

Examining the spatial effect ranges of new classes of long-lasting insecticidal nets (LLINs) on malaria infection and vector abundance: An anisotropic semivariance analysis in the context of a phase-III cluster-randomised malaria vector control trial of dual active-ingredient LLINs

Charles Thickstun

`Charles.Thickstun@uOttawa.ca`

University of Ottawa

Jacklin F Mosha

National Institute for Medical Research

Eliud Lukole

National Institute for Medical Research

Nancy S Matowo

National Institute for Medical Research

Elizabeth Mallya

Kilimanjaro Christian Medical University College

Jacklin Martin

National Institute for Medical Research

Alphaxard Manjurano

National Institute for Medical Research

Cindy Feng

Dalhousie University

Immo Kleinschmidt

London School of Hygiene & Tropical Medicine

Franklin W Mosha

Kilimanjaro Christian Medical University College

Mark Rowland

London School of Hygiene & Tropical Medicine

Monica Taljaard

Ottawa Hospital Research Institute

Natacha Protopopoff

Research Article

Keywords: Malaria, Cluster-Randomised Control Trial, Vector control, Community effect, Buffer, Semivariance, Spatial analysis

Posted Date: September 23rd, 2026

DOI: <https://doi.org/10.21203/rs.3.rs-7762367/v1>

License: © ⓘ This work is licensed under a Creative Commons Attribution 4.0 International License.
[Read Full License](#)

Additional Declarations: No competing interests reported.

Abstract

Background

At high levels of population coverage with long-lasting insecticidal nets (LLINs), reductions in malaria vector populations can create a community effect, protecting individuals in an area who do not sleep under a net themselves. In cluster-randomised trials evaluating new LLINs, spatially localised reductions in malaria transmission may impact nearby clusters unless carefully designed, leading to attenuated treatment effect estimates. Unsampled buffer areas are commonly used to mitigate contamination, but no consensus on optimal buffer size exists. Using data from a phase-III cluster-randomised trial in northern Tanzania assessing three dual active-ingredient LLINs against a pyrethroid-only LLIN, our study aims to determine the spatial form of LLIN intervention effects on malaria infection and vector abundance.

Methods

Using cross-sectional data (July 2020; 18 months post-intervention) from a cluster-randomised malaria vector control trial, we measured malaria infection and commonly associated clinical, household, environmental, and geographic factors in 5955 children from 3188 households across four geographically contiguous areas. Data on vector abundance and associated factors were additionally collected from a subset of 789 households between September and December 2020. Mixed-effects logistic and negative binomial regression models were constructed to predict malaria infection in children and vector abundance in households, respectively. Model residuals were used to compute robust semivariance estimates and variogram models, accounting for anisotropic trends present in the data.

Results

We identified malaria infection in 2738 children (46.0%) and captured an average of 4.13 malaria vectors per trap night—predominantly *Anopheles funestus* sensu lato (80.7%). Range estimates for malaria infection model residuals varied from 1452m (95%CI = 1360–1545; Py-Pyriproxyfen LLIN) to 7833m (4413–11250; Pyrethroid-only LLIN) and vector abundance model residuals varied from 1139m (1100–1178; Py-Pyriproxyfen LLIN) to 4085m (1216–6954; Py-Chlorfenapyr LLIN). The Pyrethroid-only LLIN and Py-Pyriproxyfen LLIN malaria infection models were largely non-spatial in nature (RNE = 88.4% (84.8–92.4) and 91.0% (88.9–93.0), respectively) and the Py-Chlorfenapyr LLIN vector abundance model had no significant spatial form (68.1%, 50.9–100.0).

Conclusions

The results of this study describe the spatial form of community effects induced by LLIN interventions in certain contexts—potentially driven by the relative efficacy of intervention effects on local vector populations. Modelled range estimates uniformly exceed common buffer distances, although the proportion of variation explained by spatial dependence was quite low for three models. In designing

cluster buffers, future vector control trials should consider the spatial dispersion patterns of local vector populations and identify how they intend to control for any contamination that may occur.

Background

Malaria is a vector-borne acute febrile disease caused by *Plasmodium spp.* parasites that afflicts more than 249 million people annually, mainly in sub-Saharan Africa [1]. While malaria has been a major World Health Organization (WHO) elimination focus for decades, recent trends have shown a resurgence in malaria cases, in part due to an increased vector resistance profile to the current class of WHO approved insecticides used in the manufacture of long-lasting insecticidal nets (LLINs) [2]. Pyrethroid-only bednets, which were the preferred class of insecticide treated nets from 2003–2022 [3, 4], have been compared against new dual active-ingredient (Dual AI) LLINs which combine multiple chemical agents in the production of LLINs and have demonstrated superiority to pyrethroid only nets in areas with high pyrethroid resistance [5–9].

As new Dual AI LLINs are deployed widely, a renewed focus has been placed on the spatial and community effects exhibited by previous generations of LLINs and how these may impact future trial results [10–15]. A wealth of studies have shown a significant reduction of malaria cases and vector abundance following community distribution of LLINs [16–23]. While these community-level protective effects have become an essential element of malaria vector control measures in large-scale distribution campaigns, they can pose a complication in comparative intervention trials where the goal is to identify the protective effect that an intervention provides to communities in one trial arm, compared to communities allocated to another. In cluster-randomised control trials (cRCTs), where community ‘clusters’ from multiple trial arms can be geographically intermingled, the primary concern has become whether the community-level effects are spatially bound to their intervention clusters [10–15]. The WHO Vector Control Advisory Group (VCAG) guidance on the design of malaria vector control trials has recommended that trials build a buffer area around intervention clusters to prevent contamination [24], but there is very little empirical evidence to support a choice of buffer size.

In this study, we employ the semivariogram (hereinafter ‘variogram’) to describe the spatial form of LLIN intervention community effects on malaria infection and vector abundance, controlling for both statistical confounders and coincident spatial trends in the study area [25]. The variogram plots the dissimilarity of data points as a function of distance, providing a basis to fit candidate models that define a structure for the spatial form of the community effect [26]. By fitting variogram curves in concentrated areas of high sampling density for each of four separate LLIN products, we seek to establish explicit range estimates for the spatial effects of these interventions on malaria infection and vector abundance in northern Tanzania to inform more defined effect ranges for future trial buffer areas.

Methods

Setting

Misungwi is a district in the Mwanza region of Northwestern Tanzania. Home to just under half a million people [27], Misungwi encompasses 2400 square kilometres along the eastern shore of the Bay of Mwanza and contains a mix of rural and peri-urban villages. Many villages in the district are situated in close proximity to Lake Victoria, which provides a source of subsistence and economic activity, but also an increased risk of malaria [28]. The 2022 Tanzania census found that 48.2% (225337) of individuals in Misungwi district were under the age of 15 and these proportions were consistently higher in rural areas [27]. A 2018 sample of children under fifteen in Misungwi district found a malaria infection prevalence of 44.2% shortly following the long rainy season when malaria infection prevalence is expected to be highest [29].

The primary malaria vector species in the district is *Anopheles funestus* sensu lato (sl), with *An. gambiae* sensu stricto (ss) occupying small geographical pockets, most predominantly in the northern areas not under consideration in this study [30]. *Anopheles arabiensis* (part of the *An. gambiae* sl complex) is also present in the area but not substantially implicated in malaria transmission [30]. High levels of resistance to pyrethroids have been identified in *Anopheles* spp. in the study area, and both species composition and resistance profiles have demonstrated micro-scale geographic variation [31, 32].

Misungwi Dual AI LLIN Trial

This study was nested within a phase-III cluster-randomised malaria vector control trial to assess the efficacy of three novel LLIN formulations as compared to a standard pyrethroid only LLIN [33]. Key features and the primary trial results are described in detail elsewhere (ClinicalTrials.gov identifier: NCT03554616) [29, 33]. Briefly, the study evaluated the efficacy of three novel LLINs: Royal Guard® LN (pyriproxyfen 225mg/m² + alpha-cypermethrin 261mg/m²), Interceptor® G2 LN (200mg/m² chlorfenapyr + alpha-cypermethrin 100mg/m²), and Olyset™ Plus LN (piperonyl-butoxide (PBO) 400mg/m² + permethrin 800mg/m²) compared to a standard Interceptor® LN (alpha-cypermethrin 200mg/m²). The trial assessed malaria infection prevalence by malaria rapid diagnostic test (CareStart™ malaria rapid diagnostic test (mRDT) targeting detection of histidine-rich protein 2 (HRP2), DiaSys, Wokingham, UK) in 50 children aged 0.5–14 years over six cross-sectional surveys (at baseline and 12-, 18-, 24-, 30-, and 36-months post-intervention) in each of 84 trial clusters (86 at baseline) comprised of geographically proximal hamlets. In the current study, we analysed data from the 18-month post-intervention survey.

LLIN type and use were measured by self-report and confirmed by visual inspection of hanging nets by study enumerators. Entomological outcomes were assessed by single trap-night of vector species by Centers for Disease Control (CDC) miniature light traps in eight households per cluster every three months over the duration of the trial. Unsampled buffer areas were established around study clusters in accordance with VCAG guidelines on malaria vector control trials [24], with a minimum distance of 600m between each sampled household and any households in a separate trial cluster.

Outcome measures and covariates

The primary outcomes of interest for these analyses are malaria infection, defined as positive indication of infection with any *Plasmodium spp.* parasite by mRDT, and vector abundance, defined as total female *Anopheles spp.* mosquitoes collected by CDC miniature light trap during one trap night at each household location. Directly collected covariates of interest were identified by a survey of previously published literature [34–38] and include basic demographic characteristics for each child (age, sex, recent antimalarial treatment, and bednet use), household construction materials and potential points of vector ingress (number of doors and windows, eave construction, and window screening), head of household level of education, and durable household assets.

A complete data dictionary of variables and coded levels included in the analysis dataset can be found in Suppl 1.

Geographic data

Household coordinate locations were captured during census mapping by handheld global positioning device (Garmin Legend e-trex). Elevation, Normalised Difference Vegetation Index (NDVI), and Distance to Lake Victoria were derived from externally sourced geodata to provide additional contextual information relevant to malaria infection prevalence and vector abundance.

Elevation data was retrieved from the ALOS 3D World 30m resolution Digital Surface Model [39].

NDVI data for the region was retrieved from the United States Geological Survey Earth Resources Observation and Science Center Visible Infrared Imaging Radiometer Suite [40]. Ten-day overlapping average NDVI surfaces were compiled at 375m resolution and sampled to household points at five-day increments. NDVI values for the entomological model were calculated ten days prior to the household trap night and epidemiological values were calculated twenty days prior to the clinical sample date to account for mosquito and parasite development times [41].

Planar distance to Lake Victoria was computed for each household in the study area using the Near (Analysis) tool in ArcGIS Pro 3.2 (ESRI, Redlands, California) [42]. Measures were calculated in straight-line distance, irrespective of geographic features, to provide a uniform continuous measure of proximity to the lake. Exact boundary data for Lake Victoria were computed based on administrative boundaries retrieved from the GADM 4.1 database of global administrative areas [43]. All geographic data were projected into Africa Equidistant Conic (ESRI:102023) to most accurately preserve distance estimates in the analysis [44].

Epidemiological and entomological data collection

While the trial was appropriately powered to detect differences in the efficacy of the Dual AI LLINs [45], substantially more datapoints are required to produce robust variogram estimates, especially when anisotropic trends may be present [46]. To ensure an adequate sample for modelling the epidemiological

and entomological outcomes, we intensively oversampled four geographically-contiguous areas (hereafter referred to as ‘superclusters’), one for each trial arm, by combining adjacent trial clusters that happened to be randomly allocated to the same intervention arm (Fig. 1). Households in buffer areas were included in the oversample and all sampled households received randomly allocated trial nets in January of 2019.

Figure 1 Study area. Map showing the study site of the Misungwi Dual AI LLIN Trial and location on the southern shore of Lake Victoria. Supercluster areas are highlighted and inset maps show sampled household locations (saturated points) against the locations of unsampled households in the same supercluster area. Grey areas indicate trial clusters not used in this study and dark grey areas represent trial buffer areas. The dashed lines in Superclusters C and D show the boundaries where multiple trial clusters were joined into one Supercluster for the purposes of this study.

Following the standard trial sampling process, a total of 620 additional households (170 each from superclusters A and B, and 140 from C and D) were selected for oversampling from the four supercluster areas through a weighted random process during the cross-sectional survey conducted 18 months after net distribution (July-August 2020). To maintain a spatially uniform distribution for the sample within each supercluster, a proportional sample was selected based on the total number of households in the core and buffer areas. All households with at least one child under 15 were entered into a Python script using the ‘random.sample’ module [47]. Separate lists were used for each supercluster core/buffer arrangement. Previously selected households were included in the calculation of proportions and derived sample sizes but were excluded from the random selection process to prevent duplicates.

Due to a lower-than-expected number of households with eligible children in the supercluster oversample (83%), an additional 40 households were selected from each supercluster and sampled for epidemiological outcomes in early September. Data from the main study 18-month post intervention cross-sectional sample was merged with the oversample data to produce the final dataset for the analyses in this study. Entomological sampling was conducted only in the supercluster areas, between September and December 2020, using CDC light traps following the same methods as in the main trial. All households in the supercluster areas that consented to participate in epidemiology data collection were included in the entomology sample. Malaria vector species were identified morphologically as *An. funestus* sl or *An. gambiae* sl using an identification key [48].

Statistical analyses

Descriptive statistics

Descriptive statistics were computed for each variable under consideration using SAS 9.4 (SAS Institute, Cary, North Carolina). Categorical variables with small cell sizes were collapsed to improve model estimability. Cases with missing outcome, model covariate, or geographic data were removed. A relative wealth index for the study population was constructed from durable household assets and utility

features by principal components analysis using standard computation methods [49]. All variables, including outcomes, were examined for spatial autocorrelation by normalised inverse-distance weighted Moran's I [50].

Regression models

Residuals from a well-fit regression model indicate the remaining variability of an outcome after known factors have been taken into account (i.e., how much would the odds of malaria infection or vector abundance differ between sampling points if the influence of correlating factors were removed) [51]. These residuals are also a reflection of any unmeasured covariates which are related to the outcomes but are missing from the model. A variogram of regression model residuals therefore represents how the dissimilarity of those unexplained factors varies depending on the distance between sampling locations [26]. Unless somehow specifically modelled, any community effect present due to an intervention (or lack thereof) should be captured as variance in the model residuals. If the community effect has a spatial trend, as is expected from previous research, its form may be shown by a variogram of model residuals.

In order to investigate the spatial pattern of intervention community effects in this study, we therefore model variograms using residuals from a robust regression model [52]. We first construct regression models for malaria infection and for vector abundance to control for commonly identified confounding factors and mitigate the effects of any underlying spatial trends that may impact the variogram estimation.

A mixed-effects logistic regression model was computed in SAS 9.4 to evaluate the relationship between *Plasmodium spp.* infection in children and the identified characteristics of interest described above to control for potential confounding. Geographically derived model covariates measuring elevation, NDVI, and distance from Lake Victoria were included to capture the expected underlying first-order spatial trends relating to these factors, and sampling week was included to account for potential seasonal variation over the sampling period. Reported use of any LLIN the previous night by sampled children was included to account for the personal protective effect of the bednet [53]. Household-level random effects were included to control for clustering of sampled children within households, but trial clusters were not included to ensure the variance related to LLIN intervention community effects was captured in the model residuals and enable subsequent variogram estimation of their spatial structure.

The malaria vector abundance model was similarly determined with several key differences: vectors were modeled on a negative binomial distribution, child and behavioural characteristics were removed in favour of household construction characteristics more likely associated with vector abundance, and no random effects were included as only one trap night was conducted at each household location.

Randomised Quantile Residuals (RQRs) [54] were computed using the 'DHARMA' package in R to assess model fit [55]. Descriptive quantile-quantile (QQ) plots were produced for scaled ordinary and

randomised quantile residuals and additive quantile regressions were conducted on rank transformed model predictions for the 25, 50, and 75th quantiles using the 'qgam' package to identify under/overdispersion or heteroscedasticity in the models [56].

Variogram estimation

Ordinary residuals from the epidemiological and entomological models were used to estimate variograms of residual localised effects for malaria infection and malaria vector abundance, respectively [57], to provide a measure of the LLIN intervention effects at each household location. For each supercluster, initial omnidirectional variogram models were fit in SAS 9.4 using a robust fourth-root M-estimator [58] for calculation of semivariance to protect against outliers and limit the influence of distributional and sampling irregularities [59]. In the malaria infection variogram, two observations excessively skewed the distribution of the model residuals and were removed to improve model fit [60].

Variogram models under consideration in this study provide us with estimates for three parameters: the nugget, scale, and range (Fig. 2). The nugget defines the sampling dissimilarity at distance zero—effectively capturing the portion of the variogram model that is not defined by spatial separation. The scale, inversely, indicates the amount of dissimilarity that is defined only by the distance between sampling points. Finally, the range estimate is the distance of separation between sampling points at which the spatial form has reached the sill, a global dissimilarity beyond which pairs are spatially independent.

Figure 2 Variogram model forms Standardised representations of the variogram candidate models used in this study. All models presented have a parameterised nugget of 0.2, a scale of 0.8, and a range, or effective range, estimate of 4.0 based on model construction.

Variogram curves were fit by weighted sum of squared errors to exponential, gaussian, spherical, or sine wave effect model forms in SAS 9.4 [61]. Note that due to their asymptotic construction, the exponential and gaussian model range estimates are not directly comparable with other model parameters and must be scaled to an 'effective range' for approximate comparison [61].

Each omnidirectional variogram was assessed for both zonal and geometric anisotropic trends. Anisotropy is present when a spatial process is not uniform across all directions [62]. This angular dependence inhibits accurate construction of the spatial process in the omnidirectional model and requires further correction. To assess directionality, variograms were computed with 45-degree angle tolerances in each of 180 degrees using the same candidate model form that was selected in the omnidirectional analysis. Range estimates for each directional variogram were smoothed with a 10-point moving average and examined for the presence, and type, of anisotropy. Superclusters exhibiting zonal anisotropy were recomputed on their principal axis with one kilometre directional transects. Geometric anisotropy was corrected by reprojecting household coordinate locations into pseudo-isotropic space [26].

Final variograms are presented with parameter estimates and 95% confidence intervals, as well as details on the modelled forms and any anisotropic correction applied. Residual Nugget Effects (RNE) were computed for each variogram to evaluate the relative spatial impact of each model and expressed as a percentage to indicate the proportion of variation defined by the non-spatial process [63].

Results

Supercluster characteristics and sample population

Characteristics of the supercluster areas are described in Table 1. Supercluster B was the smallest cluster sampled by every measure recorded (3.84km², 3288 population). Supercluster C had the largest physical area (6.01km², 10466m sampled data distance) and population (6079), but Supercluster A had the highest household and population density (188.7 and 1044.6 per square kilometer, respectively). Superclusters B and C had comparable proportions of eligible households between the main- and over-samples, while A and D had lower ineligibilities in the oversample data. Supercluster D had the highest refusals in both samples (1.1% and 3.5%, respectively). Complete sampling details can be found in Suppl 2.

Table 1
Supercluster characteristics and sample population

Trial cluster ID(s)	Supercluster A	Supercluster B	Supercluster C	Supercluster D
	64	57	61,62	67,73
Intervention allocation	Py-PBO LLIN	Py-Chlorfenapyr LLIN	Pyrethroid-only LLIN	Py-Pyriproxyfen LLIN
Maximum sampled data distance in meters	7098	6947	10466	8155
Bounded census area in square kilometers	3.95	3.84	6.01	5.01
Households per square kilometer	188.7	128.7	175.1	180.4
Population per square kilometer	1044.6	856.9	1011.5	1026.6
Census population*	4124	3288	6079	5143
Census households with at least one child < 15*	745	494	1052	904
Total censused children < 15*	1954	1608	2966	2591
Target sample				
Main cross-sectional sample households	45	45	90	90
Oversample households (round 1)	170	170	140	140
Oversample households (round 2)	40	40	40	40
Total household sample target	255	255	270	270
Oversample entomology householdst	209	202	201	203
Sample population				
Households	206	193	200	200
Children	379	362	377	2065
Entomology households	204	193	195	197

Trial cluster ID(s)	Supercluster A	Supercluster B	Supercluster C	Supercluster D
	64	57	61,62	67,73
ID = Identification, LLIN = Long-Lasting Insecticidal Net. Py-PBO = Pyrethroid-Piperonyl Butoxide. Py-Chlorfenapyr = Pyrethroid-Chlorfenapyr. Py-Pyriproxyfen = Pyrethroid-Pyriproxyfen.				
*Trial census was conducted in 2018 and may not reflect exact age distributions at time of sample.				
†Entomology targeted only households that consented to the household survey.				

Table 1 **Supercluster characteristics and sample population**

Epidemiology sample characteristics

The final study sample comprised 5955 children from 3188 households in 84 clusters. A total of 2738 children (46.0%) tested positive for malaria infection by mRDT in the clinical sample (Table 2). Seven hundred and six children (11.9%) were treated with artemisinin-based combination therapy (ACT) in the two weeks prior to sampling and 4683 (78.6%) slept under a bed net the night prior to clinical sampling. Most household heads have a primary education (2249, 71.1%), with 22.1% of households having no formal parental education (n = 706). Just over a third (1167, 36.6%) of households have completely plastered walls, and 1988 (62.4%) have closed eaves. Only 208 households (6.5%) had animals sleeping inside.

Table 2

Characteristics of sampled children and households across intervention arms, 18-months post-intervention / N = 5955 children, 3188 households

Intervention allocation	Supercluster A	Supercluster B	Supercluster C	Supercluster D	All Other Clusters
	Py-PBO LLIN	Py-Chlorfenapyr LLIN	Pyrethroid-only LLIN	Py-Pyriproxyfen LLIN	*
Individual characteristics					
Malaria infection prevalence, positive mRDT	132/379 (35%)	143/362 (40%)	210/374 (56%)	188/377 (50%)	2065/4463 (46%)
Children aged 0.5–1 year old	41/379 (11%)	47/362 (13%)	56/374 (15%)	52/377 (14%)	525/4463 (12%)
Female	196/379 (52%)	198/362 (55%)	198/374 (53%)	183/377 (49%)	2220/4463 (50%)
Treated with ACT in the past two weeks	29/379 (8%)	20/362 (6%)	35/374 (9%)	41/377 (11%)	581/4463 (13%)
Slept under any bednet the previous night	290/379 (77%)	304/362 (84%)	330/374 (88%)	314/377 (83%)	3445/4463 (77%)
Household characteristics					
Households where the head of household has no formal education	44/206 (21%)	46/193 (24%)	42/200 (21%)	47/200 (24%)	527/2389 (22%)
Households with unplastered walls	52/206 (25%)	57/193 (30%)	61/200 (31%)	90/200 (45%)	939/2389 (39%)
Households with open eaves	32/206 (16%)	91/193 (47%)	57/200 (29%)	59/200 (30%)	961/2389 (40%)
Households where animals sleep inside the house	7/206 (3%)	18/193 (9%)	8/200 (4%)	8/200 (4%)	167/2389 (7%)
Households in the lowest wealth quintile	20/206 (10%)	53/193 (27%)	35/200 (18%)	40/200 (20%)	488/2389 (20%)
Median elevation, meters	1186 (1177–1196; 206)	1189 (1166–1216; 193)	1186 (1170–1211; 200)	1169 (1157–1184; 200)	1203 (1179–

Intervention allocation	Supercluster A	Supercluster B	Supercluster C	Supercluster D	All Other Clusters
	Py-PBO LLIN	Py-Chlorfenapyr LLIN	Pyrethroid-only LLIN	Py-Pyriproxyfen LLIN	*
above sea level (IQR; N)					1230; 2389)
Median distance to Lake Victoria, meters (IQR; N)	2190 (1626–2836; 206)	3135 (2755–3470; 193)	2792 (2346–4020; 200)	3260 (2113–4102; 200)	11003 (5446–15870; 2389)
Median week of mRDT sample collection (IQR; N)	33 (33–33; 206)	33 (33–33; 193)	33 (29–33; 200)	33 (30–33; 200)	31 (30–32; 2389)
Median NDVI, 20 days prior to mRDT sample (IQR; N)	0.42 (0.38–0.45; 206)	0.40 (0.37–0.43; 193)	0.42 (0.38–0.47; 200)	0.41 (0.39–0.45; 200)	0.45 (0.41–0.49; 2389)
Data are n/N (%), unless otherwise noted.					
LLIN = Long-Lasting Insecticidal Net. Py-PBO = Pyrethroid-Piperonyl Butoxide. Py-Chlorfenapyr = Pyrethroid-Chlorfenapyr. Py-Pyriproxyfen = Pyrethroid-Pyriproxyfen. mRDT = Malaria Rapid Diagnostic Test. NDVI = Normalised Difference Vegetation Index. ACT = Artemisinin-based Combination Therapy. IQR = Inter-quartile range.					
*Trial clusters were randomly allocated to each of the four presented intervention groups.					

Table 2 **Characteristics of sampled children and households across intervention arms, 18-months post-intervention** N = 5955 children, 3188 households

Entomology sample characteristics

A subset of 789 households was used to assess entomological outcomes in the supercluster areas only. In total, 3259 malaria vectors were captured across 789 household trap-nights. The vast majority of malaria vectors captured were *An. funestus* sl (80.8%), with *An. gambiae* sl comprising the remainder (Table 3). Some variation in species composition was noted across superclusters; 73.1% of malaria vectors identified in Supercluster B (Py-Chlorfenapyr LLIN) were *An. funestus* sl compared to 89.2% in Supercluster C (Pyrethroid-only LLIN). Sample households predominantly had improved walls (burnt brick or cement; 88.2%), completely plastered walls (55.9%), closed eaves (73.5%), and no window screens (69.2%). Only 63 (8.0%) households had animals sleeping inside. Trap nights largely did not coincide with heavy rain (2.3%) or strong winds (7.4%).

Table 3

Characteristics of entomology data collection and households across intervention arms, 18-months post-intervention / N = 3262 malaria vectors, 789 households

Intervention allocation	Supercluster A	Supercluster B	Supercluster C	Supercluster D
	Py-PBO LLIN	Py-Chlorfenapyr LLIN	Pyrethroid-only LLIN	Py-Pyriproxyfen LLIN
Entomology characteristics				
Malaria vector abundance, mean vectors per trap night (SD; N)	3.54 (6.2; 204)	3.84 (7.2; 193)	3.18 (6.5; 195)	5.96 (12.5; 197)
<i>Anopheles funestus</i> sl proportion	598/723 (83%)	544/744 (73%)	554/621 (89%)	937/1174 (80%)
Household characteristics				
Household with grass/leaves, mud, or unburnt brick walls	20/204 (10%)	26/193 (13%)	23/195 (12%)	24/197 (12%)
Households with unplastered walls	48/204 (24%)	53/193 (27%)	53/195 (27%)	70/197 (36%)
Households with open eaves	32/204 (16%)	74/193 (38%)	54/195 (28%)	49/197 (25%)
Number of doors (IQR; N)	1 (1–2; 204)	1 (1–2; 193)	1 (1–1; 195)	1 (1–2; 197)
Number of windows (IQR; N)	3 (2–4; 204)	3 (2–4; 193)	3 (2–3; 195)	3 (2–4; 197)
Households with no window screens	105/204 (51%)	149/193 (77%)	144/195 (74%)	148/197 (75%)
Households where animals sleep inside the house	7/204 (3%)	18/193 (9%)	8/195 (4%)	8/197 (4%)
Households that cook inside	12/204 (6%)	19/193 (10%)	11/195 (6%)	21/197 (11%)
Households in the lowest wealth quintile	20/204 (10%)	49/193 (25%)	34/195 (17%)	39/197 (20%)
Median elevation, meters above sea level (IQR; N)	1186 (1176–1196; 204)	1189 (1166–1216; 193)	1187 (1171–1212; 195)	1169 (1156–1176; 197)

Intervention allocation	Supercluster A	Supercluster B	Supercluster C	Supercluster D
	Py-PBO LLIN	Py-Chlorfenapyr LLIN	Pyrethroid-only LLIN	Py-Pyriproxyfen LLIN
Median distance to Lake Victoria, meters (IQR; N)	2208 (1636–2840; 204)	3149 (2768–3487; 193)	2792 (2342–4017; 195)	3260 (2105–4087; 197)
Median week of vector trap night (IQR; N)	45 (41–47; 204)	42 (41–46; 193)	44 (42–48; 195)	43 (41–47; 197)
Median NDVI, 10 days prior to vector trap night (IQR; N)	0.37 (0.33–0.46; 204)	0.35 (0.33–0.46; 193)	0.36 (0.32–0.45; 195)	0.38 (0.33–0.55; 197)
Proportion of households with light rain during trap night	47/204 (23%)	93/193 (48%)	56/195 (29%)	41/197 (21%)
Proportion of households with light wind during trap night	105/204 (51%)	98/193 (51%)	113/195 (58%)	100/197 (51%)
Data are n/N (%) or mean (SD), unless otherwise noted.				
LLIN = Long-Lasting Insecticidal Net. Py-PBO = Pyrethroid-Piperonyl Butoxide. Py-Chlorfenapyr = Pyrethroid-Chlorfenapyr. Py-Pyriproxyfen = Pyrethroid-Pyriproxyfen. SD = Standard Deviation. sl = <i>sensu lato</i> . NDVI = Normalised Difference Vegetation Index. IQR = Inter-quartile range.				

Table 3 **Characteristics of entomology data collection and households across intervention arms, 18-months post-intervention** N = 3262 malaria vectors, 789 households

Model residual diagnostics

Ordinary and randomised quantised model residuals from the mixed-effects logistic regression malaria infection and negative binomial vector abundance models are presented in Fig. 3. Ordinary residuals for both models show expected deviations from normality, given the non-normal distributions used in their construction. RQR values mapped much more closely to normality, with only the vector abundance model showing slight deviations. Five vector abundance model prediction values (0.6%) were outside of simulated parameters and the model shows some slight, but significant, undervaluing of the predicted 75th quantile regression. All data points in the malaria infection model were within expected values.

Figure 3 Residual diagnostic plots For all plots, dashed lines represent ideal locations for normally distributed data. In the third column, outlying model predictions are highlighted in orange and solid lines represent quantile regressions with shaded areas showing their 95% confidence intervals.

Variogram models

Final variogram models were plotted to visualise the spatial form of the malaria infection and vector abundance residuals in each supercluster area (Fig. 4). Two malaria infection residual models were best fit to exponential forms (Py-PBO LLIN, Pyrethroid-only LLIN), one vector abundance residual model was best fit to a spherical form (Pyrethroid-only LLIN), and all other malaria infection and vector abundance residual models were fit to sine hole effect forms. No final variogram model was best fit by a gaussian form in this study.

Figure 4 Variogram estimates Fitted variogram models of the residuals from malaria infection and vector abundance regression models (columns) for each supercluster area (rows). Point estimates show the lagged robust semivariance estimates for each distance class. Solid lines represent the best weighted sum of squared errors variogram model fit. Dashed lines and shaded areas show the modelled estimate and 95% confidence interval for variogram range effects. Dot-dash lines represent effective range estimates for models with asymptotic range constructions.

Variogram parameter estimates and confidence intervals, as well as any anisotropic correction applied, are presented in Table 4. Most variogram models required some form of anisotropic correction.

Table 4

Variogram parameter estimates for malaria infection and vector abundance model residuals

Py-PBO LLIN	Malaria Infection	Vector Abundance
Model form	Exponential	Sine Hole Effect
Anisotropic correction (degrees rotation; scale)	Zonal (0; 1.00:1)	Zonal (0; 1.00:1)
Nugget estimate, robust semivariance	1.14 (1.08–1.20)	0.57 (0.55–0.59)
Scale estimate, robust semivariance	1.64 (1.55–1.73)	0.49 (0.46–0.53)
Range estimate, meters	3132 (2643–3624)*	1444 (1366–1523)
RNE proportion	40.9 (38.4–43.6)	53.5 (50.8–56.3)
Py-Chlorfenapyr LLIN		
Model form	Sine Hole Effect	Sine Hole Effect
Anisotropic correction (degrees rotation; scale)	Zonal (45; 1.00:1)	None (0; 1.00:1)
Nugget estimate, robust semivariance	2.32 (2.27–2.37)	0.71 (0.71–0.71)
Scale estimate, robust semivariance	1.04 (0.96–1.12)	0.33 (0.00–0.68)
Range estimate, meters	2002 (1846–2158)	4085 (1216–6954)
RNE proportion	69.1 (67.0–71.2)	68.1 (50.9–100.0)
Pyrethroid-only LLIN		
Model form	Exponential	Spherical
Anisotropic correction (degrees rotation; scale)	None (0; 1.00:1)	Geometric (81; 1.54:1)
Nugget estimate, robust semivariance	2.74 (2.74–2.74)	0.36 (0.31–0.41)
Scale estimate, robust semivariance	0.36 (0.23–0.49)	0.79 (0.73–0.85)
Effective range estimate, meters	7833 (4413–11250)*	1379 (1211–1547)
RNE proportion	88.4 (84.8–92.4)	31.4 (26.7–36.0)
Py-Pyriproxyfen LLIN		
Model form	Sine Hole Effect	Sine Hole Effect
*Effective range estimate.		

Py-PBO LLIN	Malaria Infection	Vector Abundance
Anisotropic correction (degrees rotation; scale)	Geometric (163; 1.39:1)	Geometric (15; 1.38:1)
Nugget estimate, robust semivariance	2.65 (2.60–2.71)	0.83 (0.78–0.88)
Scale estimate, robust semivariance	0.26 (0.20–0.32)	0.51 (0.46–0.56)
Range estimate, meters	1452 (1360–1545)	1139 (1100–1178)
RNE proportion	91.0 (88.9–93.0)	61.9 (58.2–65.6)
Data are estimate (95%CI) unless otherwise noted.		
LLIN = Long-Lasting Insecticidal Net. Py-PBO = Pyrethroid-Piperonyl Butoxide. Py-Chlorfenapyr = Pyrethroid-Chlorfenapyr. Py-Pyriproxyfen = Pyrethroid-Pyriproxyfen. RNE = Residual Nugget Effect.		
*Effective range estimate.		

Table 4 Variogram parameter estimates for malaria infection and vector abundance model residuals

Variogram models of malaria infection residuals had consistently significant parameter estimates across all superclusters ($p < 0.0001$). Range estimates for the malaria infection models varied from 1452m (95% CI = 1360–1545) for Py-Pyriproxyfen LLIN, to 7833m (4413–11250) for Pyrethroid-only LLIN. The Py-PBO LLIN malaria infection model had a substantially lower nugget estimate at 1.14 (1.08–1.20) than other malaria models, which remained relatively consistent between 2.32 (2.27–2.37, Py-Chlorfenapyr LLIN) and 2.74 (2.74–2.74, Pyrethroid-only LLIN). Residual Nugget Effects were quite high in the Py-Pyriproxyfen LLIN (RNE = 91.0%, 95% CI = 88.9–93.0), Pyrethroid-only LLIN (88.4%, 84.9–92.4) and Py-Chlorfenapyr LLIN (69.1%, 67.0–71.2) models, suggesting a relatively small spatial effect. The Py-PBO LLIN model demonstrated a comparatively smaller RNE of 40.9% (38.4–43.6).

Parameter estimates for variogram models of vector abundance residuals were also largely significant ($p < 0.0001$), with the noted exception of the Py-Chlorfenapyr LLIN model scale parameter ($p = 0.0635$). Among the remaining models, range estimates varied from 1139m (1100–1178) for the Py-Pyriproxyfen LLIN to 1444 (1366–1523) for the Py-PBO LLIN. The Py-Chlorfenapyr LLIN range estimate was substantially greater than all other vector abundance model range estimates at 4085m but also had a dramatically larger confidence interval (1216–6954) than other models. Vector abundance nugget estimates were generally smaller than their residual malaria infection counterparts, with the exception of the Py-PBO LLIN, which was slightly higher (53.5%, 50.8–56.3). Residual Nugget Effects were notably lower in the Py-Pyriproxyfen LLIN (61.9%, 58.2–65.6) and Pyrethroid-only LLIN (31.4%, 26.7–36.0) vector abundance models. Due to the non-significant scale estimate for the Py-Chlorfenapyr LLIN vector abundance model, the RNE estimate suggests that this may be a purely non-spatial process (68.1%, 50.9–100.0).

Discussion

Summary of key findings

While VCAG guidance underscores the potential for intervention community effects to extend beyond cluster boundaries and cause contamination between trial arms, the exact form of these effects is not well enough understood to provide guidance on how large buffer areas should be to encapsulate these effects [24]. The results of this study describe the spatial signature of community, or mass effects, on malaria infection and vector abundance in four different LLIN intervention settings. Detectable community effects were present in most superclusters for both modelled outcomes with relatively consistent spatial distance signatures. Modelled range estimates in this study are largely clustered between 1–3km, with two notable exceptions. The malaria infection model for Supercluster C (Pyrethroid-only LLIN) and vector abundance model for Supercluster B (Py-Chlorfenapyr LLIN) had range estimates substantially in excess of three kilometres (7833m and 4085m, respectively).

Three variogram models had RNE confidence intervals crossing into the 90% range (100% in one case)—suggesting that these spatial processes are almost entirely negligible compared to the residual non-spatial variation in the modelled areas [63]. In the cases of the malaria infection models for Pyrethroid-only LLIN and Py-Pyriproxyfen LLIN, these are likely due to the relatively limited effectiveness of these LLIN interventions in the study area 18 months post-intervention [29]. The lower RNE estimates in the vector abundance models for these interventions suggests that the LLIN community effect on local vector populations is at least noticeable, even if it does not translate to a similar effect on malaria. These interventions were statistically indistinct in their impact on malaria and vector abundance in the study area—likely due to the limited sterilisation effect of pyriproxyfen on *An funestus* sl (24%)—which reinforce the similarities between these interventions in the present study [29, 32].

Most fitted omnidirectional variograms exhibited some non-monotonic properties (i.e., they demonstrated some periodicity rather than consistently increasing over the spatial process). While it is not uncommon practice to ignore the effects of these periodicities, they can be indicative of more complex anisotropic trends [64]. Our further analysis uncovered substantial zonal anisotropy in superclusters A (Py-PBO) and B (Py-Chlorfenapyr LLIN)—such that variogram range estimates were not estimable along entire axes. We additionally identified evidence of geometric anisotropy in superclusters C (Pyrethroid-only LLIN) and D (Py-Pyriproxyfen LLIN).

The presence of anisotropic trends is not inherently indicative of some form of directional process in the LLIN community effects—indeed, anisotropies are commonly present in spatial variables or even spatial point processes [65] and must simply be sufficiently corrected in order to develop accurate model variogram estimates [26]. Given that the suggested mechanisms of action that cause a community effect in LLIN interventions are not directionally-informed [53], it seems unlikely to suppose that directional effects present in these analyses are inherent to LLIN community effects but are rather statistical artefacts introduced by setting-specific elements of the current study.

One plausible explanation for the geometric anisotropy present in superclusters C and D is the advection effects of surface winds which can cause downwind dispersal of mosquito populations [66]. Surface winds in the study area exhibit a seasonal, diurnal pattern, with overnight surface winds predominantly originating in the South and South-East during the long dry season (June-August) and the North and East during the short rains (October-December) (Fig. 5) [67]. The relative alignment of the geometric anisotropy identified in the malaria infection and vector abundance residual models with the dominant overnight winds at their time of data collection suggests that these winds could be dispersing vector populations along the anisotropic angle—functionally stretching the LLIN community effect along this axis.

Figure 5 Comparison of seasonal overnight surface wind patterns in Misungwi District. Arrows represent the circular average overnight (18:00–06:00) hourly wind direction at 0.1° gridded locations. Hourly data on wind direction was obtained from the US National Centers for Environmental Information Integrated Surface Dataset for the 34 most proximal weather stations and interpolated by inverse-distance weighting in ArcGIS Pro 3.5 [68, 69]. Supercluster areas are highlighted.

The topographic characteristics of the supercluster areas may also have impacted the directionality of LLIN community effects in this study. Households in the superclusters are largely clustered along major transport corridors and the peripheries of river valleys. These locations provide economic opportunities—and relative protection from seasonal floodplains—but create a non-random distribution of household locations along directional transects. While this does not present a direct impact on the estimation of variograms for sampled data, studies have shown that mosquito dispersal may have intentional directional factors, especially anthrophilic vector species which may seek human settlements specifically in search of a bloodmeal [70]. The arrangement of households in the study area may have driven directionality in the host-seeking behaviour of vector species along directional axes.

The location of breeding sites in buffer areas may also play a substantive role in the presence of contamination effects between trial clusters, as dispersal ranges are likely to be centred around these locations [71], causing adjacent clusters to partially share vector populations. Early entomological studies of mosquito flight ranges found that female *An. gambiae* dispersed an average of 1.03km when released from central locations in a village, with those released in outlying areas flying about 50% further on average (1.58km) [72].

Comparison with other studies

The findings in these analyses are largely in agreement with other studies that have examined the spatial impact of LLIN interventions—although not in all contexts [16–23]. This study joins a host of previous efforts in attempting to directly quantify these community effects and establish spatial range estimates in cRCTs [73]. While early examinations of these effects were largely focused on establishing the existence of a community effect from vector control interventions [17–21], more recent studies have begun using advanced simulation and spatial models to make inference on the community effect ranges and their impact on trial design [10–12, 15]. These studies have provided crucial evidence on the spatial

nature of vector control interventions but have largely remained focused on the re-examination of single-intervention trials from a period where no comparator net was used in the analysis of intervention effects. The lack of any intervention as a comparator allows for a cleaner examination of the spatial intervention effects in the contexts examined but represents an impossible scenario in the context of modern trial design. Modern trial control interventions must meet current WHO standard of care for malaria prevention in the context under study [24].

Two early explorations of malaria vector control effect ranges in Kenya share notable similarities with our current study in both design and results. A 2003 study in Asembo, on the eastern shore of Lake Victoria, explored five malaria-related outcomes (clinical cases, anaemia, mortality, high parasitaemia, and haemoglobin), grouping households for analysis based on distance to the nearest discordant household in the study area—that is the nearest household not in the same intervention group [18]. The authors present a gradient of protection across 300m distance lags for each of these outcomes. They further found evidence of a community protective effect extending beyond cluster boundaries for high parasitaemia, anaemia, and haemoglobin at sufficient coverage levels, but only explored these effects within 300m of intervention compounds [18].

A 2000 study in Kilifi is more directly comparable in its construction of design. Households were categorised based on the estimated degree of bednet usage from households within increasing distance lags of 0.5km and assessed odds of hospital malaria admission in children by Cox proportional hazards models, controlling for two likely spatial confounding variables [19]. These analyses demonstrated a local reduction in for children in intervention zones extending 1.0-2.0km, even among a subset of children who were not issued an intervention net. The consistency of these distance measures is particularly notable in the Kilifi study, considering the differences in major vector populations in the region [74].

A previous study conducted by this team on the spatial effects of LLIN and Indoor Residual Spraying interventions used variograms to assess malaria infection data from a malaria vector control cRCT, four months post-intervention in a comparable setting [14]. This study found slightly shorter effective range distances for LLIN interventions on malaria infection (Median; IQR = 1168m; 829–1504), but did not have the data density required to examine vector populations [14]. The longer malaria infection model effective range estimates in our current study could be due to a number of factors; the most likely being some combination of a smaller number of sampling areas and a later sampling period post-intervention.

Strengths and limitations

Developing clear spatial range estimates for the community effects of LLIN interventions is essential for the design of future cluster-randomised vector control trials and may have implications for the roll-out of LLIN distribution campaigns. In particular, modelling the spatial effects of LLIN interventions is crucial to establish guidance and control for contamination between clusters in future trial designs [24]. In this study, we have intensively collected data to examine the spatial impact on malaria vector abundance and malaria infection for each of four types of LLINs currently recommended in sub-Saharan Africa for

malaria control. The development of variogram models for both malaria infection and vector abundance has allowed us to examine the localised impact of each LLIN intervention by deriving estimates for the variability of entomological and epidemiological outcomes at small spatial scales, the amount that the intervention effects reduce the variability over distance, and—most importantly for this analysis—established clear spatial range estimates for the impact of each LLIN intervention in the context of a modern cRCT.

The timing of this analysis has some substantive implications for the interpretation of the results. Generally, LLINs are expected to wane in protective efficacy over their lifespan, due to a combination of physical integrity and degradation of the insecticide [75, 76]. Samples in this study were taken at the 18-month post-intervention cross-sectional survey, after which a reasonable decay of LLIN efficacy is to be expected. Furthermore, the initial survey was intended to be completed in June of 2020, just following the major rains in the region, and during a period of high expected vector activity (and subsequently, high expected malaria infection) [77]. Unfortunately, COVID-19 interruptions in 2020 necessitated the delay of data collection during this time, resulting in epidemiological outcomes being assessed during the dry season (July-September) and the entomological data collection continuing into December. Both of these timing concerns are limiting on the effect estimates presented in this analysis—lower LLIN efficacy and lower expected outcome events in both models. It would be prudent to assume that the spatial effects of these interventions would be stronger in the early stages of LLIN deployment, and during peak periods of malaria and vector activity.

Of key importance in the interpretation of the presented variogram estimations is the limited sample of trialed intervention clusters. In order to establish sufficient comparability between clusters in the main study which targeted comparative intervention effects, up to two children in 30 random households from each of 84 clusters were sampled in each of four cross-sectional surveys over a period of two years [29]. While substantially more households were recruited in the supercluster oversample to establish the necessary spatial density of data for variogram analyses, only six study clusters were included in this intensive sampling. As comparative power increases only marginally through increasing cluster sizes [78], this study was not powered to make explicit statistical comparisons between intervention group ranges. Care should be taken in directly comparing the trialed interventions.

The design of this study does not allow for the complete disaggregation of the effect of interventions from any random error that may be introduced at the cluster level by unknown factors. While we have taken great care to include a robust set of likely spatial confounding covariates, unmeasured spatially trending factors (e.g., mosquito breeding sites, insecticide resistance, etc.) likely contribute to some of the spatial signal presented in these analyses. The inherent statistical impacts from the inclusion of cluster hierarchy on within-cluster variation would likely eliminate any spatial structure for variogram estimation. Previous research using a variation of this method found similar results in a setting with distinct geographic, cultural, and entomological characteristics [14], supporting the use of these outcome measures as intervention effects.

Finally, Supercluster B (Py-Chlorfenapyr LLIN) appeared to be exhibiting some form of spatial nonstationarity that was not adequately controlled for—creating difficulty in fitting an adequate variogram to the semivariance estimates [79]. The malaria infection model was, at least somewhat, corrected by assessing the data along a single anisotropic transect—consistent with the assumption of zonal anisotropy. Unlike supercluster A (Py-PBO LLIN), where the same zonal anisotropic trend was identified in both the malaria infection and vector abundance models, the vector abundance model for supercluster B appears largely indistinct between the omnidirectional and zonal anisotropic models. Whether this is due to the nature of the intervention, or some factor outside the variables considered in this analysis is unclear. The presence of some unknown, spatially-trending confounding factor could introduce non-stationarity uncontrolled by the regression model. The high distance estimate suggests a range consistent with our expectations of the Py-Chlorfenapyr LLIN intervention, given the performance of the net in the PAMVERC Misungwi Dual AI LLIN trial [29], but the large confidence interval makes it challenging to make confident statements on the exact range of the spatial effect.

Implications for research and practice

The leading theoretical basis for a community effect in single-pyrethroid LLIN interventions is rooted in reducing the vectorial capacity of mosquitoes through mass-killing or induced dispersal of vector populations [53]. This theory relies heavily on the flight ranges of local vector populations—especially over limited time scales—as the reduction in vector populations from such an effect should only be detectable with respect to an expected population dispersion. Extended time scales may allow for more distant impacts on vector populations—but only if mass-killing is not the primary mechanism of action supporting the effect. Mosquitoes need to come into direct contact with an LLIN to be subject to pyrethroid- or chlorfenapyr-induced mortality, meaning that any immediate reduction in vector populations due to the mass-killing of mosquitoes could only exist within the flight range of the vectors in question. Our study found lower vector densities per trap night than a pre-intervention study in the same area (4.13 vs 8.04) [30], and a complete analysis of the comparative effect of LLIN intervention arms in the area supports a major reduction in vector populations—especially in the Py-Chlorfenapyr LLIN group [32].

While numerous studies have attempted to quantify the dispersal ranges of mosquito species directly through mosquito mark-release-recapture (MMRR) methods [71, 72, 80], precise data on *Anopheles* species dispersal ranges remains limited. An effort to compile the diverse array of MMRR studies globally found 800 studies from 161 sources—only 12 of which reported recapture distances for female *Anopheles spp.* mosquitoes (Mean; SD = 1323.3m; 1587.8), Median; IQR = 500m; 250–1751) [81]. Although limited in quantity, these distance estimates align with our findings—supporting the theory that community effects will be at least somewhat bounded by mosquito dispersal patterns.

The consistently larger nugget estimates in the malaria infection models is in alignment with expectations given the malaria vector populations must serve as a mediating factor between the LLIN interventions and malaria infection. Factors driving malaria infection must therefore include the local entomological indices—and any associated factors driving the same. Further to this, true measurement

errors are more likely to exist in the quantification of malaria infection—previous studies in comparable settings show approximately 90% specificity for HRP2 detection by mRDT [82, 83] which is likely contributing to higher nugget effects in the malaria models [84].

Variogram models can be highly site-specific and may have factors that are not indicative of other areas—especially given the large presence of pyrethroid resistance in the current study [30, 31]. Exact model forms and anisotropic trends are unlikely to be identical across diverse study areas, but the relative consistency of range estimates in alignment with the theoretical underpinnings of LLIN intervention community effects suggests that these ranges are likely to be generalisable to most areas with similar vector species compositions [53].

While this study is not equipped to make representative comparisons of intervention arms, the presence of estimable community effects on malaria infection in the Py-PBO LLIN (RNE = 40.9%) and Py-Chlorfenapyr LLIN (69.1%) models is in relative alignment with the performance of these LLIN interventions—although the effects of the Py-PBO LLIN were declining at this point in the study area [29]. A study of resistance profiles in the area suggests that pyrethroid and Py-PBO nets contributed to increased insecticide resistance over their deployment [31], theoretically accelerating this decline in efficacy. Future studies estimating variogram ranges should consider examining the impact of declining LLIN efficacy on community effects over time.

Conclusions

This study computed robust anisotropically-corrected variogram models to describe the spatial structure of community intervention effects on malaria infection and vector abundance from four different LLIN interventions, 18 months post-intervention. In our analyses, all variogram range estimates exceed the buffer sizes established for the PAMVERC Misungwi Dual AI LLIN trial analysis—indeed far exceeded in some cases [33]. This would infer the presence of some degree of contamination effect between trial intervention clusters that could potentially bias comparative analyses of trial arms to the null. While some suggestion as to the amount of contamination can be gleaned from the scale parameters for each variogram model, the exact impact on between-group differences would require interpolated estimates of the model forms across the study area and will be the subject of future study. Modelled community effect range estimates generally aligned with expected mosquito dispersal ranges. This agreement with the current leading theoretical basis for LLIN community effect interventions [53] suggests a greater emphasis should be placed on understanding the dynamics of local vector populations in the design of future malaria vector control trials.

Abbreviations

ACT

Artemisinin-based combination therapy

AIRR

Adjusted Incidence Rate Ratio
AOR
Adjusted Odds Ratio
CDC
Centers for Disease Control
CI
Confidence Interval
cRCT
Cluster-randomised control trial
Dual AI
Dual active-ingredient
HRP2
Histidine-rich protein 2
IQR
Inter-Quartile Range
LLIN
Long-lasting insecticidal net
MMRR
Mosquito mark-release-recapture
mRDT
Malaria rapid diagnostic test
NDVI
Normalised Difference Vegetation Index
PAMVERC
Pan-African Malaria Vector Research Consortium
PBO
Piperonyl-butoxide
Py-Chlorfenapyr
Pyrethroid and Chlorfenapyr
Py-PBO
Pyrethroid and Piperonyl Butoxide
Py-Pyriproxyfen
Pyrethroid and Pyriproxyfen
QQ
Quantile-quantile
RNE
Residual Nugget Effect
RQR
Randomised Quantile Residuals
SD

Standard Deviation

sl

sensu lato

ss

sensu stricto

UK

United Kingdom

VCAG

Vector Control Advisory Group

WHO

World Health Organization

Declarations

Ethics approval and consent to participate

Approval for this study was granted by the University of Ottawa Office of Research Ethics and Integrity (File #H-05-19-4411).

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Funding

for this study was awarded to Dr. Protopopoff by the United Kingdom Research and Innovation Medical Research Council Joint Global Health Trials Scheme (grant #: MR/R006040/1). The funding source for this study had no involvement in the study design, data collection, analysis, interpretation, development of the manuscript, or the decision to publish.

Author Contribution

CT, JFM, NP, and MAK conceptualised the study and constructed the methods of analysis. JFM, EL, NM, EM, JM, and NP conducted data collection. CT, EL, NM, and EM curated the data. CT analysed the data and produced the first draft of the manuscript and figures. JFM, CF, MT, NP, and MAK critically evaluated the analysis methods and provided revisions for the first draft of the manuscript. CT, JFM, EL, NM, EM,

JM, AM, CF, IK, FWM, MR, MT, NP, and MAK revised the manuscript. All authors reviewed and approved the manuscript prior to publication. CT, MAK, and NP accessed and verified the data used for these analyses and all authors had access to the data used in the study.

Acknowledgement

The authors of this study are deeply grateful to the people of Misungwi, for welcoming our trial team into their community and homes, and to the field teams, for the grueling effort required to collect and process such a large oversample in a short timeframe. We would also like to express our gratitude to the United Kingdom Research and Innovation Medical Research Council Joint Global Health Trials Scheme for providing the funding for this study.

Data Availability

The datasets used in these analyses are held and managed by the Pan African Malaria Vector Ecology Research Consortium (info@pamverc.or.tz). Suppl 1 provides a summary of the dataset that can be made available to researchers. Requests should be accompanied by a detailed analysis plan and approval from a respected Research Ethics Board.

References

1. World malaria report. 2023. Geneva: World Health Organization; 2023 Nov. p. 283. Report No.
2. Kleinschmidt I, Bradley J, Knox TB, Mnzava AP, Kafy HT, Mbogo C, et al. Implications of insecticide resistance for malaria vector control with long-lasting insecticidal nets: a WHO-coordinated, prospective, international, observational cohort study. *Lancet Infect Dis*. 2018;18(6):640–9. 10.1016/S1473-3099(18)30172-5.
3. World Health Organization. WHO guidelines for malaria, 16 October 2023 [Technical documents] [Internet]. World Health Organization. 2023 Oct. p. 396. Report No.: WHO/UCN/GMP/ 2023.01 Rev.1. Available from: <https://www.who.int/publications/i/item/guidelines-for-malaria>
4. Global Partnership to Roll Back Malaria, editor. Insecticide-treated mosquito net interventions: a manual for national control programme managers. Geneva: World Health Organization; 2003. 114 p.
5. Accrombessi M, Cook J, Dangbenon E, Yovogan B, Akpovi H, Sovi A, et al. Efficacy of pyriproxyfen-pyrethroid long-lasting insecticidal nets (LLINs) and chlorfenapyr-pyrethroid LLINs compared with pyrethroid-only LLINs for malaria control in Benin: a cluster-randomised, superiority trial. *Lancet*. 2023;401(10375):435–46. 10.1016/S0140-6736(. 22)02319-4 PubMed PMID: 36706778.
6. Ngufor C, N'Guessan R, Fagbohoun J, Odjo A, Malone D, Akogbeto M, et al. Olyset Duo® (a Pyriproxyfen and Permethrin Mixture Net): An Experimental Hut Trial against Pyrethroid Resistant *Anopheles gambiae* and *Culex quinquefasciatus* in Southern Benin. *PLoS ONE*. 2014;9(4):e93603. 10.1371/journal.pone.0093603.

7. Protopopoff N, Mosha JF, Messenger LA, Lukole E, Charlwood JD, Wright A, et al. Effectiveness of piperonyl butoxide and pyrethroid-treated long-lasting insecticidal nets (LLINs) versus pyrethroid-only LLINs with and without indoor residual spray against malaria infection: third year results of a cluster, randomised controlled, two-by-two factorial design trial in Tanzania. *Malar J*. 2023;22(1):294. 10.1186/s12936-023-04727-8.
8. Mosha JF, Matowo NS, Kulkarni MA, Messenger LA, Lukole E, Mallya E, et al. Effectiveness of long-lasting insecticidal nets with pyriproxyfen–pyrethroid, chlorfenapyr–pyrethroid, or piperonyl butoxide–pyrethroid versus pyrethroid only against malaria in Tanzania: final-year results of a four-arm, single-blind, cluster-randomised trial. *Lancet Infect Dis*. 2024;24(1):87–97. 10.1016/S1473-3099(. 23)00420-6 PubMed PMID: 37776879.
9. Gleave K, Lissenden N, Chaplin M, Choi L, Ranson H. Piperonyl butoxide (PBO) combined with pyrethroids in insecticide-treated nets to prevent malaria in Africa. *Cochrane Database Syst Reviews*. 2021;510.1002/14651858.CD012776.pub3.
10. Silkey M, Homan T, Maire N, Hiscox A, Mukabana R, Takken W, et al. Design of trials for interrupting the transmission of endemic pathogens. *Trials*. 2016;17(1):278. 10.1186/s13063-016-1378-1.
11. Jarvis CI, Multerer L, Lewis D, Binka F, Edmunds WJ, Alexander N et al. Spatial Effects of Permethrin-Impregnated Bed Nets on Child Mortality: 26 Years on, a Spatial Reanalysis of a Cluster Randomized Trial [Internet]. 2019 Dec 4. 10.4269/ajtmh.19-0111
12. Multerer L, Glass TR, Vanobberghen F, Smith T. Analysis of contamination in cluster randomized trials of malaria interventions. *Trials*. 2021;22(1):613. 10.1186/s13063-021-05543-8.
13. Benjamin-Chung J, Li H, Nguyen A, Barratt Heitmann G, Bennett A, Ntuku H, et al. Extension of efficacy range for targeted malaria-elimination interventions due to spillover effects. *Nat Med*. 2024;30(10):2813–20. 10.1038/s41591-024-03134-z.
14. Thickstun C, Lukole E, Mosha JF, Manjurano A, Kleinschmidt I, Mosha FW, et al. Inter-cluster contamination: a semivariance analysis of community effect ranges of malaria vector control interventions in a four-armed malaria trial in Muleba, Tanzania. *Malar J*. 2025;24(1):1. 10.1186/s12936-025-05438-y.
15. Multerer L, Vanobberghen F, Glass TR, Hiscox A, Lindsay SW, Takken W, et al. Estimating intervention effectiveness in trials of malaria interventions with contamination. *Malar J*. 2021;20(1):1. 10.1186/s12936-021-03924-7.
16. Komazawa O, Kaneko S, K’Opiyo J, Kiche I, Wanyua S, Shimada M, et al. Are Long-Lasting Insecticidal Nets Effective for Preventing Childhood Deaths among Non-Net Users? A Community-Based Cohort Study in Western Kenya. *PLoS ONE*. 2012;7(11):e49604. 10.1371/journal.pone.0049604.
17. Gimnig JE, Kolczak MS, Hightower AW, Vulule JM, Schoute E, Kamau L, et al. Effect of permethrin-treated bed nets on the spatial distribution of malaria vectors in western Kenya. *Am J Trop Med Hyg*. 2003;68(4suppl):115–20. 10.4269/ajtmh.2003.68.115.

18. Hawley WA, Phillips-Howard PA, Kuile FOT, Terlouw DJ, Vulule JM, Ombok M, et al. Community-wide effects of permethrin-treated bed nets on child mortality and malaria morbidity in western Kenya. *Am J Trop Med Hyg.* 2003;68(4suppl):121–7. 10.4269/ajtmh.2003.68.121.
19. Howard SC, Omumbo J, Nevill C, Some ES, Donnelly CA, Snow RW. Evidence for a mass community effect of insecticide-treated bednets on the incidence of malaria on the Kenyan coast. *Trans R Soc Trop Med Hyg.* 2000;94(4):357–60. 10.1016/S0035-9203(00)90103-2.
20. Maxwell CA, Msuya E, Sudi M, Njunwa KJ, Carneiro IA, Curtis CF. Effect of community-wide use of insecticide-treated nets for 3–4 years on malarial morbidity in Tanzania. *Tropical Med Int Health.* 2002;7(12):1003–8. 10.1046/j.1365-3156.2002.00966.x.
21. Binka FN, Indome F, Smith T. Impact of spatial distribution of permethrin-impregnated bed nets on child mortality in rural northern Ghana. *Am J Trop Med Hyg.* 1998;59(1):80–5. 10.4269/ajtmh.1998.59.80 PubMed PMID: 9684633.
22. Escamilla V, Alker A, Dandolo L, Juliano JJ, Miller WC, Kamthuzza P, et al. Effects of community-level bed net coverage on malaria morbidity in Lilongwe, Malawi. *Malar J.* 2017;16(1):142. 10.1186/s12936-017-1767-2.
23. Malvisi L, Troisi CL, Selwyn BJ. Analysis of the spatial and temporal distribution of malaria in an area of Northern Guatemala with seasonal malaria transmission. *Parasitol Res.* 2018;117(9):2807–22. 10.1007/s00436-018-5968-6.
24. VCAG. How to design vector control efficacy trials: Guidance on phase III vector control field trial design provided by the Vector Control Advisory Group. Geneva: World Health Organization, Vector Control Advisory Group; 2017. pp. 1–62.
25. Matheron G. Principles of geostatistics. *Econ Geol.* 1963;58(8):1246–66. 10.2113/gsecongeo.58.8.1246.
26. Diggle P, Ribeiro PJ. *Model-based Geostatistics.* Springer; 2007. p. 242.
27. Tanzania National Bureau of Statistics. 2022 Population and Housing Census - Administrative units Population Distribution and Age and Sex Distribution Reports [Internet]. Tanzania; 2022 Dec. Report No. Available from: <https://www.nbs.go.tz/index.php/en/census-surveys/population-and-housing-census/852-2022-population-and-housing-census-administrative-units-population-distribution-and-age-sex-reports>
28. Duguay C, Mosha JF, Lukole E, Mangalu D, Thickstun C, Mallya E, et al. Assessing risk factors for malaria and schistosomiasis among children in Misungwi, Tanzania, an area of co-endemicity: A mixed methods study. *PLOS Global Public Health.* 2023;3(11):e0002468. 10.1371/journal.pgph.0002468.
29. Mosha JF, Kulkarni MA, Lukole E, Matowo NS, Pitt C, Messenger LA, et al. Effectiveness and cost-effectiveness against malaria of three types of dual-active-ingredient long-lasting insecticidal nets (LLINs) compared with pyrethroid-only LLINs in Tanzania: a four-arm, cluster-randomised trial. *Lancet.* 2022;399(10331):1227–41. 10.1016/S0140-6736(21)02499-5.

30. Matowo NS, Martin J, Kulkarni MA, Mosha JF, Lukole E, Isaya G, et al. An increasing role of pyrethroid-resistant *Anopheles funestus* in malaria transmission in the Lake Zone. *Tanzan Sci Rep*. 2021;11(1):1. 10.1038/s41598-021-92741-8.
31. Messenger LA, Matowo NS, Cross CL, Jumanne M, Portwood NM, Martin J, et al. Effects of next-generation, dual-active-ingredient, long-lasting insecticidal net deployment on insecticide resistance in malaria vectors in Tanzania: an analysis of a 3-year, cluster-randomised controlled trial. *Lancet Planet Health*. 2023;7(8):e673–83. 10.1016/S2542-5196(. 23)00137-7 PubMed PMID: 37558348.
32. Matowo NS, Kulkarni MA, Messenger LA, Jumanne M, Martin J, Mallya E, et al. Differential impact of dual-active ingredient long-lasting insecticidal nets on primary malaria vectors: a secondary analysis of a 3-year, single-blind, cluster-randomised controlled trial in rural Tanzania. *Lancet Planet Health*. 2023;7(5):e370–80. 10.1016/S2542-5196(. 23)00048-7 PubMed PMID: 37164513.
33. Mosha JF, Kulkarni MA, Messenger LA, Rowland M, Matowo N, Pitt C, et al. Protocol for a four parallel-arm, single-blind, cluster-randomised trial to assess the effectiveness of three types of dual active ingredient treated nets compared to pyrethroid-only long-lasting insecticidal nets to prevent malaria transmitted by pyrethroid insecticide-resistant vector mosquitoes in Tanzania. *BMJ Open*. 2021;11(3):e046664. 10.1136/bmjopen-2020-046664.
34. Kibondo UA, Renju J, Lukole E, Mosha JF, Mosha FW, Manjurano A, et al. Factors associated with malaria infection among children after distribution of PBO-pyrethroid synergist-treated nets and indoor residual spraying in north-western Tanzania. *PLoS ONE*. 2023;18(12):e0295800. 10.1371/journal.pone.0295800.
35. Mosha JF, Lukole E, Charlwood JD, Wright A, Rowland M, Bullock O, et al. Risk factors for malaria infection prevalence and household vector density between mass distribution campaigns of long-lasting insecticidal nets in North-western Tanzania. *Malar J*. 2020;19(1):297. 10.1186/s12936-020-03369-4.
36. West PA, Protopopoff N, Rowland M, Cumming E, Rand A, Drakeley C, et al. Malaria Risk Factors in North West Tanzania: The Effect of Spraying, Nets and Wealth. *PLoS ONE*. 2013;8(6):e65787. 10.1371/journal.pone.0065787.
37. Bousema T, Drakeley C. Determinants of Malaria Transmission at the Population Level. *Cold Spring Harb Perspect Med*. 2017;7(12):a025510. 10.1101. /cshperspect.a025510 PubMed PMID: 28242786; PubMed Central PMCID: PMC5710096.
38. Accrombessi M, Akogbeto MC, Dangbenon E, Akpovi H, Sovi A, Yovogan B, et al. Malaria Burden and Associated Risk Factors in an Area of Pyrethroid-Resistant Vectors in Southern Benin. *Am J Trop Med Hyg*. 2022;107(3):681–8. 10.4269/ajtmh.22-0190. PubMed PMID: 35895353; PubMed Central PMCID: PMC9490648.
39. JAXA. ALOS Global Digital Surface Model ALOS World 3D – 30m (AW3D30) [Digital Surface Model] [GeoTIFF]. [cited 2024 Jan 10]. Available from: https://www.eorc.jaxa.jp/ALOS/en/dataset/aw3d30/aw3d30_e.htm

40. U.S. Geological Survey (USGS) Earth Resources Observation And Science (EROS) Center. eVIIRS NDVI [Jpg,tif]. U.S. Geological Survey; 2021 [cited 2024 Jan 10]. Available from: <https://www.usgs.gov/centers/eros/science/usgs-eros-archive-vegetation-monitoring-eros-visible-infrared-imaging> 10.5066/P9Q3B2A7
41. Rossati A, Bargiacchi O, Kroumova V, Zaramella M, Caputo A, Garavelli PL. Climate, environment and transmission of malaria. *Infez Med*. 2016;24(2):93–104. PubMed PMID: 27367318.
42. Near. (Analysis)—ArcGIS Pro | Documentation [Internet]. [cited 2021 Dec 1]. Available from: <https://pro.arcgis.com/en/pro-app/latest/tool-reference/analysis/near.htm>
43. GADM [Internet]. [cited 2021 Dec 1]. Available from: <https://gadm.org/>
44. Kessler F, Battersby S. *Working with Map Projections: A Guide to their Selection*. Boca Raton: CRC; 2019. p. 317. 10.1201/9780203731413.
45. Hayes RJ, Moulton LH. *Cluster randomised trials*. Second edition. Boca Raton: CRC Press; 2017. 397 p. (Chapman & hall/crc biostatistics series).
46. Webster R, Oliver MA. Sample adequately to estimate variograms of soil properties. *J Soil Sci*. 1992;43(1):177–92. <https://doi.org/10.1111/j.1365-2389.1992.tb00128.x>.
47. random — Generate pseudo-random numbers — Python 3.9.2 documentation [Internet]. [cited 2021 Mar 21]. Available from: <https://docs.python.org/3/library/random.html>
48. Coetzee M. Key to the females of Afrotropical Anopheles mosquitoes (Diptera: Culicidae). *Malar J*. 2020;19(1):1–20. 10.1186/s12936-020-3144-9.
49. Vyas S, Kumaranayake L. Constructing socio-economic status indices: how to use principal components analysis. *Health Policy Plann*. 2006;21(6):459–68. 10.1093/heapol/czl029.
50. Moran PAP. Notes on Continuous Stochastic Phenomena. *Biometrika*. 1950;37(1/2):17–23. 10.2307/2332142.
51. Hoaglin DC, Mosteller F, Tukey JW, editors. *Understanding robust and exploratory data analysis*. Wiley classics library ed. New York: Wiley; 2000. p. 447. (Wiley classics library).
52. Banerjee S, Carlin BP, Gelfand AE. *Hierarchical modeling and analysis for spatial data*. Second edition. Boca Raton: CRC Press, Taylor & Francis Group; 2015. 562 p. (Monographs on statistics and applied probability; no. 135).
53. Lines J, Chitnis N, Paintain L. How insecticide-treated nets (ITNs) work: The biological mechanisms by which ITNs give personal- and community-level protection against malaria [Internet]. Zenodo; 2022 Mar [cited 2024 Jul 10]. Report No. Available from: <https://zenodo.org/records/6393253> 10.5281/zenodo.6393253
54. Dunn PK, Smyth GK. Randomized Quantile Residuals. *J Comput Graphical Stat*. 1996;5(3):236–44. 10.1080/10618600.1996.10474708.
55. Hartig F, Lohse L, leite M, de DHARMa S. Residual Diagnostics for Hierarchical (Multi-Level / Mixed) Regression Models [Internet]. 2024 [cited 2025 Jul 7]. Available from: <https://cran.r-project.org/web/packages/DHARMa/index.html>

56. Fasiolo M, Griffiths B, Wood SN, Zaffran M, Goude Y, Nedellec R. qgam: Smooth Additive Quantile Regression Models [Internet]. 2025 [cited 2025 Jul 8]. Available from: <https://cran.r-project.org/web/packages/qgam/index.html>
57. Cressie NAC. Statistics for spatial data. Revised edition. New York: John Wiley & Sons, Inc; 2015. 900 p.
58. Cressie N, Hawkins DM. Robust estimation of the variogram: I. Math Geol. 1980;12(2):115–25. 10.1007/BF01035243.
59. Omre H. The Variogram and its Estimation. In: Verly G, David M, Journel AG, Marechal A, editors. Geostatistics for Natural Resources Characterization: Part 1 [Internet]. Dordrecht: Springer Netherlands; 1984 [cited 2024 Jun 4]. pp. 107–25. Available from: https://doi.org/10.1007/978-94-009-3699-7_7 doi:10.1007/978-94-009-3699-7_7.
60. Krivoruchko K. Spatial statistical data analysis for GIS users. Redlands, Calif. Esri; 2011.
61. SAS. SAS/STAT® 13.2 User's Guide. SAS Institute Inc; 2014.
62. Journel AG, Huijbregts CJ. Mining geostatistics. New York: Academic Press;; London; 1978. p. 600.
63. Trangmar BB, Yost RS, Uehara G. Application of Geostatistics to Spatial Studies of Soil Properties. In: Brady NC, editor. Advances in Agronomy [Internet]. Academic Press; 1986 [cited 2024 Jun 2]. pp. 45–94. Available from: <https://www.sciencedirect.com/science/article/pii/S0065211308606732> 10.1016/S0065-2113(08)60673-2
64. Journel AG, Froidevaux R. Anisotropic hole-effect modeling. Math Geol. 1982;14(3):217–39. 10.1007/BF01032885.
65. Rajala T, Redenbach C, Särkkä A, Sormani M. A review on anisotropy analysis of spatial point patterns. Spat Stat. 2018;28:141–68. 10.1016/j.spasta.2018.04.005. One world, one health.
66. Endo N, Eltahir EAB. Modelling and observing the role of wind in Anopheles population dynamics around a reservoir. Malar J. 2018;17(1):48. 10.1186/s12936-018-2197-5.
67. Nicholson SE, Hartman AT, Klotter DA. On the Diurnal Cycle of Rainfall and Convection over Lake Victoria and Its Catchment. Part II: Meteorological Factors in the Diurnal and Seasonal Cycles [Internet]. 2021 Nov 1. 10.1175/JHM-D-21-0085.1
68. National Centers for Environmental Information (NCEI) [Internet]. 2021 [cited 2025 May 8]. Global Hourly - Integrated Surface Database (ISD). Available from: <https://www.ncei.noaa.gov/products/land-based-station/integrated-surface-database>
69. Lott JN, Baldwin R. The FCC Integrated Surface Hourly Database, a New Resource of Global Climate Data. In: Observed Climate Change II: Data and Extremes [Internet]. Asheville, NC: American Meteorological Society; 2002 [cited 2025 May 8]. Available from: <https://ams.confex.com/ams/annual2002/webprogram/Paper27792.html>
70. Abdel-Malek AA, Abdel-Aal MA. Study of the dispersion and flight range of Anopheles sergenti Theo. in Siwa Oasis using radioactive isotopes as markers. Bull World Health Organ. 1966;35(6):968–73. PubMed PMID: 4381759.

71. Thomson MC, Connor SJ, Quiñones ML, Jawara M, Todd J, Greenwood BM. Movement of *Anopheles gambiae* s.l. malaria vectors between villages in The Gambia. *Med Vet Entomol.* 1995;9(4):413–9. 10.1111/j.1365-2915.1995.tb00015.x.
72. Gillies MT. Studies on the dispersion and survival of *Anopheles gambiae* Giles in East Africa, by means of marking and release experiments. *Bull Entomol Res.* 1961;52(1):99–127. 10.1017/S0007485300055309.
73. Jarvis C, Di Tanna GL, Lewis D, Alexander N, Edmunds WJ. Spatial analysis of cluster randomised trials: a systematic review of analysis methods. *Emerg Themes Epidemiol.* 2017;14(1):12. 10.1186/s12982-017-0066-2.
74. Mbogo CNM, Baya NM, Ofulla AVO, Githure JI, Snow RW. The impact of permethrin-impregnated bednets on malaria vectors of the Kenyan coast. *Med Vet Entomol.* 1996;10(3):251–9. 10.1111/j.1365-2915.1996.tb00739.x.
75. Azizi S, Martin J, Mbewe NJ, Msapalla A, Mwacha S, Joram A, et al. Evaluation of Durability as a Function of Fabric Strength and Residual Bio-Efficacy for the Olyset Plus and Interceptor G2 LLINs after 3 Years of Field Use in Tanzania. *Trop Med Infect Disease.* 2023;8(8):8. 10.3390/tropicalmed8080379.
76. Lukole E, Cook J, Mosha JF, Messenger LA, Rowland M, Kleinschmidt I, et al. Protective efficacy of holed and aging PBO-pyrethroid synergist-treated nets on malaria infection prevalence in north-western Tanzania. *PLOS Global Public Health.* 2022;2(10):e0000453. 10.1371/journal.pgph.0000453.
77. Craig MH, Snow RW, le Sueur D. A Climate-based Distribution Model of Malaria Transmission in Sub-Saharan Africa. *Parasitol Today.* 1999;15(3):105–11. 10.1016/S0169-4758(99)01396-4.
78. Hayes RJ, Bennett S. Simple sample size calculation for cluster-randomized trials. *Int J Epidemiol.* 1999;28(2):319–26. 10.1093/ije/28.2.319.
79. Armstrong M. Common problems seen in variograms. *J Int Assoc Math Geol.* 1984;16(3):305–13. 10.1007/BF01032694.
80. Midega JT, Mbogo CM, Mwambi H, Wilson MD, Ojwang G, Mwangangi JM, et al. Estimating Dispersal and Survival of *Anopheles gambiae* and *Anopheles funestus* Along the Kenyan Coast by Using Mark–Release–Recapture Methods. *J Med Entomol.* 2007;44(6):923–9. 10.1093/jmedent/44.6.923.
81. Guerra CA, Reiner RC, Perkins TA, Lindsay SW, Midega JT, Brady OJ, et al. A global assembly of adult female mosquito mark-release-recapture data to inform the control of mosquito-borne pathogens. *Parasites Vectors.* 2014;7(1):276. 10.1186/1756-3305-7-276.
82. Rogier E, Bakari C, Mandara CI, Chiduo MG, Plucinski M, Nace D, et al. Performance of antigen detection for HRP2-based malaria rapid diagnostic tests in community surveys: Tanzania, July–November 2017. *Malar J.* 2022;21(1):361. 10.1186/s12936-022-04383-4.
83. Diallo MA, Diongue K, Ndiaye M, Gaye A, Deme A, Badiane AS, et al. Evaluation of CareStart. Malar HRP2/pLDH (Pf/pan) Combo Test Malar low transmission region Senegal *Malar J.* 2017;16(1):1.

Figures

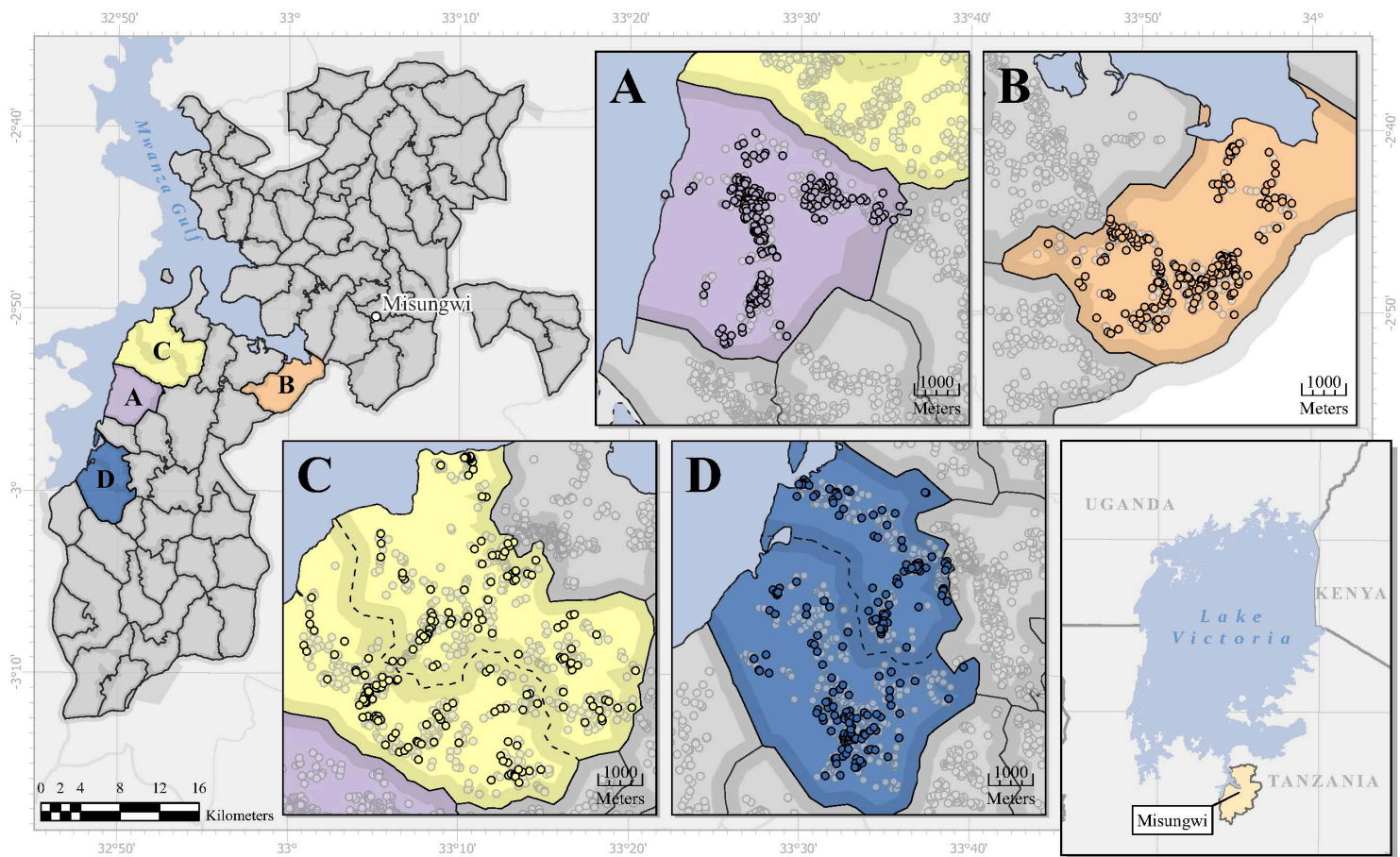


Figure 1

Study area. Map showing the study site of the Misungwi Dual AI LLIN Trial and location on the southern shore of Lake Victoria. Supercluster areas are highlighted and inset maps show sampled household locations (saturated points) against the locations of unsampled households in the same supercluster area. Grey areas indicate trial clusters not used in this study and dark grey areas represent trial buffer areas. The dashed lines in Superclusters C and D show the boundaries where multiple trial clusters were joined into one Supercluster for the purposes of this study.

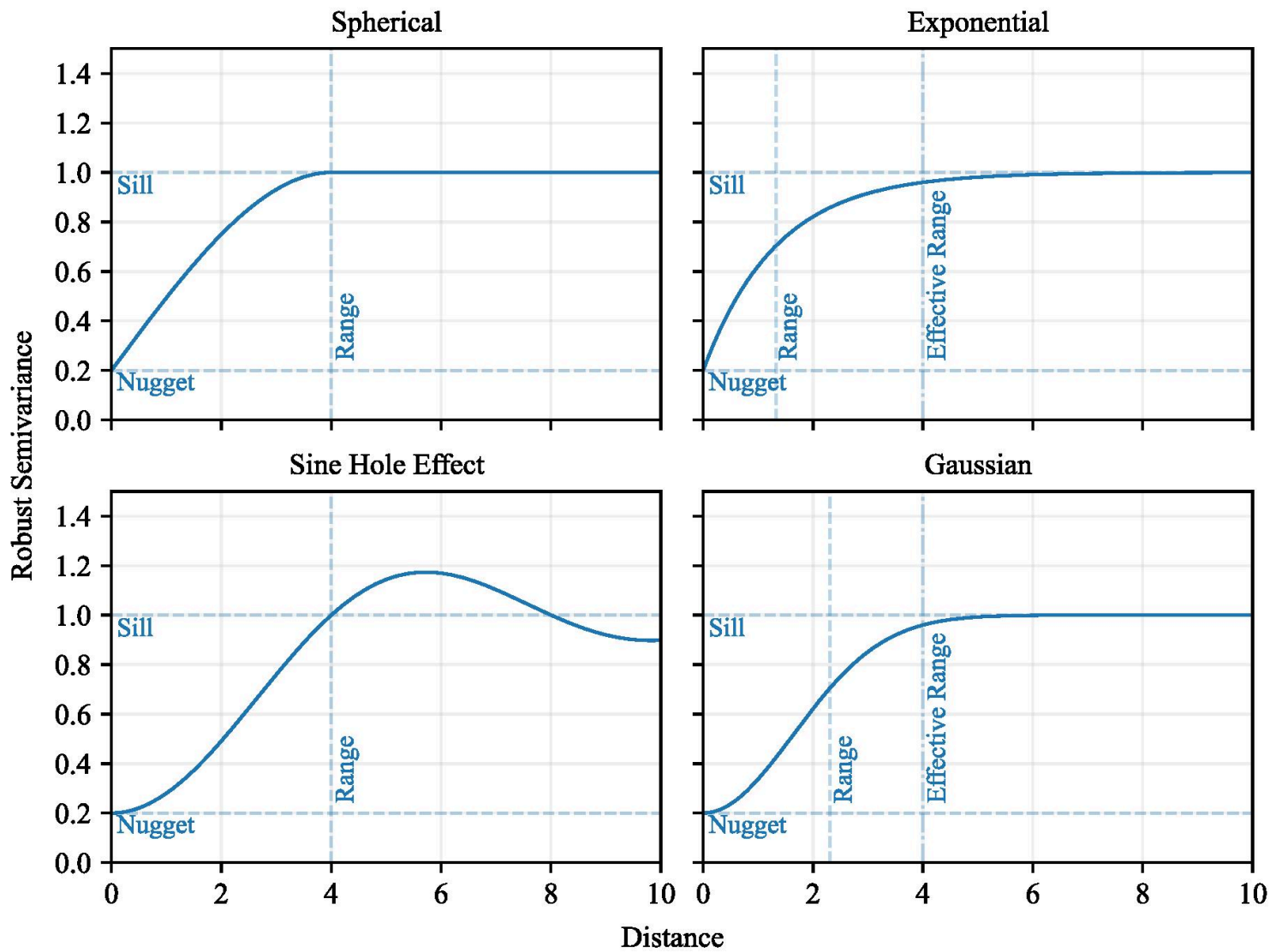


Figure 2

Variogram model forms Standardised representations of the variogram candidate models used in this study. All models presented have a parameterised nugget of 0.2, a scale of 0.8, and a range, or effective range, estimate of 4.0 based on model construction.

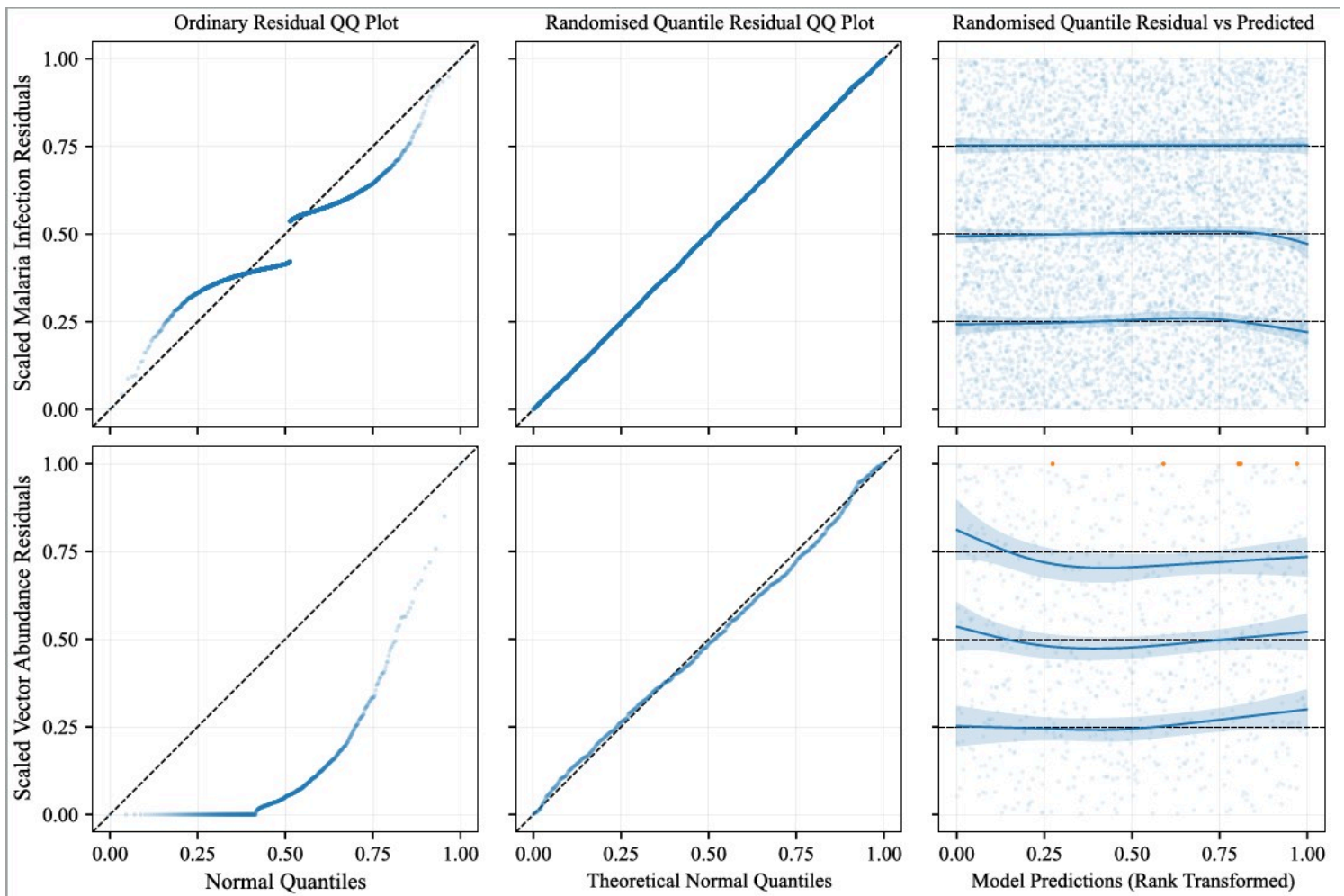


Figure 3

Residual diagnostic plots For all plots, dashed lines represent ideal locations for normally distributed data. In the third column, outlying model predictions are highlighted in orange and solid lines represent quantile regressions with shaded areas showing their 95% confidence intervals.

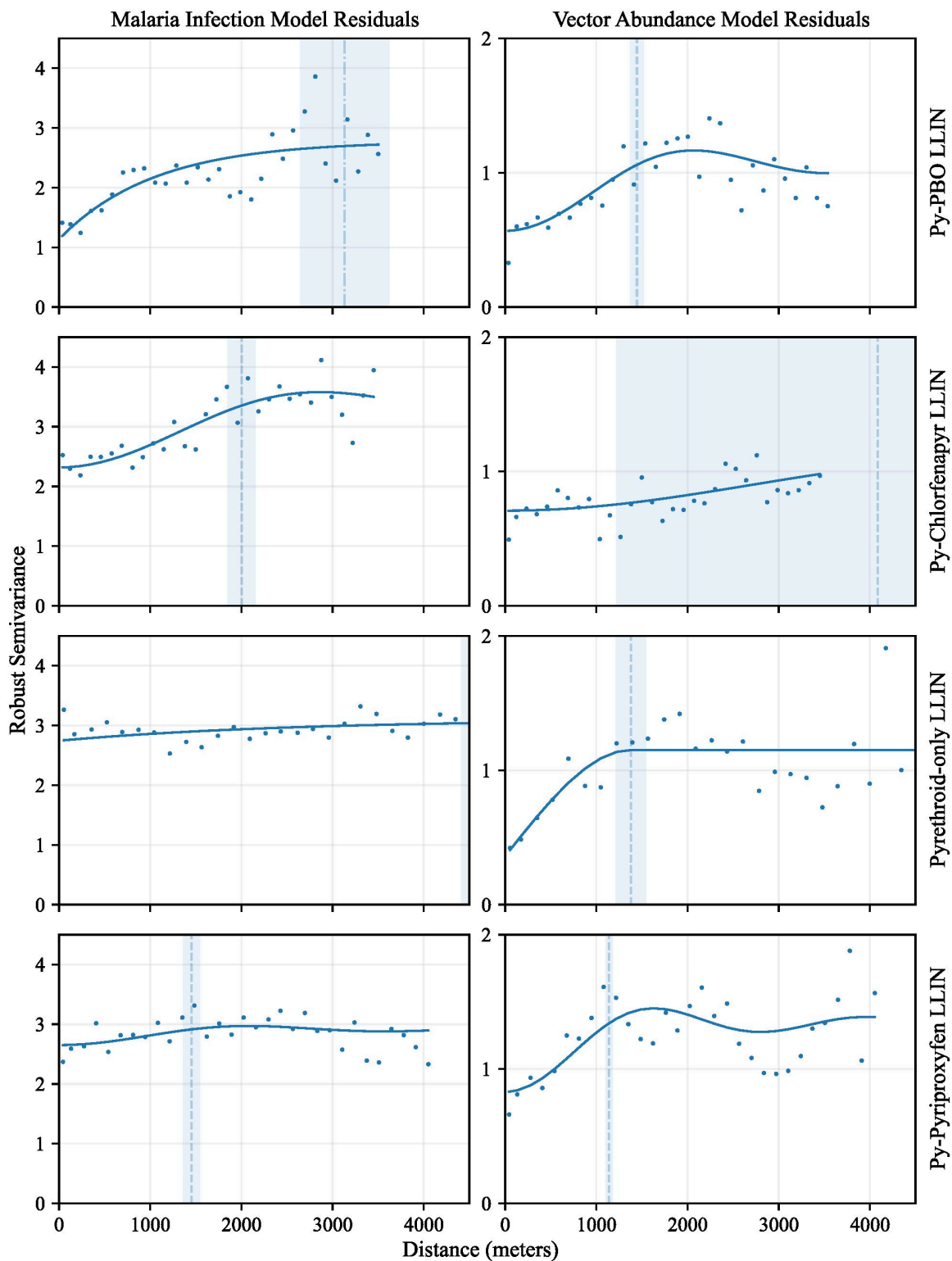


Figure 4

Variogram estimates Fitted variogram models of the residuals from malaria infection and vector abundance regression models (columns) for each supercluster area (rows). Point estimates show the lagged robust semivariance estimates for each distance class. Solid lines represent the best weighted sum of squared errors variogram model fit. Dashed lines and shaded areas show the modelled estimate

and 95% confidence interval for variogram range effects. Dot-dash lines represent effective range estimates for models with asymptotic range constructions.

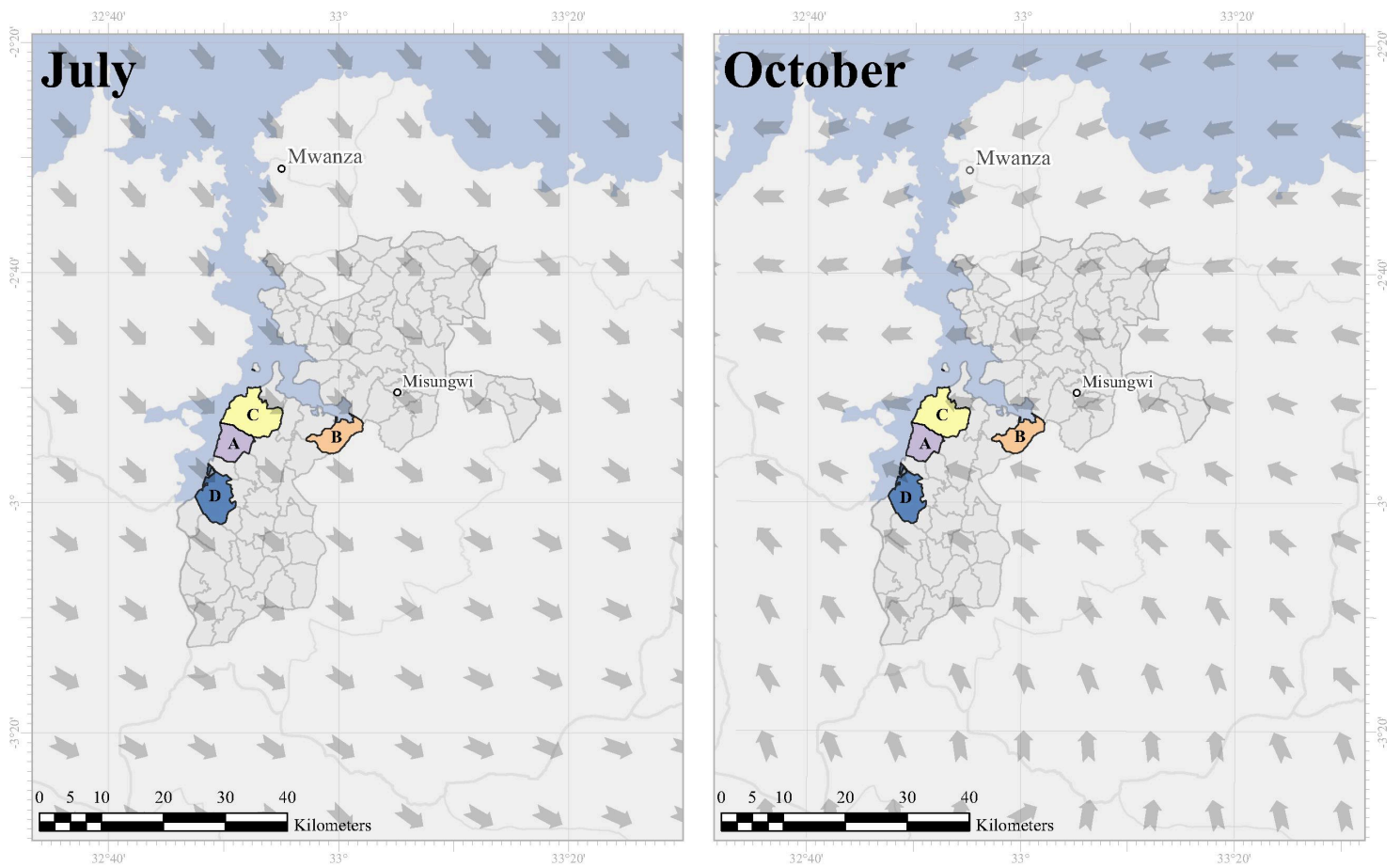


Figure 5

Comparison of seasonal overnight surface wind patterns in Misungwi District. Arrows represent the circular average overnight (18:00-06:00) hourly wind direction at 0.1° gridded locations. Hourly data on wind direction was obtained from the US National Centers for Environmental Information Integrated Surface Dataset for the 34 most proximal weather stations and interpolated by inverse-distance weighting in ArcGIS Pro 3.5 [68,69]. Supercluster areas are highlighted.

Supplementary Files

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

- [ThickstunExaminingthespatialeffectrangesofDualAILLINTablesRevision1.docx](#)
- [Suppl1Datadictionary.xlsx](#)
- [Suppl2Superclustersamplingbreakdownbycluster.pdf](#)
- [Suppl3Superclustersamplingtimeline.pdf](#)
- [Suppl4Additionaltables.docx](#)