



# A Bayesian multinomial modeling of spatial pattern of co-morbidity of malaria and non-malarial febrile illness among young children in Nigeria

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**Background:** Children in developing countries continue to suffer mortality and morbidity from a number of illnesses, among which are malaria and non-malarial febrile illnesses, which epidemiologically overlap. We examined the spatial pattern and risk factors of co-morbidity of malaria and non-malarial febrile illness among children aged 6–59 months in Nigeria.

**Method:** Using data from the 2010 Nigeria Malaria Indicator Survey, we considered the co-morbidity of malaria and non-malarial febrile illness among the children as mult categorical and selected a mixed multinomial logit model capable of incorporating covariates of different types. Inference was Bayesian, based on mult categorical linear mixed-model representation.

**Results:** We found that the risk of co-morbidity of malaria and non-malarial febrile illness increases as a child advances in age while the risk of non-malarial fever reduces after about 32 months of age. Area of residence (urban or rural), wealth index and type of roofing material used in the dwelling are other important risk factors for the co-morbidity found in this study. Further, children from four of Nigeria's 37 states are at high risk of malaria.

**Conclusions:** Disease preventive measures need to be intensified, with more focus on rural areas and the poor. Campaigns for use of insecticide-treated bed nets need be more aggressive in all Nigerian states.

**Keywords:** Effective disease management, Insecticide-treated net, Malaria endemic regions, Nigeria, *Plasmodium falciparum*, Spatial analysis

## Introduction

Children in developing countries continue to suffer mortality and morbidity from a number of illnesses among which are malaria and non-malarial febrile illness, which epidemiologically overlap. Malaria is one of the major human infectious diseases; it is endemic in more than 100 countries, with approximately 300 million clinical cases and 2 million fatalities per year.<sup>1</sup> The geographical location of Nigeria makes the climate suitable for malaria transmission throughout the country. Children under the age of 5 years and pregnant women are vulnerable. More than 60% of outpatient visits in Nigeria are prompted by malaria symptoms.<sup>2</sup>

Fever or pyrexia is a documented elevation of axillary body temperature to  $\geq 37.5^{\circ}\text{C}$ . It is most often a response to infection (bacterial, viral, rickettsial, fungal or parasitic), although a variety of other causes include neoplasms, vascular disease, trauma,

immunological, endocrine, metabolic and haematological disorders, and physical agents.<sup>3</sup> Although fever can be caused by many infections in tropical Africa, the proportion of fevers attributable to malaria is often high, ranging from 30% to 60%.<sup>4,5</sup> Estimates suggest that malaria is the cause of symptoms in as many as 43% of children presenting to health facilities in Africa with fever.<sup>6</sup> Of the several parasites that cause malaria, *Plasmodium falciparum* is responsible for the most severe form of the disease, and accounts for 90–98% of malaria infections in Nigeria.<sup>7,8</sup> The WHO recently recommended artemisinin combination therapy (ACT) for *P. falciparum* malaria in all regions with drug-resistant malaria. However, presumptive treatment of fever with antimalarials is widely practised to reduce malaria-attributable morbidity and mortality. Presumptive treatment is particularly common at lower-level health facilities where microscopy and rapid diagnosis test kits are not readily available or

where health workers assume all childhood fever to be a result of malaria.<sup>6,9-11</sup> This practice means that many ill children may be inappropriately treated, resulting in wastage of limited drug stocks. Prompt and accurate diagnosis remains the key to effective disease management.<sup>1</sup>

Several studies have reported the incidence and determinants of malaria and non-malarial febrile illness among young children and pregnant women in Nigeria.<sup>7,12-14</sup> However, few studies have modelled the co-morbidity and little is known about the geographical overlaps. A broader understanding of the co-morbidity processes would support the development of better and more cost-effective control measures. Appropriate, evidence-based use of scarce resources requires adequate knowledge of the subset of the population that is at high risk, and of the geographical variability of the risk factors. To this end, our study analysed data arising from the 2010 Nigeria Malaria Indicator Survey, the first of a series of surveys that take a nationally representative sample of the prevalence of malaria, fever symptoms and other illnesses among children aged <5 years. We also aimed to quantify the residual spatial variations in the overlapping of co-morbidity of malaria and non-malarial febrile illness after taking other characteristics of the children into account. Spatial modelling has been a valuable approach for quantifying district- and state-specific effects on outcomes.

We adopted a flexible Bayesian modelling approach that allows investigation of how individual, household and district- and state-specific random effects shape the co-morbidity of non-malarial febrile illness and malaria among young children in Nigeria. Considering that, epidemiologically, malaria and non-malarial febrile illness overlap, we considered the co-morbidity as a multi-categorical outcome and proposed a multinomial modelling approach within the Bayesian framework that allows for separate treatment of the outcomes against a control group. Multinomial models have been extended to incorporate spatial random effects, to cater for unstructured heterogeneity that may be present in the data, and spatially structured variations within the framework of generalised linear models.<sup>15-17</sup> A similar technique has been adopted to study epidemiological outcomes in developing countries.<sup>18,19</sup>

## Methods

### Data

This study relies on data from the 2010 Nigeria Malaria Indicator Survey (NMIS).<sup>20</sup> With technical assistance from ICF International through Measure DHS, the nationally representative survey was implemented by the National Population Commission (NPC) and the National Malaria Control Program (NMCP) alongside other partners. The survey was designed to provide information on malaria indicators and malaria prevalence at national and state level.

Details of the sampling procedure for the survey have been reported elsewhere.<sup>20</sup> Briefly, samples were realised through a two-stage probability sampling technique. At the first stage, 240 clusters were selected from the sampling frame used during the 2006 Population and Housing Census of the Federal Republic of Nigeria. At the second stage, an average of 26 households was selected in each cluster by equal probability sampling. A total of 6197 households were selected, and of these, 5986 were

occupied at the time of survey. Of the occupied households, 5895 were successfully interviewed, yielding a response rate of 99%. All children aged 6-59 months in the households were eligible to be tested for malaria.

The 2010 NMIS incorporated three biomarkers: anaemia testing, malaria testing using a rapid diagnostic test (RDT), and the preparation on microscope slides of thick blood smears and thin blood films ('gold standard'). After obtaining informed consent from the child's parent or guardian, blood samples were collected using a microcuvette to obtain a drop of blood from a finger prick (or a heel prick in the case of young children with small fingers) to perform on-the-spot RDT for malaria and to prepare the gold-standard blood smears and films. The RDT was done using the Paracheck Pf test (Orchid Biomedical Systems, Goa, India), which tests for *P. falciparum*. The test includes a loop applicator that comes in a sterile packet. A tiny portion of blood is captured on the applicator and placed in the well of the device; results are available in 15 min. The prepared blood smears and films were dried and then fixed with analar methanol. The field teams carefully packed the slides in sturdy slide boxes for collection by a laboratory scientist and transport to the laboratory. Giemsa staining of the slides was carried out at the laboratory, and the presence and species of malaria parasite determined by microscopic examination. To assess the children's fever status, the field teams measured axillary body temperature. A temperature of  $\geq 37.5^{\circ}\text{C}$  was considered to constitute fever.

The data analysed came from 4944 children for whom a record was available of non-malarial febrile illness and malaria from the 2010 survey.<sup>20</sup> Questions on place of residence, mother's educational level, household wealth index, ethnicity, sex of the child, number of household members, age of the child, age of household head, number of rooms available for sleeping, type of roofing material of the dwelling, ownership and use of bed nets, geographical region, and state of residence at the time of the survey were included in the survey.

The household wealth index was calculated using data on the household's ownership of consumer goods, characteristics of the dwelling, source of drinking water, sanitation facilities, and other characteristics that relate to a household's socioeconomic status. Each of these assets was assigned a weight (factor score) generated through principal component analysis, and the resulting asset scores were standardised in relation to a standard normal distribution with a mean of zero and standard deviation of one. Each household was then assigned a score for each asset, and the scores were summed for each household. Individuals were ranked according to the total score of the household in which they resided. The sample was then divided into quintiles from one (poorest) to five (richest).

Administratively, Nigeria is divided into six geopolitical zones, each comprising six states (totalling 36 states altogether) and a Federal Capital Territory (FCT), Abuja.

### Statistical analysis

Let  $Y_{ijk}$  and  $\pi_{ijk}$  be the illness status and probability of co-morbidity of malaria and non-malarial febrile illness ( $k=1$ ), malaria only ( $k=2$ ), non-malarial fever only ( $k=3$ ), and no illness ( $k=4$ ) for child  $j$  in location (state)  $i$ . We assumed that  $Y_{ijk}$  follows a multinomial distribution, i.e.,  $Y_{ijk} \sim MN(1, \pi_{ijk})$  where  $\pi_{ijk} = (\pi_{ij1}, \pi_{ij2}, \pi_{ij3}, \pi_{ij4})'$ . Given some categorical covariates,  $v_{ij}$ , metrical covariates,  $x_{ij}$  and state-specific random effect,  $s_{ik}$ , the probability of

co-morbidity can be modelled thus:

$$\pi_{ijk} = \frac{\exp(\eta_{ijk})}{1 + \sum_{l=1}^k \exp(\eta_{ijl})} \quad k = 1, 2, 3 \quad (1)$$

where the predictor,  $\eta_{ijk}$ , is given by

$$\eta_{ijk} = v_{ij}\beta_k + f_k(x_{ij}) + s_{ik} \quad (2)$$

The term  $\beta_k$  is the vector of parameters and  $f_k$  is a smooth function for the covariates that are continuous and assumed non-linear, for each of the status categories  $k$ . In this case study, we adopted the logit link and set the last category (no illness) as reference. The state random effect can further be split into two components: one that incorporates structured (correlated) spatial effects and another that allows for unstructured (uncorrelated) spatial effects such that  $s_{ik} = \phi_{ik} + \varphi_{ik}$ .

To estimate smooth effect functions and model parameters, we used the empirical Bayesian approach, as developed by Fahrmeir and Lang<sup>15</sup> and Lang and Brezger.<sup>21</sup> For all functions and parameters, appropriate prior functions were assigned. For fixed effect parameters,  $\beta_k$ , we assumed diffuse priors,  $p(\gamma) \propto \text{const}$  while a Bayesian P-splines prior is assumed for the non-linear smooth functions. The basic assumption behind the P-splines approach is that the unknown smooth function  $f$  can be approximated by a spline of degree  $l$  defined on a set of equally spaced knots within the domain of  $x$ .<sup>22</sup> Such a spline can be written in terms of a linear combination of basis function (B-spline), i.e.  $p(z) = \sum_{j=1}^J \beta_j B_j(z)$  where  $B_j(z)$  are B-splines. Smoothness of the basis function is achieved by a first- or second-order random walk model. We adopted the second-order random walk in this study i.e.  $\beta_j = 2\beta_{j-1} - \beta_{j-2} + \varepsilon_t$  with Gaussian error  $\varepsilon_t \sim N(0, \tau_\varepsilon^2)$ . The variance  $\tau_\varepsilon^2$  controls for the smoothness of  $f$ .

For the structured spatial effects, we chose a Gaussian Markov random field prior.<sup>23</sup> The priors define areas as neighbours if they share a common boundary and neighbouring areas are assumed to have similar patterns, such that the mean of area  $i$  is assumed to be an average of neighbouring areas, with variance as a function of neighbours and spatial variance. The unstructured heterogeneity term was estimated using exchangeable normal priors,  $u_{ijk} \sim N(0, \tau_b^2)$ , where  $\tau_b^2$  is a variance component that incorporates over-dispersion and heterogeneity.

Inference was based on multicategorical linear mixed-model representation where the variance components  $\tau_\varepsilon^2$ , corresponding to the inverse smoothing parameters in a frequentist approach, are estimated via restricted maximum likelihood/marginal likelihood estimation. In the mixed model representation, a variance component model is obtained where the variances are considered as unknown constants to be estimated from their marginal likelihood. The regression coefficients are estimated via the modified Fisher scoring, yielding posterior mode estimates. Detailed information about the modelling approach of categorical space data via restricted likelihood can be found in Kneib and Fahrmeir<sup>24</sup> and Fahrmeir, Kneib and Lang.<sup>25</sup>

Sensitivity to the choice of priors and hyperparameters was investigated in this paper for various values of hyperparameters  $a$  and  $b$  of the inverse gamma distribution. However, results do not show remarkable difference to the various choices of priors.

## Results

Table 1 presents the descriptive analysis of the co-morbidity of malaria and non-malarial febrile illness based on household characteristics of the children. Overall, about 60% (2972/4944) of the children had malaria, non-malarial febrile illness (subsequently in this section termed 'fever') or both. About 22% (1100/4944) had either malaria or fever only, and another 16% (793/4944) suffered from both. Among children from rural areas, a greater percentage had malaria (36.3%, 945/3592), whereas fever was more frequent in the urban areas (24.3%; 328/1352). Among the children whose parents had no education, about 27% (717/2676) had malaria while 19% (512/2676) had fever. Children from the richest households suffered the fewest episodes of fever and malaria (6%, 58/921). More than half (56%, 511/921) of those from the richest households had no illness. About 18% (181/982) of children from households of two to four individuals had malaria, compared with 24% (593/982) of children from households of seven or more. In contrast, 26% (251/982) of those from households of two to four had fever compared with 20% (486/2460) of those from households of seven or more. Our findings also show that the percentage of children with malaria increased with increase in the number of sleeping rooms. However, the proportion of children who had both malaria and fever did not vary with number of rooms. As expected, the percentage of children who had malaria was higher among households without bed nets (24%; 537/2241) compared with those who possessed them (21%; 557/2681). Nevertheless, the proportion of the children who had malaria, fever or both was higher among those who had slept under a bed net the night before the survey than in those who had not.

Results of the fixed effects covariates are presented in Table 2, which shows the odds ratios and corresponding 95% confidence intervals. The odds that a child would have malaria, fever or both were significantly lower for children who lived in urban areas compared with their counterparts in rural areas. The odds of having malaria, fever or both were not significant for those whose parents had primary or secondary education, compared with children whose mothers had no education. Those whose parents attained a higher educational level were 50% less likely to have malaria compared with those whose mothers had no education (OR=0.50, CI: 0.30–0.81). Findings for fever and both fever and malaria were not significant. Children from the Yoruba ethnic group were 79% more likely to have malaria (OR=1.79, CI: 1.12–2.87), Igbo children were 53% less likely (OR=0.47, CI: 0.281–0.785) while the result is not significant for the Hausa/Fulani children, when compared with those from other ethnic groups. Findings on fever show that the Yoruba children were 32% (OR=0.68, CI: 0.46–0.99) less likely to have had fever; Hausa children were 58% (OR=1.58, CI: 1.16–2.13) more likely to have done so, while findings were not significant for Igbo children compared with children from the other ethnic groups. Comparing the same sets of children, those from the Yoruba group were about 80% (OR=1.80, CI: 1.01–3.20) more likely to have had both malaria and fever. Compared with children from the poorest households, those from the richest households were 36% (OR=0.64, CI: 0.48–0.86) less likely to have malaria, and 39% (OR=0.61, CI: 0.43–0.85) less likely to have both conditions. Households in the mid-range of the wealth index were 29% (OR=1.29, CI: 1.06–1.54) more likely to have malaria and 47% (OR=1.47, CI: 1.19–1.82) more likely to have both

**Table 1.** Demographic/biosocial characteristics of respondents to the 2010 Nigeria Malaria Indicator Survey<sup>a</sup>

Parameter	Malaria only	Fever <sup>b</sup> only	Fever <sup>b</sup> and malaria	No illness	Children
Area of residence					
Rural	945 (36.3)	751 (20.9)	663 (18.5)	1233 (34.4)	3592
Urban	155 (11.5)	328 (24.3)	130 (9.6)	739 (54.7)	1352
Mother's education					
No education	717 (26.8)	512 (19.1)	510 (19.1)	937 (35.0)	2676
Primary	177 (20.5)	202 (23.4)	131 (15.1)	354 (41.0)	864
Secondary	193 (16.1)	297 (24.7)	139 (11.6)	572 (47.6)	1201
Higher	13 (6.4)	68 (33.7)	12 (5.9)	109 (54.0)	202
Data missing					1
Ethnicity					
Hausa/Fulani	228 (17.3)	354 (26.8)	330 (25.0)	408 (30.9)	1320
Igbo	84 (12.4)	178 (26.2)	80 (11.8)	338 (49.7)	680
Yoruba	143 (30.9)	66 (14.3)	66 (14.3)	188 (40.6)	463
Other	645 (26.1)	479 (19.4)	314 (12.7)	1036 (41.9)	2474
Data missing					7
Wealth index					
Poorest	253 (28.1)	157 (17.5)	170 (18.9)	319 (35.5)	899
Poorer	265 (29.1)	169 (18.5)	169 (18.5)	306 (33.6)	912
Mid-range	283 (25.2)	255 (22.7)	218 (19.4)	368 (32.7)	1124
Richer	199 (18.3)	246 (22.6)	175 (16.1)	468 (43.0)	1088
Richest	100 (10.9)	252 (27.4)	58 (6.3)	511 (55.5)	921
Household members					
2–4	181 (18.4)	251 (25.6)	147 (15.0)	403 (41.0)	982
5–6	326 (21.7)	342 (22.8)	232 (15.4)	602 (40.1)	1502
≥7	593 (24.1)	486 (19.8)	414 (16.8)	967 (39.3)	2460
Rooms for sleeping					
≥3	563 (25.5)	458 (20.8)	345 (15.6)	839 (38.0)	2205
2	339 (20.1)	391 (23.0)	284 (16.7)	683 (40.2)	1697
1	198 (19.0)	230 (22.1)	164 (15.7)	450 (43.2)	1042
Dwelling's roofing material					
Thatch	308 (28.7)	196 (18.2)	212 (19.7)	359 (33.4)	1075
Zinc	622 (19.4)	749 (23.3)	467 (14.5)	1376 (42.8)	3214
Other	170 (26.0)	134 (20.5)	114 (17.3)	237 (36.2)	655
Bed net owned					
No	537 (24.0)	466 (20.8)	355 (15.8)	883 (39.4)	2241
Yes	557 (20.8)	611 (22.8)	436 (16.3)	1077 (40.2)	2681
Missing					22
Bed net used					
No	704 (22.9)	621 (20.2)	484 (15.8)	1263 (41.1)	3072
Yes	394 (37.7)	451 (24.5)	303 (16.3)	694 (37.7)	1842
Data missing					30
Sex					
Male	553 (22.1)	551 (22.0)	416 (16.6)	981 (39.2)	2501
Female	547 (22.4)	528 (21.6)	377 (15.4)	991 (40.6)	2443
Total	1100 (22.2)	1079 (21.8)	793 (16.1)	1972 (39.9)	4944

<sup>a</sup> Data are n or n (%).<sup>b</sup> Non-malarial febrile illness.

conditions. Similarly, children from the poorer households were 26% (OR=1.26, CI: 1.03–1.54) more likely to have malaria. Other results on the wealth quintiles were not significant.

Findings on number of household members show that the odds of having malaria, fever or both conditions were higher but not significantly so for children from households of five to six members

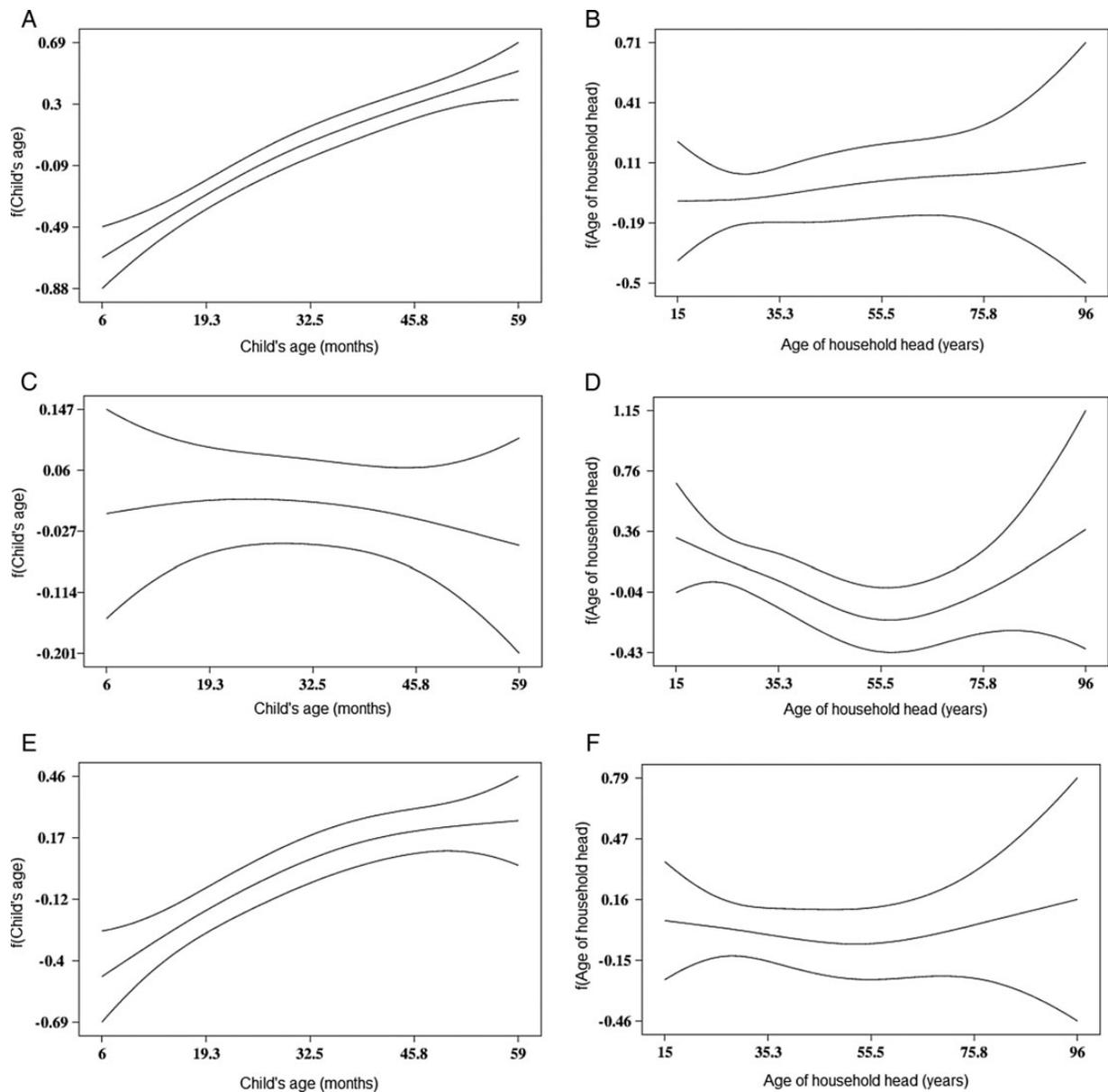
**Table 2.** Chance of a child having malaria, non-malarial febrile illness or both: OR (95% CI) for fixed-effects covariates, derived from the 2010 Nigeria Malaria Indicator Survey

Parameter	Malaria vs No sickness	Fever <sup>a</sup> vs No sickness	Fever <sup>a</sup> and malaria vs No sickness
Area of residence			
Rural	1	1	1
Urban	0.62 (0.52–0.74)	0.83 (0.73–0.95)	0.63 (0.51–0.77)
Mother's education			
No education	1	1	1
Primary	1.162 (0.922–1.464)	1.042 (0.872–1.244)	1.16 (0.91–1.49)
Secondary	1.192 (0.954–1.491)	0.910 (0.115–1.070)	1.04 (0.81–1.32)
Higher	0.495 (0.304–0.806)	1.250 (0.948–1.647)	0.748 (0.452–1.238)
Ethnicity			
Other	1	1	1
Hausa\Fulani	0.991 (0.651–1.509)	1.575 (1.163–2.132)	1.027 (0.639–1.652)
Igbo	0.470 (0.281–0.785)	1.087 (0.773–1.530)	0.658 (0.367–1.178)
Yoruba	1.793 (1.119–2.874)	0.677 (0.463–0.990)	1.799 (1.013–3.197)
Wealth index			
Poorest	1	1	1
Poorer	1.259 (1.027–1.543)	0.908 (0.742–1.111)	1.066 (0.847–1.342)
Mid-range	1.288 (1.060–1.565)	1.152 (0.960–1.382)	1.467 (1.186–1.815)
Richer	0.986 (0.796–1.220)	1.021 (0.843–1.237)	1.247 (0.992–1.568)
Richest	0.644 (0.481–0.864)	1.153 (0.910–1.461)	0.606 (0.432–0.851)
Household members			
2–4	1	1	1
5–6	1.059 (0.929–1.207)	1.038 (0.922–1.169)	1.040 (0.902–1.199)
≥7	0.956 (0.830–1.102)	0.836 (0.732–0.956)	0.894 (0.765–1.045)
Rooms for sleeping			
≥3	1	1	1
2	1.004 (0.884–1.140)	1.017 (0.906–1.142)	0.936 (0.781–1.121)
1	0.842 (0.715–0.993)	0.858 (0.738–0.997)	1.048 (0.914–1.201)
Roofing material			
Other	1	1	1
Thatch	1.296 (1.040–1.614)	1.117 (0.892–1.399)	1.432 (1.125–1.821)
Zinc	0.891 (0.750–1.059)	0.877 (0.742–1.037)	0.898 (0.743–1.086)
Bed net owned			
No	1	1	1
Yes	0.871 (0.763–0.995)	0.911 (0.806–1.031)	1.030 (0.892–1.188)
Bed net used			
No	1	1	1
Yes	1.087 (0.949–1.245)	1.204 (1.064–1.363)	0.994 (0.859–1.150)
Sex			
Male	1	1	1
Female	0.969 (0.891–1.054)	0.977 (0.902–1.057)	0.913 (0.833–1.002)

<sup>a</sup> Non-malarial febrile illness.

compared with those from households of two to four members. Those from households of seven and above were less likely to have suffered from one or both of the conditions, although the difference was significant only for fever. Compared with children from households that had three or more sleeping rooms, those from households with only one room were 16% (OR=0.84, CI: 0.72–0.99) and 14% (OR=0.86, CI: 0.74–0.99) less likely to have suffered

from malaria and fever respectively, while the odds for both conditions were not significant. Results for those who had two rooms were not significant. With regard to type of roofing material, children living in a house with a roof of thatch were significantly more likely to have suffered from malaria or both malaria and fever than were those from households where other materials were used. Where zinc was used, children in the household were



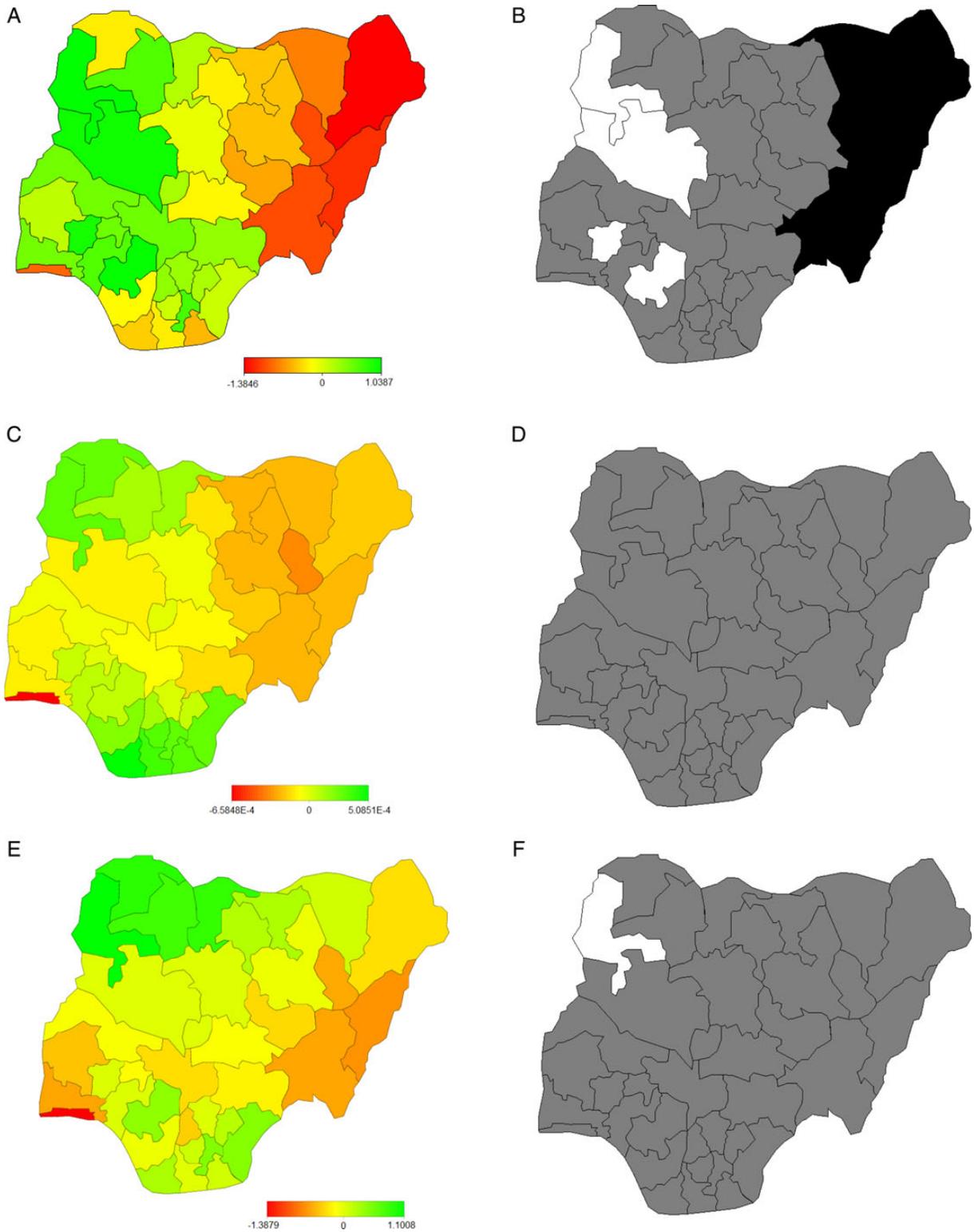
**Figure 1.** Non-linear effects of child's age and age of household head on co-morbidity. (A,B) The chance of a child having malaria only; (C,D) chance of non-malarial febrile illness only; (E,F) chance of both non-malarial fever and malaria. Based on data from the 2010 Nigeria Malaria Indicator Survey.

less likely to have suffered from either one or both conditions, albeit none of the differences was significant. Children from households that owned bed nets were significantly less likely to have suffered from malaria compared with those without nets. However, the odds were not significant for having fever or both fever and malaria. With regard to use of a bed net the previous night, the survey shows that the odds of having malaria or both malaria and fever were not significant for children who slept under a bed net compared with those who did not. However, the odds of these children having fever were significantly higher. Findings on sex of the children show that, although the female children were less likely to have had one or both conditions, none of the variation was significant.

The non-linear effects of a child's age and the age of the household head are presented in Figure 1, which shows the

posterior modes and 95% CI. Our findings show that the odds of having malaria or both malaria and fever increased as the child's age increased, while those of fever alone increased slightly with age until 28 months, after which the odds drop. The likelihood of the child having malaria increased with increasing age of the household head. However, the findings for fever revealed a U-shaped pattern, signifying that from a relatively high level with a household head aged 15 years, the likelihood of a child having fever reduced as the head of household's age increased up until around age 55 years, after which it started rising again. The likelihood that a child had both malaria and fever started to increase as the household head reached around 55 years of age.

The geographical patterns of our findings are shown in Figure 2.



**Figure 2.** Maps of states of Nigeria showing spatial effects on co-morbidity, based on data from the 2010 Nigeria Malaria Indicator Survey. Significance is assessed using posterior modes (A,C,E) and 95% CI (D,E,F). (A,B) The odds of a child having malaria only are significantly higher in four states (Niger, Kebbi, Osun and Edo), and significantly lower in the five neighbouring north eastern states of Taraba, Adamawa, Borno, Yobe and Gombe. (C,D) The odds of having non-malarial febrile illness alone are not significant for any state. (D,E) The odds of having both non-malarial fever and malaria are significantly higher only in Kebbi state.

## Discussion

This study was designed to examine the geographical pattern and determinants of co-morbidity of malaria and non-malarial febrile illness among children in Nigeria <5 years of age. It is essential to explore these factors because in developing countries terminal illness in children <5 years of age is often characterised by co-morbidity.<sup>19,26</sup> The co-morbidity of malaria and non-malarial febrile illness was considered a multicategorical response variable and a mixed multinomial logit model, capable of incorporating explanatory variables of different types while at the same time quantifying residual spatial effects, was considered appropriate. The formulation of structuring a binary to multicategorical response variable is appropriate considering the epidemiological overlap of the diseases. The results provide evidence of geographical impact on childhood health and can therefore serve as guiding tool for policy formulation and execution.

Place of residence plays an important role in the spread of diseases among young children in Nigeria. We found that children residing in urban areas in Nigeria are less likely to test positive for malaria, non-malarial febrile illness or both conditions when compared with their counterparts in rural areas. Poor perception and knowledge of malaria and its control and of bacterial infections is prevalent among people living in rural areas. For instance, it has been reported that ownership and use of bed nets is significantly lower among rural dwellers than it is in urban areas in Nigeria.<sup>12</sup> Moreover, in most rural areas in Nigeria there is a dearth of health professionals who could provide necessary information on disease prevention methods, although two-thirds of the Nigerian population live in rural areas.<sup>27</sup> Such factors as education and socioeconomic status, often measured by wealth index, have been reported in many studies as major determinants of disease prevention measures. A higher level of education has been associated with improved knowledge and practice with regard to strategies for preventing and treating malaria and other diseases.<sup>7,13,28</sup> Although our findings on malaria are similar to those reported in published studies, we could not establish any significant difference in the risks of non-malarial febrile illness or co-morbidity of non-malarial fever and malaria among the different educational levels considered.

Other studies have found that sociocultural factors are associated with health beliefs for fever and other childhood diseases.<sup>29–31</sup> Children from the Yoruba ethnic group have a high likelihood of being infected with malaria and having both malaria and non-malarial febrile illness, but are at low risk of non-malarial fever alone. In contrast, Igbo children are at lower risk for malaria, while Hausa/Fulani children are at high risk of non-malarial febrile illness. It has been found that, in Nigeria, the use of insecticide-treated nets to prevent malaria was four times higher in the coastal south (Niger Delta), where most of the Igbo live, than it was in the arid north (Sahel Savannah).<sup>28</sup> Also, possession of insecticide-treated nets and their use by children <5 years of age and pregnant women was least common among the Yoruba households living in southwestern Nigeria and hence there was a high risk of malaria among them.<sup>20,32</sup> The Hausa and Fulani groups are disproportionately exposed to infectious diseases. The nomads among them are often isolated from disease prevention campaigns, because of factors such as dispersion and mobility, which collectively create specific problems regarding the delivery of healthcare, social services and education. They

have been virtually excluded from primary health services although, consistent with our findings, fever has been their most frequently cited health challenge.<sup>33,34</sup>

We have found that ownership of a bed net significantly reduces the risks of malaria, while children who slept under a net the night before the survey were at high risk of having non-malarial fever. The use of insecticide-treated nets is considered one of the most cost effective methods of malaria prevention in highly endemic areas and their usage has been the main method of malaria prevention adopted in Nigeria. Free distribution of long-lasting insecticidal nets is conducted through campaigns, public health facilities and non-governmental organisations. To achieve the goal of universal access to the at-risk population of children, considerable efforts and resources are still required to make the nets available and easily accessible. In a study in western Kenya, there was no notable association found, as in our case, between the use of some preventive measures, including bed nets, and malaria risks.<sup>35</sup> Campaigns to enlighten families on the benefits of regular bed-net use need to be intensified to attain the desired results. Our findings have also shown that households with more than six members and those using one room for sleeping are at lower risk of fever symptom. The design of a house, including the roofing material, significantly affects the incidence of *P. falciparum*.<sup>36</sup> Houses roofed with zinc might better protect their occupants from mosquitoes and bacterial infections than those roofed with thatch. In a study in Burkina Faso, the prevalence of *P. falciparum* was found to be twice as high among participants living in a house with a mud roof than among those living in a house roofed with iron sheet.

The non-linear effects of a child's age and the age of the household head have shown that relationships between epidemiological issues and demographic attributes are not always linear. The risks of malaria and co-morbidity of malaria and non-malarial febrile illness were found to be lower among younger children and to increase as they grew older, whereas the risk of non-malarial fever was lower for older children. In a study of Malawian children, it was observed that the risks of non-malarial febrile illness, diarrhoea and other childhood diseases/conditions were higher for younger children than for those aged 3–6 years.<sup>19</sup> Very young infants could be considered to have been breastfed and therefore protected by maternal immunity. It would therefore be necessary to target interventions such as the use of insecticide-treated nets and micronutrient supplements at all children.

Results of the spatial analyses have shown that, although variation at state level exists in co-morbidity of malaria and non-malarial febrile illness among young children in Nigeria, in only four of the country's 37 states are they at high risk of having malaria, while in one they are at a high risk of both malaria and non-malarial febrile illness. Since 2007 there have been campaigns to promote the use of long-lasting insecticide-treated nets (LLIN) through the World Bank Booster Project. The aim is to boost malaria control over 5 years in selected states where, among other resistance, *P. falciparum* resistance to chloroquine and sulphadoxine-pyrimethamine in excess of 85% has been documented. Also, there have been campaigns by other donors to boost the distribution of LLIN in some other states. Altogether, about 24 million such nets had been distributed in the country's 36 states and the Federal Capital Territory as at October 2010, when the NMIS that generated the data analysed in this study was conducted.<sup>20</sup> However, from our findings, the residual spatial

effects show a significantly lower likelihood of malaria in Adamawa, Taraba, Gombe, Borno and Yobe states, of which only Adamawa and Gombe are among the states that have been covered by the various campaigns. The implication is that the impact of efforts in this direction has not been adequately felt in most states that have been covered. This situation calls for more aggressive actions to bring about the desired results.

This study has some limitations. First, as in any cross-sectional survey, the study lacks the ability to make causal inference. The overlapping of the outcome variables studied may cause underestimation, or at least hide some associations between each of the variables and the explanatory variables, as children who suffered from both malaria and non-malarial febrile illness (793 patients) were excluded from the analyses of the individual outcomes. Also, the multinomial approach adopted may result in difficulties in estimating and interpreting results when the number of diseases increases, resulting in the rapid expansion of the number of categories to be estimated. The multivariate spatial approach may be advantageous in this regard. Further, a possible problem with one explanatory variable, the wealth index, is that households were classified into the different strata using household assets that are more likely to be found in urban areas than in rural areas. Thus, most of the rural households would have been in the lowest wealth category even if they had other wealth indicators such as livestock or farm machinery. In view of the finding that almost a quarter of the children tested had the malaria parasite, one would have expected to know if any effort was made to elicit information about asymptomatic malaria. Unfortunately this was not addressed in the survey on which our study was based. The lack of such information has inhibited the extent to which malaria programmers can address asymptomatic malaria when designing effective malaria control measures. Perhaps strategies targeting asymptomatic carriers are required to enhance effective control of malaria in Nigeria.

To conclude, greater efforts are desirable to improve the prevention of malaria and non-malarial febrile illness in Nigeria. Control strategies and interventions need to be designed to target people living in rural areas, the Hausa/Fulani and the Yorubas, and the poor. Intensified health education at grass-roots level should be provided to convince communities of the need to possess and sleep under insecticide-treated nets and of the benefits of other disease-preventive measures. Governments of each state in Nigeria should equally intensify efforts to improve the health status of their citizens.

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