ESTIMATING THE ASSOCIATION BETWEEN TYPES OF BED NET USAGE AND MALARIA INCIDENCE IN A COHORT OF CHILDREN IN KINTAMPO, GHANA

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INTRODUCTION

- Ghana faces one of the highest malaria burdens in the world.1 In 2021, there were about 5.4 million reported cases of malaria and 12,500 malaria deaths.[1]
- The phase III trial of the RTS,S/AS01 malaria vaccine was a double-blind, randomized controlled trial conducted between March 27, 2009, and January 31, 2014, at 11 sites across seven sub-Saharan countries.[2] Previous research using phase III trial data found that the combined use of the RTS,S vaccine and bed nets was more effective than using the RTS,S vaccine alone.[3] Vaccinating one child without a bed net was found to prevent more malaria cases than vaccinating a child who used a bed net.[3] However, in scenarios where RTS,S vaccines were absent, it is still not well understood whether the use of bed nets alone was associated with a reduction in malaria cases in participants. It is also not clear whether the types of bed net usage, such as imperfect versus perfect use, had different association with malaria incidence.
- Purpose: To estimate the association between types of bed net usage and malaria incidence among children in the control group of the phase III trial of RTS,S/AS01 in Kintampo, Ghana.

METHODS

Follow-up Segmentation and Malaria Episode Counting:

- The extension phase after the dose 3 was divided into three time periods, as depicted in Figure 1. The usage of the bed nets were documented during three home visits: at 12 months and 29 months after the third vaccine dose was given to the child, and one month before the trial ended.[4] Each measurement within an interval serves as a proxy for bed net usage during that time period. We counted the number of malaria episodes within each interval for every child.

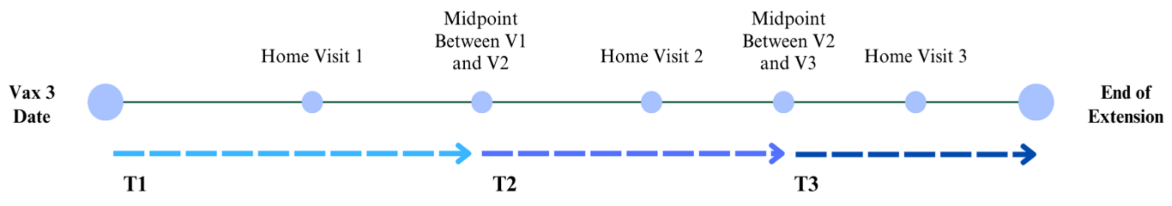

Figure 1. Timeline of Follow-up Home Visits and Data Collection Intervals.

Exposure:

- We coded bed net usage categories as follows: 0 - No bed net was observed on the child's bed, 1 - The bed net was either untreated, had at least one hole large enough to admit three fingers, or both, 2 - The bed net was treated and had no holes large enough to admit three fingers.

Outcome of Interest:

- Clinical malaria, defined in the trial as an illness accompanied by an axillary temperature of at least 37.5°C and P. falciparum asexual parasitemia (> 5000 parasites per mm³).[2]

Confounding Variables:

- Based on the literature, the age of the child, background malaria transmission intensity, and household socioeconomic status (SES) were identified as potential confounders that are likely to influence both a child's bed net usage and the number of malaria cases experienced.[3, 5-7]

➢ Household SES Index

- We used principal component analysis (**PCA**).[8] Roof type, wall type, floor type, and nighttime lights were included for PCA based on literature.[9-11] We scaled the variables and extracted the first principal component, PC_1, to generate the household SES index.

$$PC_1 = a_{11}X_1 + a_{12}X_2 + a_{13}X_3 + a_{14}X_4$$

➢ Background Malaria Incidence

- We used two machine learning (ML) algorithms—a random forest (**RF**) model and an artificial neural network (**ANN**). Our training data consisted of control-group infants' data from three study sites—Lilongwe, Malawi; Kintampo, Ghana; and Lambaréné, Gabon (n = 419). Twelve ecological variables were selected based on a study by Bell et al.[12] We included the study site as a predictor in our model to account for potential transmission heterogeneity across the sites. To tune the hyperparameters, we utilized the random search approach with 10-fold cross-validation. Finally, the model having the lowest root mean-square error (RMSE) and the highest R-squared was selected for estimating the background malaria incidence for each child in our study cohort.

➢ Baseline Age

- Time from the child's birth date to the first day of the corresponding follow-up.

Statistical Analysis: All analyses were done in RStudio for Windows, version 2023.09.1. We started with **univariate analysis** that estimated the association between types of bed net usage and malaria incidence without adjusting for any confounders. We then conducted a **multivariate analysis** that controlled for potential confounders to determine if and how the estimates changed. We added a random intercept to account for within-subject correlation since each child can have more than one observation. For both analyses, we used a mixed-effects Poisson regression model.

$$1) \quad \ln(E[Y]) = \beta_0 + \beta_1 * Imperfect\ Bed\ Net\ Use + \beta_2 * Perfect\ Bed\ Net\ Use + \ln(Follow\ up\ Days) + b_{pid[i]}$$

$$2) \quad \ln(E[Y]) = \beta_0 + \beta_1 * Imperfect\ Bed\ Net\ Use + \beta_2 * Perfect\ Bed\ Net\ Use + \beta_3 * Age + \beta_4 * Household\ SES + \beta_5 * Background\ Malaria\ Incidence + \ln(Follow\ up\ Days) + b_{pid[i]}$$

RESULTS

After removing incomplete data, 666 records from 242 children were included in the final analysis.

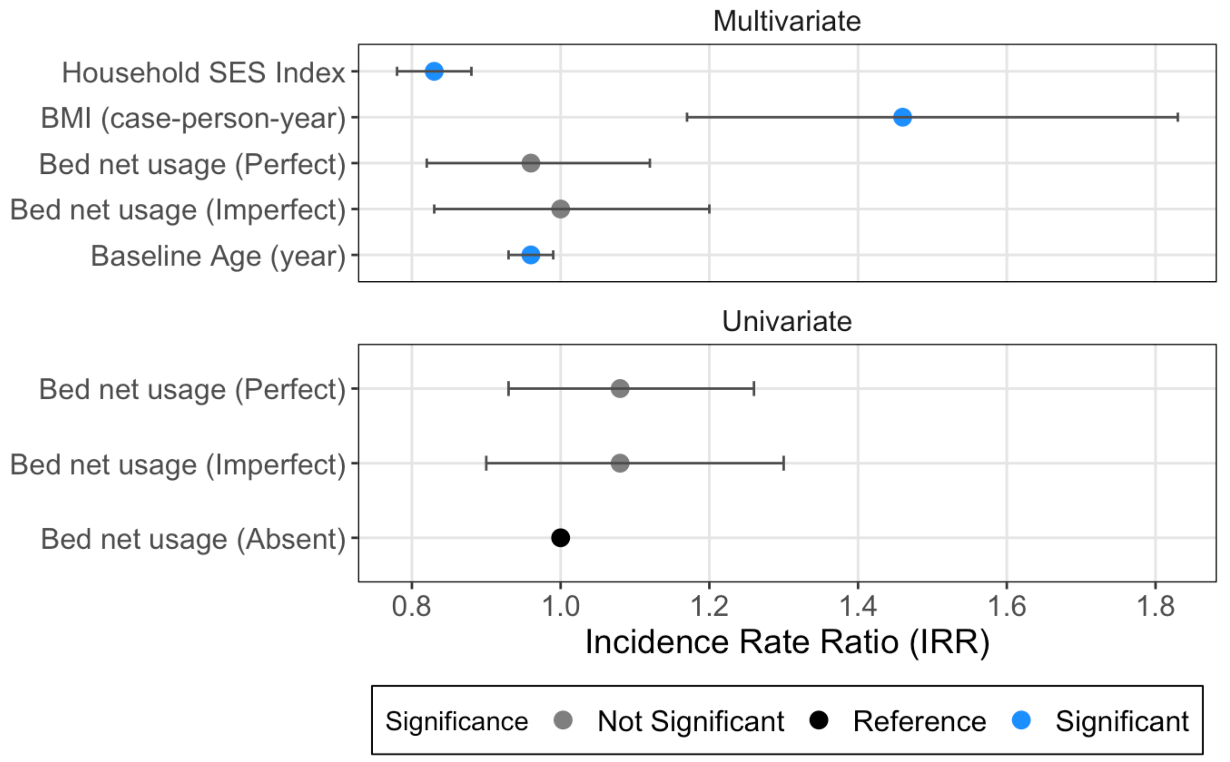
Multivariate
Household SES Index
BMI (case-person-year)
Bed net usage (Perfect)
Bed net usage (Imperfect)
Baseline Age (year)
Univariate
Bed net usage (Perfect)
Bed net usage (Imperfect)
Bed net usage (Absent)
0.8
1.0
1.2
1.4
1.6
1.8
Incidence Rate Ratio (IRR)
Significance
Not Significant
Reference
Significant

Figure 2. Incidence Rate Ratios of Malaria by Bed Net Usage and Control Variables.

Variable	Loading
Wall Type	0.595
Roof Type	0.590
Floor Type	0.324
Nighttime Lights	0.439

Figure 3. Loadings of Household Characteristics on the First Principal Component.

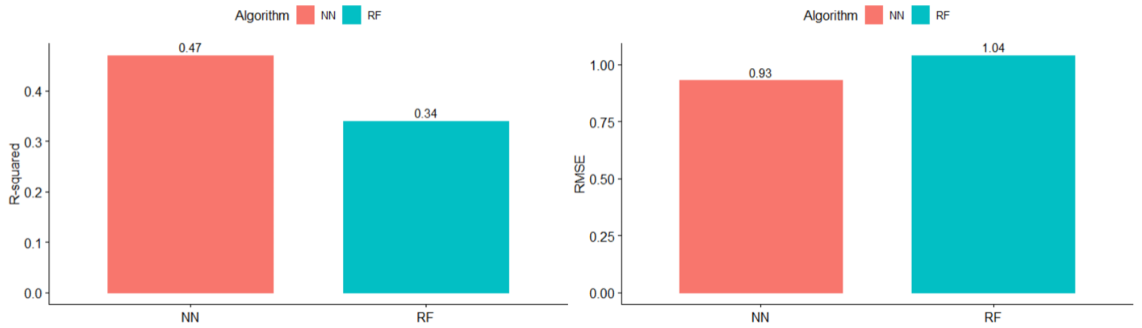

Figure 4. Comparison of Performance Between Machine Learning Algorithms.

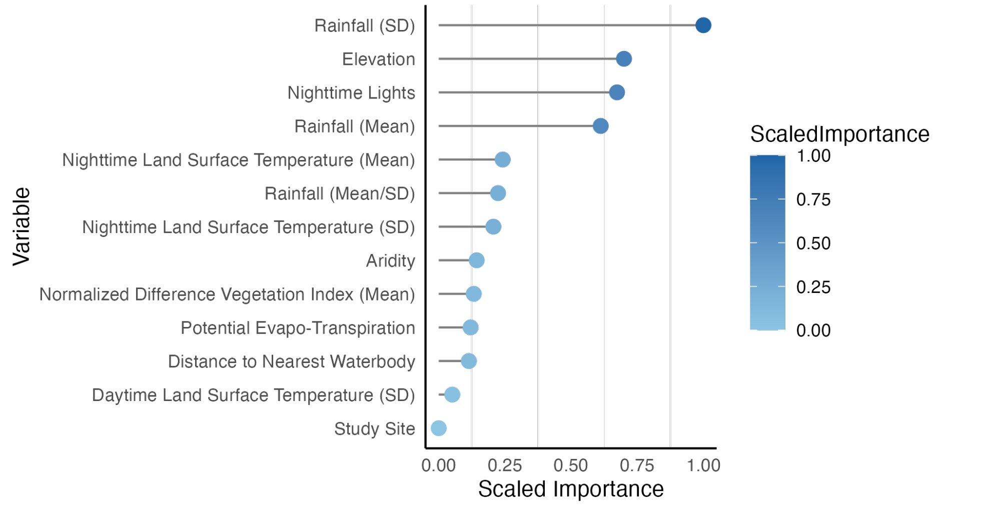
Rainfall (SD)
Elevation
Nighttime Lights
Rainfall (Mean)
Nighttime Land Surface Temperature (Mean)
Rainfall (Mean/SD)
Nighttime Land Surface Temperature (SD)
Aridity
Normalized Difference Vegetation Index (Mean)
Potential Evapo-Transpiration
Distance to Nearest Waterbody
Daytime Land Surface Temperature (SD)
Study Site
Variable
Scaled Importance
ScaledImportance
1.00
0.75
0.50
0.25
0.00

Figure 5. Permutation Feature Importance Plot for the Neural Network Model.

- We conducted a sensitivity analysis by varying the way of segmenting the extension phase. We employed the same unadjusted mixed-effects Poisson model and results remained consistent.

CONCLUSIONS

- Our univariate and multivariate analyses did not reveal a significant impact of bed net usage on malaria incidence in either model. Future studies could benefit from data with more consistent measurements of bed net usage in an controlled environment.
- Our analysis suggests that targeted interventions in Ghana should prioritize resources and support for younger children and households with lower socioeconomic status, as well as for children living in areas with higher estimated background malaria transmission intensity. This will allow us to enhance the overall effectiveness of existing interventions and reduce the burden of this disease among the most vulnerable populations.

REFERENCES

1. WHO. World Malaria Report, 2023. Geneva: World Health Organization (WHO); 2023.
2. Efficacy and safety of RTS,S/AS01 malaria vaccine with or without a booster dose in infants and children in Africa: final results of a phase 3, individually randomised, controlled trial. The Lancet. 2015;386(9988):31-45. doi:10.1016/S0140-6736(15)60721-8
3. Bell GJ, Loop M, Topazian HM, et al. Case reduction and cost-effectiveness of the RTS,S/AS01 malaria vaccine alongside bed nets in Lilongwe, Malawi. Vaccine. 2020;38(25):4079-4087. doi:10.1016/j.vaccine.2020.04.031Ol
4. RTS,S Clinical Trials Partnership. Supplementary appendix of "Efficacy and safety of RTS,S/AS01 malaria vaccine with or without a booster dose in infants and children in Africa: final results of a phase 3, individually randomised, controlled trial." Lancet. 2015;386(9988):31-45. doi:10.1016/S0140-6736(15)60721-8.
5. Akello AR, Byagamy JP, Etajak S, Okadhi CS, Yeka A. Factors influencing consistent use of bed nets for the control of malaria among children under 5 years in Soroti District, North Eastern Uganda. Malaria Journal. 2022;21(1):363. doi:10.1186/s12936-022-04396-z
6. Sonko ST, Jaiteh M, Jafali J, et al. Does socio-economic status explain the differentials in malaria parasite prevalence? Evidence from The Gambia. Malaria Journal. 2014;13(1):449. doi:10.1186/1475-2875-13-449
7. Khagayi S, Desai M, Amek N, et al. Modelling the relationship between malaria prevalence as a measure of transmission and mortality across age groups. Malaria Journal. 2019;18(1):247. doi:10.1186/s12936-019-2869-9
8. Vyas S, Kumaranayake L. Constructing socio-economic status indices: how to use principal components analysis. Health Policy and Planning. 2006;21(6):459-468. doi:10.1093/heapol/czl029
9. Gyaase S, Asante KP, Adeniji E, Boahen O, Cairns M, Owusu-Agyei S. Potential effect modification of RTS,S/AS01 malaria vaccine efficacy by household socio-economic status. BMC Public Health. 2021;21(1):240. doi:10.1186/s12889-021-10294-x
10. Escamilla V, Alker A, Dandalo L, et al. Effects of community-level bed net coverage on malaria morbidity in Lilongwe, Malawi. Malaria Journal. 2017;16(1):142. doi:10.1186/s12936-017-1767-2
11. Pérez-Sindín XS, Chen THK, Prishchepov AV. Are night-time lights a good proxy of economic activity in rural areas in middle and low-income countries? Examining the empirical evidence from Colombia. Remote Sensing Applications: Society and Environment. 2021;24:100647. doi:10.1016/j.rsase.2021.100647
12. Bell GJ, Goel V, Essone P, et al. Malaria Transmission Intensity Likely Modifies RTS, S/AS01 Efficacy Due to a Rebound Effect in Ghana, Malawi, and Gabon. The Journal of Infectious Diseases. 2022;226(9):1646-1656. doi:10.1093/infdis/jiac322

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