, between 2014 – 2016, the coverages dropped below recommended which latter coincided with an increase of malaria cases (73), by this supporting the need for achieving the minimum coverage for it to become effective. Despite us using a six month of residual efficacy for the estimated protection period compared to to the individual time of spraying, there have been reports of lower (62) and higher protection periods (74), which can extend the protection period throughout the peak transmission period. Besides, the slow-acting insecticides: neonicotinoids, were recently made available for malaria vector control and brought-in the need to extend the 24-hour mortality reading to additional 48 hrs and up to 72 hrs (75) and 120 hrs (76) post-exposure, the so-called delayed mortality, which can prolong the residual efficacy in a certain way.

4.1.3 Socio-demographic characteristics of the IRS in Mozambique

As for the sociodemographic characteristics of IRS targeted dwellings, our results from the 2018 DHS MIS data showed that there's an association of IRS status and the place of residence and that households in the rural areas were more likely to be targeted for IRS. As for malaria and IRS, our results showed that people who tested positive for malaria were almost equally likely to receive IRS when compared to those who tested negative (OR 1.16, 95%CI 0.72 – 1.88) and it differs from the analysis conducted by Ozougwu, L. in 2018 with the Nigeria DHS data, where sprayed households were less likely to test positive for malaria (OR 0.89, 95%CI 0.47 – 1.72) (77).

Qualitative studies on adherence towards IRS in Mozambique have showed that reasons for acceptance of IRS included the perception of reduction of insect population, trust on health care and government and disease avoidance (78,79). However, in southern Mozambique, the reasons for non-adhrence to IRS included absence of household decision makers upon visit of spraying teams, lack of understanding of IRS procedures and mosquito control and short notice (79); whereas in northen Mozambique, acceptance was jeopardized by negative experience from previous campaings, political-partisian conflicts and the laborious process of setting up the household as well as preference towards ITNs rather than IRS (78). Some of the factors could be solved with more effective and tailored Information Education Communication (IEC) campaings on targeted areas for IRS (e.g.: lack of understanding of IRS procedures, mosquito control and negative experience from previous campaings), while other will require political will and commitment from Government and political parties.

The recent scale-up of IRS to two additional provinces of southern Mozambique (Gaza and Inhambane) under the umbrella of the MOSASWA initiative might have influenced the results found in the present study, by decreasing malaria prevalence in that region and intensifying IRS implementation, therefore making huge progress towards malaria elimination in southern Mozambique, as seen in recent publications by Galatas & Saúte *et al.* 2020 (80) despite being the result of various interventions (both epidemiological and entomological) and collaboration among partners with same vision (11).

4.2 Strengths and Limitations

We believe that our core strength lays on the fact we are the pioneers on investigating how the implementation strategies can influence the effective protection by indoor residual spraying, and we also believe that these findings will help malaria modellers to build better predictive models when taking into count IRS as an intervention. The analysis of the 2018 DHS MIS data using robust statistical techniques allowed us to thoroughly investigate the sociodemographic characteristics of the targeted dwellings for IRS in Mozambique, which latter allowed us to confirm some achievements of some ongoing projects such as the MOSASWA initiative.

The limitations identified on the present study were related to both the study design and the dataset used in the analysis: (i) for data analysis, the lack of including hierarchical Bayesian space-time modelling in order to determine the optimal implementation strategy; (ii) we only assumed the residual efficacy to last about six months post spraying, whereas it could be lower and higher thus decreasing or increasing the effective protection period; (iii) as a secondary

data analysis, the lack of GIS data of the households visited during spraying made it impossible to map the spraying operations; (iv) if GBM had collected the household aggregate number on their spraying operator's forms during the visits it could have been an alternative to have the GIS data from the census 2015 and lastly (iv) since we used households as reference when calculating coverages, the secondary spraying (also known as mop-up round) was not recorded as-sprayed household but only as house sprayed, which should increase our IRS coverage. During the next iteration of this analysis, we will include population density to estimate the number of people protected/not protected by the IRS over time.

4.3 Conclusion

We have identified that the GBM has been achieving the recommended coverage for IRS during the 2016–2017 and 2017–2018 malaria seasons for malaria vector control in Magude district, southern Mozambique. The duration of spraying needs to be adjusted to the two months and to finish before the onset of the rainy season as recommended by the WHO. Furthermore, we recommend more studies on effective coverage of IRS taking into account other variables such as community compliance, delayed mortality and different wall subtracts using mathematical modelling, as well as more anthropologic studies to understand the underlying factors that decrease the odds of female-owned households being less likely to be sprayed.

With the current milestone of malaria elimination in southern Mozambique, there's need to secure long-term funding and political commitment to sustain the gains and prevent future outbreaks or re-establishment of disease in previously malaria-free areas.

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APPENDIX