

# The impact of Indoor Residual Spraying (IRS) withdrawal in the Lake Zone Regions in Mainland Tanzania. Should Tanzania withdrawal its IRS program?

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#### **Research Article**

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# Abstract

**Background:** Indoor Residual Spray (IRS) has proven to be one of the most effective malaria vector control interventions in reducing malaria transmission mainly in areas with high transmission. With the support from the US President's Malaria Initiative (PMI), Tanzania has gone through expansion of IRS implementation with different insecticides from one district in 2007 to 18 districts in 2012. However, due to financial constraints this was followed by IRS withdrawal to 6 districts by 2021 - with planned further withdrawal in 2022 – 2023 down to 2 districts.

**Method:** The retrospective analysis is performed to understand the impact of IRS withdrawal based on DHIS2 malaria incidence per 1000 population data. Data is subjected to interrupted time series (ITS) based on monthly periods to investigate whether the effect due to IRS withdrawal is statistically significant or not. The analysis helps to examine the changes in level and/or trend before, during, and after IRS withdrawal.

**Results:** Visual inspections on yearly time series plots indicate that withdrawing IRS after one, two, three, or even four rounds of IRS implementation results into resurgence of malaria incidence.

The interrupted time series statistical model results based on monthly data show that the difference between the trend during IRS and after withdrawal is negative and statistically significant (p < 0.001) indicating that monthly malaria incidence decreases over time during IRS. The immediate effect after the IRS is withdrawn is positive and statistically significant (p < 0.001), indicating that withdrawing IRS resulted in increased malaria incidence. The sustained effect after IRS withdrawal is positive and statistically significant (p < 0.001), indicating that passes after IRS is withdrawn, the malaria incidence increases. Overall, malaria resurgence is observed in almost all the districts in which IRS was prematurely withdrawn. Such malaria rebounds costs human lives and therefore may go beyond epidemiological concerns, raising ethical, moral and human rights issues.

**Conclusion:** Any decision to withdrawal IRS should ensure its replacement with an equally effective or superior intervention. There is currently no data to support that the new nets being rolled-out in the country are suitable alternatives to IRS; especially in areas of high malaria transmission with reported insecticide resistance. This calls for a need for endemic countries to continue collecting data in local setting on the performance of current and forthcoming "new net" products to ascertain their suitability to replace IRS.

# Background

Indoor residual spraying (IRS) and long-lasting insecticidal nets (LLINs) are the core interventions for malaria prevention in Tanzania. Available data casts doubt as to whether reductions in malaria can be sustained after IRS is discontinued. Past records from the Garki Project [1, 2] and Pare Taveta Malaria Scheme in Tanzania [3] showed similar experiences with transmission rebound setting in immediately

after cessation of IRS. Several studies in Africa have demonstrated the impact on malaria cases resurgences after IRS withdrawal in Uganda [4, 5], Kenya [6], Benin [7], Ghana [8].

Indoor Residual Spraying (IRS) with effective insecticides for the control of malaria implementation in Tanzania has recently been solely funded by the US President's Malaria Initiative (PMI) beginning in 2007 in Muleba and Karagwe districts, located in Kagera Region. The initial locations were supported in response to malaria epidemics that occurred repeatedly in 2006 and 2007. Thereafter, IRS activities were progressively expanded to cover other district councils in the Lake Victoria basin, including the remaining five district councils of Kagera Region in 2009, 2010 and 2011 reaching a peak when it covered all 18 districts of Kagera, Mwanza, and Mara regions, spraying over 1.1 million structures and protecting nearly 6.3 million people. However, from 2012/2013 PMI reduced the targeted area for IRS and by 2013/2014 about 445,000 structures were sprayed, protecting just slightly over 2 million people. Plans for year 2021 aimed at implementing IRS in six districts of Kigoma, Geita, Kagera and Mwanza regions, covering about 550,000 structures and protecting a total of 2,054,330 populations. According to PMI, the reduction in the number of structures sprayed was partly due to the switch from pyrethroids to a more expensive perimorphs-methyl CS insecticide that was in keeping with the NMCP adoption of the WHO guidance for insecticide rotation to mitigate development of resistance. Tungu et al[9] provides a comprehensive report on trends of insecticide resistance monitoring in mainland Tanzania from 2004 to 2020.

The withdrawal of IRS has been marked with a rebound in malaria transmission that threatens the gains so far achieved. This scenario not only poses epidemiological challenges but it also has moral and ethical implications. As pressure mounts for further IRS withdrawal due to limited resources, it becomes important to delve into detailed analysis of the effects of IRS withdrawal as the NMCP considers the future of IRS implementation in Tanzania. Thus, the retrospective analysis is performed to understand the impact of IRS withdrawal based on DHIS2 malaria incidence per 1000 population data. Overall, malaria resurgence is observed in almost all the districts in which IRS was prematurely withdrawn. Therefore, Tanzania should not withdraw IRS where it is being implemented, particularly in areas with high malaria burden with high malaria transmission risk. Entomological and epidemiological data should be carefully collected and used to guide IRS implementation.

# Methods

# Interrupted Time Series Design (ITSD) Analysis

The standard design to evaluate the effectiveness of an intervention is to conduct randomized controlled trials (RCTs), however, RCTs cannot always be implemented, for example to evaluate health policies or Programme targeted at population level [10]. In most national based programs, there are times where it is needed to evaluate interventions which have already been implemented by performing retrospectively analysis. These are settings with no well-defined control vs experiment group, and might not incorporate randomization [10]. In understanding that the IRS program in Tanzania was not a research study designed to answer specific research question(s), that was not the intention, the data analysis should

then be performed based on appropriate designs resembling such implementation[11]. One such design is the interrupted time series (ITSD) – which is one of the strongest, quasi-experimental approaches[12] used to evaluate longitudinal effects of interventions. ITSD is appropriate to evaluate retrospectively the impact of withdrawing IRS in Tanzania because the IRS program implementation in the Lake Regions[13] can be referred to as a natural experiment with reliable routine data recorded over a period of almost 6 years (2015–2021) spanning during IRS implementation in combination with standard LLINs. The data analysis is performed in two parts: a) descriptive analysis for visual inspection of the data based on variables of interest and expected outcome and b) statistical analysis to assess change and control for other effects leading to the observed differences in the expected outcomes.

# **Descriptive analysis**

Descriptive analysis is performed to provide summary statistics, tables, and time-series plots to familiarize with the data at different time points with and without IRS. The time series plots support visual inspections of underlying trends over time, making simple comparisons of before and after IRS withdrawal.

# **Regression analysis**

Statistical analysis is performed based on segmented regression for Interrupted Time Series (ITSD)[12] because it is appropriate for studying effects of interventions that are also based on 'natural experiment'. Segmented regression analysis described in[14] is used to investigate whether the effect due to intervention(s) shift (i.e., IRS implemented in combination with LLINs followed by IRS withdraw) is statistically significant or not. The analysis helps to examine the changes in level and/or trend before, during, and after the intervention shift. The interrupted time series statistical model Eq. 1 contain four key coefficients.

$$y=\beta_0+\beta_1t_1+\beta_2I+\beta_3t_2+\epsilon$$

Where, y is the monthly malaria incidence per 1000 population,  $\beta_0$  is the intercept (baseline level),  $\beta_1$  is the change in y associated with a month increase (representing the underlying IRS trend),  $t_1$  is the number of months passed from the start of the IRS implementation,  $\beta_2$  is the level change following the intervention shift (i.e., IRS withdrawal), I is a dummy variable indicating the IRS period (= 0) or after (= 1) IRS withdrawal,  $t_2$  is the number of months passed since IRS withdrawal, and  $\beta_3$  indicates the slope change following the IRS withdrawal. Data were organized by using Excel (Microsoft, Redmond, WA) and statistical analysis was performed by using R/RStudio [14].

We have analyzed data from Lake and Western Zone from 2015 to Aug 2021 when the DHIS2 became operational in the country focusing on districts with LLIN followed by IRS and then IRS withdrawal. Therefore, the analysis focuses on the main scenarios of interest which are further investigated using

monthly malaria incidence data. The scenario is based on districts with standard LLINs followed by with IRS implementation to show the effect of IRS combined with standard LLIN followed by IRS withdrawal; to show the effect of IRS withdrawal.

# Results

# Changes in Indoor Residual Spray implementation and a review of malaria incidence per 1000 population

Review of the retrospective malaria data incidence per 1000 population data was conducted in 23 district councils in the Lake Zone where IRS was conducted starting on 2015 due to availability of reliable data via DHIS2 to 2020.

Malaria interventions in Lake Zone have been going on with the basic standard of care being universal coverage with LLINs since 2010. Indoor Residual Spraying had earlier been introduced in 2006 in response to malaria epidemics in Muleba and Karagwe districts. Since then, district councils around the Lake zone regions have been provided with IRS protection at different times (Fig. 1C) and Fig. 2. The evolution, and coverage, scope and type of insecticide used for IRS over time and percentage of population protected in the Lake Zone regions – including displaced populations (i.e., refugee camps) is provided in Supplementary file 1.

# Yearly - Time Series Trends

The time series trends based on yearly data on malaria incidence per 1000 population for all the 5 regions in the Lake Zone are presented in Figs. 3–6. The two scenarios outlined above are first investigated through visual inspection. However, the time series plots represent several intervention statuses (color-coded) for each district from one year to the next. These scenarios are a result of intervention status change from one year to the next across different districts. As indicated in the legend and of interest to this analysis, the observed intervention status with variation across the districts are the deployment of a) IRS with LLINs, and b) withdrawing IRS and maintaining only LLINs (IRS w/LLINs m). It is important to note that other changes in the intervention particularly an introduction of Piperonyl Butoxide (PBO) nets in area with or without standard LLIN or IRS is indicated using the legend as well but the analysis for such scenarios are not included as more data is required, thus, it is out of scope and the focus is on IRS withdrawal. In all the Figs. 3–6, the primary axis represents yearly incidence per 1000 population and secondary axis the percentage population protected by IRS. The IRS spray month for each year is presented by a numeric value (i.e., 1 = Jan ... 12 = Dec).

# The impact of IRS withdrawal based on yearly data

As indicated in Fig. 3 for Mwanza region, the impact of withdrawing IRS while maintaining LLINs after three rounds (Buchosa DC) or two rounds (Kwimba DC and Sengerema DC) or one round (Misungwi) is observed by an increase in malaria incidence per 1000 population.

As indicated in Fig. 4 for Geita region, in Nyang'hwale DC the impact of IRS is observed in 2017 where IRS was implemented in February followed by increase in maria incidence perhaps due to late spray in 2018 followed by IRS withdrawal - though a slight decrease is observed in 2020 but not below LLINs levels.

As indicated in Fig. 5 for Kagera region, the impact of withdrawing IRS after one round (Biharamulo DC and Muleba DC), three rounds (Bukoba DC and Missenyi DC) and after four rounds (Ngara DC) is clearly observed by the increase of malaria incidence.

As indicated in Fig. 6 for Mara Regions, the impact of withdrawing IRS and maintaining LLINs after one round in Rorya DC (2016) and three rounds in Butiama DC (2018) and Musoma DC (2018) is observed by an increase of malaria incidence over time following the IRS withdrawal.

Overall, key observations are noted from the yearly time series plots (Fig. 2 to 6) the data presented indicates that a) withdrawing IRS after one, two, three, or even four rounds result into resurgence of malaria incidence as indicated in Mara (Rorya DC, Butiama DC, Musoma DC). The districts where IRS was implemented followed by withdrawal is investigated further using monthly time series plots.

# Monthly – Time series Plots

The monthly time series plots are also used to provide visual inspection of the impact of IRS withdrawal. Although the visual inspections maybe used to show the difference between shifting of interventions in different districts, it is important to investigate whether the difference observed is statistically significant or not. Therefore, the statistical analysis is performed based on monthly data to provide more observations suitable for running a robust statistical model. Therefore, monthly time series trends are presented under each accompanied by statistical model results. The data for 2021 from January to August is also included in the monthly based analysis.

Implementation of IRS combined with standard LLIN followed by IRS withdrawal; to show the effect of IRS withdrawal.

Figure 7 presents malaria monthly incidence data per 1000 population before and after IRS is withdrawn for different IRS rounds. The impact of withdrawing IRS (vertical line) after one (A), two (B), and three (C) round(s) is clearly observed in Kagera - Muleba DC, Mwanza - Kwimba DC, and Mara - Butiama DC respectively – based on the observed resurgence of malaria incidence.

The monthly time series plot presented in Fig. 7 provides a clear picture of the impact of withdrawing IRS. However, the interrupted time series statistical model was deployed to assess the difference during IRS implementation and after withdrawal. The model results indicate that the difference between the trend during IRS and after withdrawal is negative and statistically significant (p < 0.001) - indicating that monthly malaria incidence decreases over time during IRS. For each month that passes, the malaria incidence decreases at a log mean of -0.30 (-0.34, -0.27), 95% Confidence Interval (CI), -0.08 (-0.09, -0.07), 95% CI, and – 0.02 (-0.03, -0.02), 95% CI on the index in Muleba, Kwimba, and Butiama DC respectively.

The immediate effect after the IRS is withdrawn is positive and statistically significant (p < 0.001) - indicating that withdrawing IRS increased the malaria incidence at log of 1.38 (1.20, 1.58), 95% CI, 0.41 (0.07, 0.74), 95% CI, and 0.51 (0.36, 0.66), 95% CI in Muleba, Kwimba, and Butiama DC respectively.

The sustained effect after IRS is withdrawn is positive and statistically significant (p < 0.001) - indicating that each day that passes after IRS is withdrawn, the malaria incidence increases at a log mean of 0.32 (0.29, 0.36), 95% CI, 0.13 (0.08, 0.17), 95% CI, 0.04 (0.03, 0.06), 95% CI and points on the index in Muleba, Kwimba, and Butiama DC respectively. Additional figures with almost similar trends exhibiting the same scenario are provided in Supplementary file 2.

## Discussion

Our findings based on visual inspection of yearly malaria incidence data per 1000 population indicate that IRS withdrawal results into resurgence of malaria. Statistical analysis based on monthly malaria incidence data per 1000 confirm the visual inspection where almost all the districts where IRS was withdrawing resulted into malaria resurgence after one, two, three, and even four rounds of IRS implementation. These results are not so different from previous studies conducted in Africa as demonstrated by the following publications in Uganda [4, 5, 15], Benin [7, 16], and Ghana[8, 17].

The WHO recommendation on IRS Implementation Phases [18] shows that the consolidation phase which allows a shift from total IRS coverage to targeted IRS coverage is to be introduced when the annual parasite Index (API) is down to < 5/1000 and malaria parasite prevalence (PP) is < 1%. However, the current data in Tanzania indicates that the estimated national average annual parasite incidence (API) is 122/1000 and malaria parasite prevalence is 7.5%, which are well above the WHO's recommended threshold of API < 5/1000 and PP < 1% respectively. However, the country has been withdrawing IRS from a number of councils regardless of the guidance

Most endemic African countries including Tanzania, have persistent resource constraints to ensure broad and sustainable coverage of the IRS, consequently facing difficult decisions on how to maintain IRS as a key vector control strategy. Contending with such a dilemma leads to premature withdrawal of IRS resulting in undesirable rebound of malaria. [19, 20].

One limitation from our studies is the lack of entomological data that can also be used to assess the impact of IRS withdrawal in all the IRS districts in the Lake Zone. Despite this limitation, the following recommendations are drawn from this analysis a) both entomological and epidemiological data should be used to guide IRS implementation, b) any decision to withdraw IRS prematurely (based on WHO guideline) should ensure its replacement with an equally effective or superior intervention, c) In view of having ubiquitous mixed metabolic resistance mechanisms across the country, deployment of IRS using non-pyrethroids becomes of paramount importance not only for managing resistance, but also for successful interruption of malaria transmission, d) efforts should be made to seize opportunities to conduct trials to test different combinations of vector control interventions as replacements of IRS in the spirit of integrated vector control. This should include a combination of new generation nets using non-

pyrethroids in combination with larval source management, e) where vector control interventions including IRS are being implemented, there should be a resources mobilization plan at programme and country levels to ensure sustainability of the interventions for the implementation of Integrated Vector Control Management, including deployment of IRS. It is also important to perform a cost-effectiveness analysis on the IRS program to support the decision making process.

## Conclusion

The deployment of IRS using non-pyrethroids insecticides becomes of paramount importance not only for managing resistance, but also for successful interruption of malaria transmission. Therefore, IRS should not be withdrawn in areas where it is being implemented particularly in areas with high malaria burden with high malaria transmission risk. In addition, entomological and epidemiological data should be considered and used to guide NMCP's IRS implementation program. More importantly, any decision to withdraw the IRS should ensure its replacement with an equally effective or superior intervention.

## **Abbreviations**

IRS: Indoor Residual Spraying; PMI: President's Malaria Initiative; DHIS2: District Health Information System 2; ITSD: Interrupted Time Series Design; LLINs: long-lasting insecticidal nets; WHO: World Health Organization; PBO: Piperonyl Butoxide; DC: District Council; API: Annual Parasite Index; RCTs: Randomized Controlled Trials; RTI: Research Triangle Institute.

## Declarations

#### Ethical approval and consent to participate

Not applicable, however, as it is required by any Indoor Residual Spraying (IRS) Campaigns, community sanitization was performed by RTI project in collaboration with Tanzania National Malaria Control Program before IRS implementation.

#### **Consent for publication**

Not applicable

#### Availability of data and materials

The dataset used is available upon request or through DHIS2 for those with access.

#### Competing interests

The authors declare that there are no competing interests.

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#### Authors' contributions

All authors developed the concept for this work after a discussion through Tanzania's VCTWG meetings. DM wrote the first draft with support from all authors, DM and SK performed data analysis, all authors contributed, reviewed, and approved the final draft.

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## **Figures**



#### Figure 1

The implementation of IRS in Tanzania(A): in the Lake Zone Regions(B) within selected districts (C).



#### Figure 2

A timeline indicating a number of IRS districts and the type of insecticide sprayed from 2007 to 2020



#### Figure 3

Time series plots indicating the impact of intervention shift on malaria incidence per 1000 population for the six districts in Mwanza region from 2015 to 2020.



Figure 4

Time series plots indicating the impact of intervention shift on malaria incidence per 1000 population for the six districts in Geita region from 2015 to 2020.



#### Figure 5

Time series plots indicating the impact of intervention shift on malaria incidence per 1000 population for the eight districts in Kagera region from 2015 to 2020



#### Figure 6

Time series plots indicating the impact of intervention shift on malaria incidence per 1000 population for the eight districts in Mara region from 2015 to 2020



#### Figure 7

Time series plots based on monthly malaria incidence per 1000 population data - showing the impact of withdrawing IRS after one (A), two (B), and three round(s) (C) over time.

## **Supplementary Files**

This is a list of supplementary files associated with this preprint. Click to download.

- SupplementaryFile1.pptx
- SupplementaryFile2.pptx