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Peer Review

# Review of: "Impact of Mass Distribution of Long-Lasting Insecticide Nets on Malaria Prevention in Lindi Region, Tanzania: A Quasi-Experimental Study"

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1. Independent researcher

Using a quasi experimental design, the authors analysed the effect of a free mass distribution campaign of LLINs on malaria morbidity measured by malaria parasite rate in one of the high-prevalence regions of Tanzania. The study has merit as it adds real-world evidence of the effectiveness of an experimentally proven control tool in a particular setting.

I have a couple of general comments for the authors: 1) because of the nature of the study design and the statistical tests used, the authors should exercise caution in their causation claims as there is very limited control of confounding in their study, and 2) There is considerable plagiarism (at least 20% matched text) with the following article : *Kabeya, Theddy Kazadi, et al. "Impact of mass distribution of long-lasting insecticide nets on the incidence of malaria in Lomami, Democratic Republic of Congo (DRC): a study based on electronic health record data (2018-2019)." Pan African Medical Journal 45.1 (2023).* Plagiarism may happen accidentally. It is nevertheless unethical and unacceptable in any form. Please address these critical concerns.

**COMMENTS TO THE AUTHORS**

ON THE INTRODUCTION

1. Although the research focuses on LLINs, it would be useful to present to the reader, in brief, a comprehensive picture of the malaria control strategy in Tanzania. Some control interventions are implemented nationwide while others are targeted in space, time and/or population.
2. The authors state that in 2022, the NMCP implemented a free mass distribution campaign to further protect at-risk populations in high-prevalence regions, including Lindi. Was it standard

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(pyrethroid-only) LLINs or dual-active-ingredient LLINs (PBO-Pyrethroid-LLINs) previously tested in Tanzania (2015-2016), recommended by WHO, and currently being distributed by malaria control programs in sub-Saharan Africa? If it was PBO-Pyrethroid-LLINs, was it the first time such LLINs were distributed in the region? Please clarify.

3. The authors state in the last sentence: "This study aims to assess the malaria positivity rate before and after the mass distribution of LLINs in Lindi…", but it is unclear to what end. In view of the statements made in the discussion and conclusion, it seems that their aim was to assess a causal relationship between the LLINs mass distribution campaign and a change in MPR in the Lindi region. Please reformulate to clarify the study aim.

ON THE METHODS

1. **Section 1: Study design and setting**
    a. The rationale for the study site selection is not clearly stated in the methods section. The authors write in the second sentence of the limitations paragraph in the discussion section: "First, selection of study sites was based on data availability…". 1) Please, move this point to the methods section, 2) Clarify "data availability" and clearly explain how it prevented you from including other district councils/regions, which would have supported more robust findings.
    b. In that same sentence, the authors mention "…the small number of health facilities in the selected districts…" but gIve no indication about the number, geographical distribution of those health facilities. 1) Please include a map of the study area showing the district councils, the intervention and control groups, and locating health facilities, and 2) please clarify if health facilities in the intervention and control areas were similar in term of mean distance to health facility. This is important as the outcome measure is based on healthcare service utilisation (OPD attendance), which in turn is affected by travel time and cost (distance) to the facility. Also, the study included urban and rural areas where mean distance to health facility is unlikely to be similar.
    c. The authors state: "In this study, all health facilities in Mtama, Ruangwa and Nachingwea districts council of Lindi region <u>that participated</u> in mass distribution of LLINs were assigned into intervention group". Were there health facilities in these three district councils that did not participate in the mass distribution of LLIN? Conversely, were there

health facilities in Lindi municipal, Kilwa districts and Liwale districts that received the LLIN? Pleas clarify.

d. According to the authors, Lindi was targeted in the 2022 free LLINs mass distribution campaign because it was among the high-prevalence regions. Then, why have some district councils (the control group) in the Lindi region not been covered by this campaign? Please clarify.

e. Except the intervention under study, the reader might want to know if the intervention and control groups were comparable in respect to the other malaria control interventions. Please clarify.

f. The authors give no indication as to whether the intervention and control areas were comparable in terms of environmental (temperature, precipitation, vegetation), geographical (altitude), demographic (population density), socio-economic and behavioral (bednet use, healthcare seeking) factors known to drive malaria transmission, which may account for observed differences in the outcome to some extent.

g. Please, enrich the description of study setting with malaria transmission characteristics (stability, seasonality, main vector species, EIR...), and a description of the wet season in Lindi.

2. **Section 2: Study population, variables and study size**

a. The authors state: "Exhaustive sampling was used in this study" and "A total of 2,153,208 participants who attended at OPD...were recruited...in Lindi Region". However, they don't provide the total population from which this sample was obtained. Please provide the total population for the whole study area as well the details by study group.

b. The authors state "...the general population...who attended at outpatient department to seek malaria prevention and treatment service...". Patients seek care for symptoms and signs such as fever, not for a diagnosis. Malaria is a diagnosis. Please reformulate accordingly.

i. For instance, reformulate the following (<u>original</u>) sentence "A total of 2,153,208 participants who attended at OPD for malaria prevention and treatment service in all health facilities were recruited between September 2021 to August 2022 and September 2022 to August 2023 in Lindi Region." To (<u>suggested reformulation</u>) "A total of 2,153,208 participants who were tested for malaria at OPD in all health facilities within the Lindi Region, were recruited between September 2021 to August 2022 and September 2022 to August 2023."

ii. I would suggest ther term included instead of "recruited" as the latter term sounds like you seleted the participants collected individual-level data.

3. **Section 3 : Data collection, bias, quantitative variables** :

a. The data used in this study were extracted from the DHIS2. The authors did not collect the morbidity data in the first place. I would suggest to reformulate the title of this section as, for instance, <Data source>

b. Please clarify that the data extracted from the DHIS2 is aggregated/summary data. That has implications in the justification of the choice of the statistical methods.

c. This is the second section dealing with study variables. Please 1) avoid redundancy and, 2) describe all study variables in the same section.

d. In this paragraph, the authors mentioned data completeness in DHIS2. There are two aspects in data completeness: reporting and data elements. My understanding is that they meant health facility reporting completeness rather than data element completeness? Please clarify the "data completeness" term.

e. The last sentence of the paragraph "Also, number of confirmed malaria cases, using the rapid diagnostic testing (RDT) or the microscopy testing or both." is redundant with the preceding sentence. Please delete the redundant information.

f. In this paragraph, the authors write: "The collected data are...and malaria positive rate...". MPR is not collected data. It is calculated. Please reformulate this sentence.

g. The authors write: "Poor data completeness and coding errors on the DHIS2 may cause bias and influence the results of the study. However, DHIS2 standards state that when data completeness is 80% or more, analyses can be done». However, they gave no measure of data completeness for the study site and period. Please provide the exact data completeness level that allowed you to carry out valid analysis.

h. The authors did not measure the LLINs use rate in neither group, which is an important factor to achieve a community-level effect on malaria morbidity. Though the control group did not receive LLIN during the 2022 campaign, the authors explained that mass distribution campaigns have been conducted every three years since 2012 alongside continuous distribution mechanisms. Therefore, LLINs ownership and use is unlikely to be zero in the control group. Please clarify.

4. **Statistical methods**

a. The authors state: "Data were exported to Microsoft Excel and analyzed using SPSS for figure and table development, as well as result interpretation". The way the sentence is written suggests that the software performs the results interpretation. Please, reformulate this sentence.
b. The authors used a t-test to compare proportions, which is unusual. 1) Please provide a reference (It has been reported to be applicable and robust on summary data), 2) clearly describe the t-tests you used and provide the underlying assumptions.
c. In the data collection section, the authors stated:" DHIS2, which is the national health data management software that Lindi Region has been using for several years ago". "...for several years ago" is imprecise but it sounds like a lot of data is available. It is unclear what prevented them from using more common methods (difference-in-differences, interrupted time series...) to assess a causal relationship between the LLINs mass distribution campaign and change in the MPR. Is it because of data availability (DHIS2 rolled out in stages rather than at once in the Lindi region, then when was it fully implemented in Lindi)? Is it because data before 2021 was of poor quality, then provide a measure of the data quality. Please clarify.

5. **Research ethics**:
a. There ought to be a section on ethical considerations in the methods section. Please move the ethical considerations from the statements and declarations section to the methods section.
b. The authors use the phrase "Ethical Approval to participate": my understanding is that the ethical approval is about the clearance to proceed with the conduct of the research. What individual participation requires is informed consent. The authors could, for instance, reformulate the paragraph's title as <Ethical considerations>.
c. The authors state that ethical approval was not applicable: 1) please provide the reason it wasn't applicable and, 2) though ethical clearance may not have been required, an administrative authorization to access, extract and use the data from the government agency managing the information system likely applied. Please clarify.
d. The "Patients and public involvement" paragraph should be integrated into the ethical considerations section. Please clarify that the data extracted from the DHIS2 is in aggregated form with no personally identifiable information.

ON THE RESULTS

1. Demographic characteristics of enrolled participants :
    a. Please present the demographic characteristics of enrolled participants for the groups (intervention and the control) being compared.
    b. "In term of age group 992,765 participants were under 5 years old and 1,160,443 participants were above 5years (Table 2)". That is data from Table 1. Please correct.
    c. Table 2 does not belong to the study population demographics section
2. I can't figure out the relevance of the analysis/results presented in Table 2 and Figure 2, ie combining the intervention and control groups to compare pre and post-intervention MPR. Then, what is the purpose of having intervention and control groups ? How does it help ascertain that the observed change in MPR is associated with the intervention ? Besides, that analysis is not clearly announced in the statistical methods.
3. Table 2 and figure 1 tell the same story, which creates some redundancy in the results. Please avoid redundancy.

ON THE DISCUSSION

1. In the first paragraph, the authors state: "The observed decline in malaria cases can be attributed to several factors" and "Correct utilization was noted, and the insecticides used for impregnation remained effective." 1) They did not measure LLINs use or effectiveness and they don't provide any reference for this statement. 2) the point about LLINs effectiveness in this paragraph sounds contradictory with the declining effectiveness hypothesised in the second paragraph. Please avoid unsupported statements and be consistent in your discussion.
2. In the second paragraph, the authors discussed the rise of MPR between February and June 2023 and explained that observation by the hypothesis of a declining effectiveness of LLINs. My first point is that this result is global and does not show how the rise in malaria morbidity is shared between the intervention and control areas. So, attributing that rise to declining effectiveness of LLINs seems excessive. Second, the survival time of bed nets is above 1.5 years for both standard and dual-active-ingredient LLIN (in the cited reference) while the rise in MPR was observed between six and ten months post-campaign in the present study, which is quite a short period. Finally, how can they rule out an effect of the wet season? There is no description of the rainy seasons in the manuscript.

3. The third paragraph is very confusing with the discussion tending to stray from the study research question and findings. There is too much on LLINs durability and effectiveness. There are excessive and contradictory statements: "LLINs distribution campaign did really reverse the epidemiological situation" and then acknowledging the combination of other malaria preventive methods. How those complementary methods have been implemented in the study area should have been described earlier in the methods section. The authors made the following recommendation ("If funding gaps continue, targeted selection of high burden, more populated regions and districts should be prioritized.") for which I have two observations: 1) they are recommending something that is already implemented (targeting high-burden regions (such as Lindi), and 2) should a region be targeted just because it is highly populated? Please reformulate.
4. The fourth paragraph is also straying from the research question and findings. It actually doesn't discuss any findings of the present study and the recommendation to strengthen malaria surveillance and reporting, reactive case detection, and reactive drug administration is not supported by any of their findings neither. I would recommend dropping this paragraph.
5. Limitations: the data used in this study was obtained from the DHIS2, and the authors state "Second, though the DHIS2 database enabled us to capture a comprehensive set of delivery information, poor data completeness and coding errors on the DHIS2 can lead to bias and influence the result". Nowhere in the manuscript, they provide data quality indicators (at least completeness), for the study area and for the intervention and control areas. The authors state that "quasi-experimental study designs were used to control for confounding". That is not the purpose of this design. The attempt to control for confounding is achieved through statistical methods and t-tests do not allow controlling for confounding. The authors used t-tests in this research and should present in details the limitations of t-tests in achieving the study aim with a quasi experimental design. The general point about quasi experimental designs is that, compared to RCT, they yield weaker evidence for causal relationship.

ON THE CONCLUSION

1. When the authors state "the results of this study unequivocally demonstrate that the mass distribution of LLINs has significantly reduced the percentage of malaria cases in Lindi Region." they are making excessive claims which are, by the way, contradictory with the following statement made in the limitations paragraph of the discussion: "...unmeasured confounding may have biased results. Thus, estimates should be interpreted with caution." Assessing a causal

relationship was not clearly expressed in the study aim in the introduction, and the design and statistical methods used in this study can only suggest causation. Please, make only claims that are reasonably supported by your methods and findings.

2. When the authors state "This intervention...has also led to other positive outcomes, such as a reduction in severe malaria cases and hospital admissions", they are making unsupported claims: neither severe malaria cases, nor hospital admissions data were mentioned in the description of the study variables extracted from DHIS2 in the methods. There is no mention of severe malaria cases or hospital admissions in the results. This is surprising. Please make only claims that are supported by your methods and findings.

ON THE REFERENCES

1. The reference list contains sources that are not retrievable as they are written. Readers should have access to all references in the list. Please correct the following reference and provide an URL: <*World Health Organization (WHO). Malaria 2021 Country Profile:United Republic of Tanzania. Geneva switzerland; 2021*>
2. The reference list contains sources that are not properly cited:
    a. The full-text PDF in ResearchGate indicates that the following article was published in the International Journal of Immunology Sciences: <*George M Bwire AS. Malaria Control in Tanzania: Current status and future prospects. Researchgate.*> Please cite properly.
    b. The title of the following source is not correct: <*Yi B, Zhang L, Yin J, Zhou S, Xia Z. in malaria elimination: China's practice and global adaptions. Malar J [Internet]. 2023;22(1):1–9. Available from: doi:10.1186/s12936-023-04580-9*>. Please, check and cite properly.
    c. The following reference is a preprint: <*Li Y, Chen R, Wang J, Chen C, Yang B, Chen Y. Malaria Elimination in China: Innovative Three-Layer Strategy Applied to the Outbreak of Indigenous Cases in Sanya, Hainan. 2022;1–14.*>. Please provide the missing information (preprint server, object type, date of most recent version, date accessed, doi).
    d. The following reference is a preprint: <*Israel Wuresah A, Sciences A, Siman Elmi G, Adjuik M, Wuresah I. Long-Lasting Insecticide Nets Ownership and Malaria Morbidity in Krachi East Municipality, Ghana. 2023;1–20. Available from: doi:10.1101/2022.05.18.22275276*>. Please provide the missing information (preprint server, object type, date of most recent version, date accessed).
3. The reference list contains sources that do not support the statements they intend to:

a. Reference 1 indicates that "In Tanzania, more than 6 million malaria cases were confirmed in 2019" instead of 10.8 million as stated in the manuscript.
b. Reference 2 is a retrospective study of malaria endemicity and does not support the statement in the third sentence
c. Reference 4 is a study of the effectiveness of community ITN coverage and does not support the statement in the last sentence of the first paragraph of the introduction
d. Reference 11 is not a study conducted in Tanzania, India, and Côte d'Ivoire to assess the durability of pyrethroid-PBO LLINs
e. Reference 13 does not support the statement about the effectiveness of LLINs

4. The reference list includes secondary, instead of original sources
    a. Instead of citing reference 1, cite the original source that Is the (World malaria report 2022)
    b. Instead of citing reference 6, cite the original source (NMCP Tanzania. 2020 Annual Report)
    c. Instead of citing reference 15, cite the original source (*A Framework for Malaria Elimination_WHO,2017*)

ON THE STATEMENTS AND DECLARATIONS

Data availability: There are two contradictory points: a) you state "All data produced in the present study are available upon reasonable request to the authors" and b) you state "Data generated or analysed during this study are included in this published article." I can't see the data. Please clarify.

ON THE ABBREVIATIONS

1. Though it is helpful to provide a list of abbreviations, it should be done consistently. Your abbreviations list contains items that never appear in the body of your manuscript (TACTs, SMMSP, PPP, MDGS, LSM, IEC, IMVC, GoT, DMTs, DHP, DDT, CLWS, CHW, CQ, BCC, ACT), which is curious, and your manuscript contains abbreviations that do not appear in the abbreviations list (ITN, DHIS2). ITN and DHIS2 were never spelt out in the body of the manuscript. Alternatively, if not a requirement, you could omit that list of abbreviations and make sure you spell out in full each abbreviation at its first use.
2. Once you spell out an abbreviation in full on its first use in your manuscript, a) you need not spell it out again (check for LLINs, WHO, OPD, RDT...), and b) do use the abbreviation afterwards, that is its purpose.

ABOUT THE WORDING

1. LLIN vs ITN. Though LLIN and ITN are often used interchangeably, I would suggest you stick to one term throughout the manuscript to make the reading experience easier.
2. Experimental group vs intervention group. Though they have the same meaning, I would suggest you stick to one term throughout the manuscript to make the reading experience easier.

## Declarations

**Potential competing interests:** No potential competing interests to declare.