

Geospatial Mapping of Pediatric Febrile Illness in Uganda to Inform Precision Public Health Interventions

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Background. Febrile illness is a leading cause of morbidity and mortality among children in low- and middle-income countries, yet the spatial distribution and environmental drivers of pediatric fever in Uganda remain poorly characterized.

Methods. We analyzed data from the 2016 Uganda Demographic and Health Survey to estimate the prevalence of febrile illness among children under 5 years of age. Using a geostatistical binomial model, we evaluated associations between fever prevalence and environmental, nutritional, and sociodemographic covariates. Spatial prediction and model calibration were conducted using the PrevMap package in R, and model performance was assessed using nonrandomized probability integral transform (nrPIT) and theoretical variograms.

Results. Among 14 195 children from 685 clusters, 4990 (35.1%) were reported to have had fever in the prior 2 weeks. Predicted fever prevalence varied substantially by region and month, with highest rates in the eastern and northeastern regions and in the period following the rainy season. Covariates including poverty, anemia, rainfall (2-month lag), enhanced vegetation index (1-month lag), and seasonality significantly improved model performance and reduced spatial uncertainty.

Conclusions. Our findings reveal pronounced geographic and temporal heterogeneity in pediatric febrile illness in Uganda. Environmental and nutritional factors significantly contribute to this variation. These results support targeted, region-specific public health interventions and inform future research into the etiologic drivers of pediatric fever.

Keywords. environmental determinants; geostatistical modeling; modeling pediatric febrile illness; precision public health; spatial epidemiology.

Febrile illness is still one of the major public health problems in low- and middle-income countries (LMICs) [1]. As of 2019, over one-third of all childhood deaths were caused by fever-related diseases [2]. In LMICs, children experience an average of 40 or greater episodes of fever by 5 years of age [3]. Although advances have been made in the diagnosis and treatment of febrile illnesses globally, even among the survivors of fevers, the associated morbidity and mortality remain high [4].

It is known that infectious diseases are the leading cause of febrile illnesses in children [5]. Understanding this principle necessitates the implementation of public health interventions

aimed at preventing the transmission of infectious diseases. Many infectious causes of febrile illness, particularly vector- and water-borne diseases, are influenced by environmental and climatic factors, whereas respiratory and urinary infections may exhibit seasonality largely driven by behavioral patterns, such as increased indoor crowding during cooler or wetter months [6, 7]. Therefore, epidemiological studies that delineate and characterize the impact of these environmental and climatic factors on the occurrence and geographical distribution of febrile illnesses are highly needed [8]. Our recent analysis showed that the distribution of fever in Africa is heterogeneous and likely driven by the distinct geographical and climatic environment [9]. Previous studies have largely focused on specific etiologies of fever, such as malarial, bacterial, viral, and helminth infections, and their associations with climatic features [10–17]. Despite such analyses being useful, they are biased because they do not provide an all-inclusive picture of the environmental determinants of febrile illnesses.

Although it has been recognized as crucial to identify the environmental factors associated with febrile illness and characterize their spatial distribution, we are not aware of any study so far that has characterized the spatial distribution and environmental drivers of febrile illnesses in Uganda [18, 19]. We aim to predict the prevalence of fever cases among children under 5 years of age in Uganda using geostatistical models, while

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exploring the potential association with environmental, nutritional, and sociodemographic factors. We hypothesize that the spatial distribution of pediatric fevers in Uganda is heterogeneous and impacted by these factors. Our analyses are keys for global health efforts to identify, mitigate, and develop targeted public health interventions relevant to smaller geographical locales.

METHODS

Data Sources

Outcome Data. We utilized data from the 2016 Uganda Demographic and Health Survey (UDHS). The UDHS is a nationally representative, population-based household survey conducted every 5 years using a stratified 2-stage cluster sampling design [20]. In the 2016 UDHS, the first stage involved selecting clusters based on the 2014 Uganda National Population and Housing Census, followed by the selection of households at the second stage; this resulted in a total of 20 880 households. Data were collected by the Uganda Bureau of Statistics (UBOS) from 15 June to 18 December 2016.

All women aged 15–49 years who were either residents or visitors of the selected households were eligible for an interview. During the interviews, eligible women were asked whether their children under 5 years of age had experienced a fever in the 2 weeks preceding the survey. Fever within the preceding 2 weeks was assessed based on caregiver recall; this is consistent with the World Health Organization–standardized Demographic and Health Survey (DHS) methodology. Validation studies have demonstrated that caregiver or parental assessment of fever provides reasonably accurate estimates of measured temperature. A systematic review and meta-analysis reported a pooled sensitivity of 87.5% (95% CI: 79.3%–92.8%) and specificity of 54.6% (95% CI: 38.5%–69.9%) for tactile detection of fever in children [21]. Similarly, a primary care study found that parents' subjective assessments had a sensitivity of 93% (95% CI: 73%–99%) and specificity of 75% (95% CI: 71%–80%) compared with thermometer-measured fever [22].

Covariate Data. We examined environmental, socioeconomic, and nutritional factors as potential risk factors for childhood fever. Environmental and socioeconomic data for Uganda were obtained from publicly accessible sources. Nutritional data were derived from the 2016 UDHS, in which blood samples were collected from children aged 6–59 months in one-third of the survey's selected households to examine conditions including anemia and Vitamin A deficiency. We interpolated the proportions of children with these conditions by creating raster files using a model-based geostatistical approach [23]. Data from previous studies were also used to estimate the proportions of children under 5 years of age who were underweight, stunting, or wasting [24, 25]. All covariate values were extracted at a spatial resolution of 1 km². A detailed list

of covariate data sources is provided in the Supplementary data (Supplementary Table 1; Supplementary Figures 1–6).

Geostatistical Modeling

We developed a geostatistical model to estimate the prevalence of febrile illnesses among children under 5 years of age in Uganda from June to December 2016. Based on this model, we predicted the monthly prevalence of fever. Parameter estimation for the geostatistical model and spatial prediction were performed using the R package *PrevMap* [23]. Model validation was conducted using nonrandomized probability integral transform (nrPIT). To assess the contribution of covariates to the spatial prediction, we compared the theoretical variogram from the estimated model with and without covariates. The detailed procedure is described below.

Exploratory Analysis. First, we assessed the relationship between the empirical logit of fever cases and each covariate by fitting univariate models. The enhanced vegetation index (EVI), rainfall, standardized precipitation-evapotranspiration index, and mean temperature were monthly variables; we examined their lagged values up to 3 months before the survey month for each cluster. The optimal lag for each variable was selected based on the lowest Akaike Information Criterion (AIC) value. AIC is defined as:

$$AIC = -2l(\theta) + 2k$$

where $l(\theta)$ is the maximum log-likelihood based on the estimated parameters θ , and k is the number of parameters in the model. Covariates demonstrating a strong linear relationship with the logit of fever prevalence, as determined by visual inspection, were selected. When covariates were highly correlated, the one with the lowest AIC value was retained in the geostatistical model. Consequently, poverty, anemia, 2-month-lagged rainfall, 1-month-lagged EVI, and seasonality (defined as “rainy season” for September to November and “dry season” for June to August or December) were included [26, 27].

Geostatistical Model. In the geostatistical binomial model, we included the selected covariates as fixed effects and accounted for both spatially structured and nonspatially structured random effects, such that

$$\log \left\{ \frac{p(x_i)}{1 - p(x_i)} \right\} = \beta_o + \sum_{j=1}^4 \beta_j d_j(x_i) + S(x_i) + Z_i,$$

where $p_i(x_i)$ and $d_j(x_i)$ represent the prevalence of febrile illness and covariate values, respectively, in cluster x_i . Each covariate was standardized by subtracting the mean and dividing by the standard deviation. $S(x_i)$ is a stationary and isotropic Gaussian process representing between-cluster variation, with mean zero, variance σ^2 , and correlation function $\rho(u) = \text{Corr}(S(x), S(x')) = \exp\{-|x - x'|/\phi\}$. ϕ is the scale

parameter controlling how rapidly spatial correlation decays with increasing distance between x and x' . Z_i represents independent and identically distributed Gaussian noise with mean zero and variance τ^2 , accounting for within-cluster variation such as measurement error. Parameters were estimated using Monte Carlo maximum likelihood (MCML).

Using the geostatistical model, we predicted the monthly prevalence of febrile illness from June to December 2016 at 5 km² spatial resolution. To estimate national-level prevalence in Uganda, we generated 10 000 predictive samples for each prediction location by MCML and weighted them by population data from WorldPop. The mean and 2.5% and 97.5% quantiles of these samples were used to compute the national mean prevalence and its 95% prediction interval.

Model Validation. We assessed the calibration of the predictive distribution. Calibration is the statistical consistency between probabilistic forecasts and observations. We employed nrPIT for count data [28], adjusting it for the geostatistical model [29]. We used 30% of the dataset as a test set and compared nrPIT from the model with and without covariates.

Assessment of the Contribution of Covariates to Spatial Prediction.

To quantify the contribution of covariates to spatial prediction, we compared the theoretical variograms of random effects from the model with and without covariates. The theoretical variogram is defined as

$$\tau^2 + \sigma^2 \left(1 - \exp \left\{ \frac{|x - x'|}{\phi} \right\} \right),$$

where τ^2 , σ^2 , and ϕ are the maximum likelihood estimates from the fitted model.

RESULTS

In the 685 surveyed clusters, 4990 of 14 195 children were reported to have had a febrile illness in the 2 weeks before the survey. The crude (or unadjusted) prevalence of fever widely ranged from ~0% to 100%, with a median of 30.43% (Figure 1).

The predicted prevalence varied both temporally and spatially. Based on the model, prevalence was highest in June, declined through September, and then increased thereafter (Table 1). Overall, the eastern and northeastern regions of the country had a higher prevalence than the southern regions throughout the study period (Figure 2).

According to the nrPIT, both models, with and without covariates, were well-calibrated (Supplementary Figure 7). This justifies the use of geostatistical models, although there was no practical difference between the models. We found that the inclusion of covariates into the geostatistical model reduced the uncertainty in spatial prediction, albeit not substantially. This is evident in the theoretical variogram (Supplementary Figure 8)

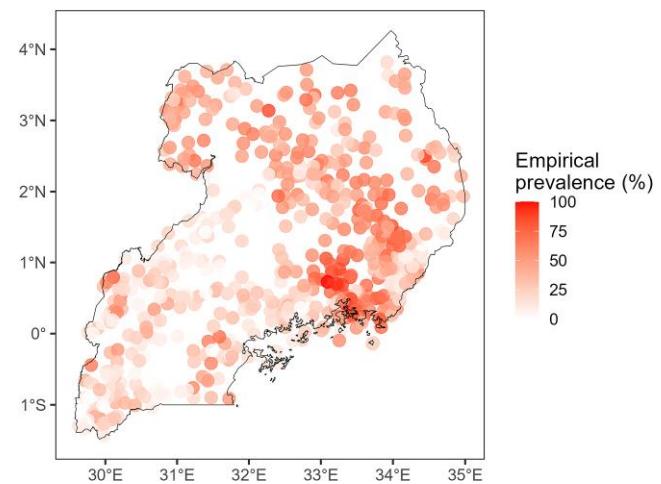


Figure 1. Crude (or unadjusted) prevalence of febrile illness among children <5 y from June to December 2016 in Uganda. The points represent the prevalence in each surveyed cluster.

Table 1. Predicted Prevalence of Febrile Illness Among Children <5 Years From June to December 2016 in Uganda.

Month	Predicted Prevalence (%)	95% Prediction Interval
June	43.30	42.45–44.14
July	39.49	38.62–40.45
August	37.15	36.31–37.96
September	29.43	28.7–30.25
October	29.85	29.07–30.67
November	31.84	31.06–32.63
December	38.99	38.06–39.83

The 95% prediction interval is derived from Monte Carlo maximum likelihood.

and parameter estimates (Supplementary Tables 2 and 3), as covariates reduced ϕ and τ^2 by explaining some of the spatial correlation exhibited in the data.

DISCUSSION

Using a geospatial modeling approach, we found that the prevalence of fever in Uganda exhibited both spatial and temporal distribution. Poverty, anemia, rainfall, and vegetation index were major factors contributing to these dynamics. These findings are crucial for public health interventions and identifying children at-risk for infectious diseases. They can guide future interventions tailored toward specific geographic regions with the greatest need.

Previous studies on febrile illnesses in LMICs have primarily focused on social, demographic, and economic factors associated with the epidemiology of childhood fevers [1, 9]. However, most have lacked analyses of environmental or climatic drivers of infectious diseases, which are major causes of fevers worldwide [5]. Our study goes beyond these limitations and provides

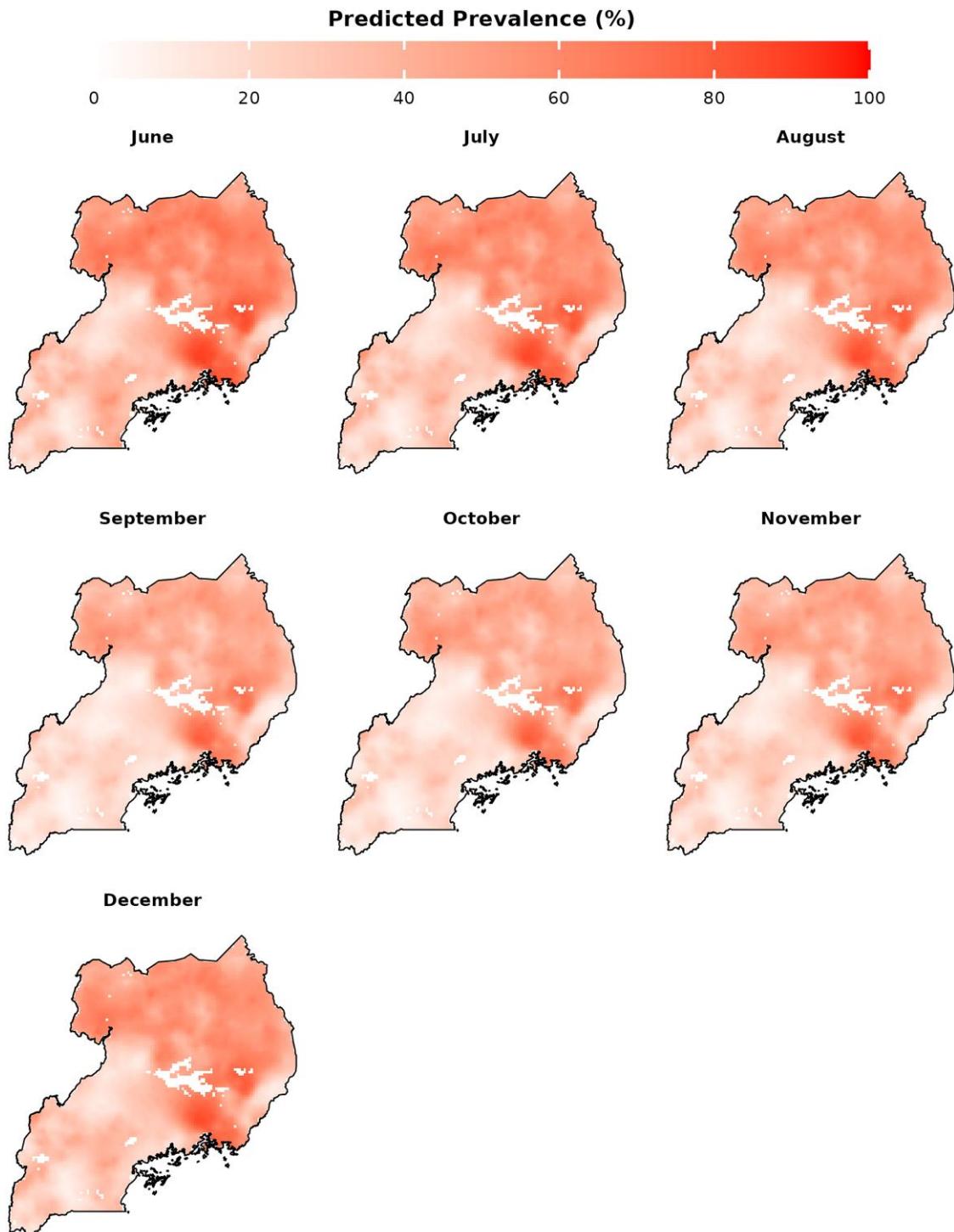


Figure 2. Predicted prevalence of febrile illness among children <5 y from June to December 2016 in Uganda. The prediction is at a 5 km resolution based on the geo-statistical model accounting for covariates.

critical evidence of key etiological and nutritional factors fundamental to known drivers of infections. We used fever as a proxy for infectious diseases in Uganda, implying that unstudied viral, protozoal, spirochaetal, and bacterial infections may be linked to precipitation.

Our findings can guide future research, pinpointing optimal locations and timing for biospecimen sampling of children or environments to identify key drivers of childhood febrile illness. They align with a growing body of literature demonstrating that climatic variability affects a wide spectrum of infectious

diseases beyond malaria [30, 31]. Extreme rainfall and humidity have been associated with meningococcal meningitis [32], and nontyphoidal *Salmonella* bacteremia [33]. Temperature fluctuations have been linked to meningitis incidence worldwide [34]. Collectively, these studies underscore that infectious-disease burdens are increasingly shaped by climate dynamics—a trend that supports integrating meteorologic and geospatial surveillance into pediatric fever monitoring and epidemic preparedness.

The positive association between febrile illness and EVI is not unexpected [35–38], as disease vectors like mosquitos thrive in dense vegetation and bushes. Therefore, strategies to prevent infections in the identified hotspots should focus on clearing bushes from near homesteads or incorporating the spraying strategies that were effective at eliminating malaria in the United States in the 1950s [39, 40].

While previous studies have explored the impact of poverty and malnutrition on infectious diseases at an individual level [41, 42], the most impactful interventions for both vector-borne and environment-driven infections are those applied at a regional or mass scale. While nutrition and vaccination programs are implemented nationally, geospatial risk mapping can refine the timing and geographic prioritization of outreach, such as intensifying malaria vector-control or immunization efforts in eastern and northeastern Uganda during high-risk rainy months. Such region-specific optimization aligns with evidence that coordinated vaccination campaigns designed to achieve herd immunity have far greater impact than interventions targeting individuals [43, 44].

Undernutrition undermines both adaptive and innate immunity, making opportunistic infections more common in affected individuals [45, 46]. Therefore, to effectively address febrile illnesses in LMICs, prioritizing proper nutrition is crucial. Our findings identify hotspots of febrile illnesses in Uganda that could benefit not only from improved treatment access but also enhanced nutrition through governmental and nongovernmental efforts [25]. Although the 2016 UDHS remains the most recent nationally geocoded dataset with environmental covariates, future analyses incorporating the completed 2022 DHS will allow assessment of changes in spatial risk under current warming trends. Ongoing climate change may intensify or shift the observed associations between rainfall, vegetation, and pediatric fever. Although there is no quick fix for poverty, population-based interventions like mandated food supplementation (eg, iodized salt, folate-fortified corn flour), access to clean public water sources, and immunizations can counteract the influence of personal wealth or household income [41, 47–49].

Our study has several strengths. Firstly, we employed robust model-based geostatistical methods for accurate mapping. Secondly, we incorporated key environmental, nutritional, and sociodemographic variables that are known to influence

infectious diseases; inclusion of these factors fine-tuned our model. Thirdly, our approach yielded actionable outcomes, guiding public health interventions by advising researchers on optimal sampling times and locations for fever cases in Uganda. Lastly, we included a large sample of participants (over 10 000) in our modeling approach, thereby providing a stronger statistical power.

Nevertheless, our findings should be interpreted with caution, bearing in mind inherent limitations. Firstly, we did not include all etiological factors that could influence the distribution of vectors that are associated with most infectious diseases in sub-Saharan Africa. Secondly, these findings cannot be generalizable to all sub-Saharan Africa due to differences in genetics, environments, political capital, social behaviors, economics, and the underlying herd immunity from immunizations. Comprehensive studies that incorporate all sub-Saharan countries are better positioned to address climate and infectious diseases in the region. Finally, fever ascertainment was based on caregiver report rather than direct thermometer measurement. Although this approach follows standardized DHS methodology, it introduces potential misclassification bias due to subjective perception. However, prior validation studies have shown that caregiver tactile and subjective assessments correlate reasonably well with objectively measured fever, with sensitivities exceeding 85% in both meta-analytic and primary-care evaluations [21, 22].

CONCLUSIONS

We identified extensive within-country spatial variation in the prevalence of febrile illness among children in Uganda, while highlighting associations with rainfall, poverty, EVI, and anemia. These findings may inform targeted public health policies for fever management and generate hypotheses for future etiologic research.

Supplementary Data

Supplementary materials are available at [Open Forum Infectious Diseases](#) online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Notes

Author Contributions. M. S., P. S., and C. F. had full access to all data in the study and take responsibility for the integrity and accuracy of the data analysis. Concept and design: P. S., M. S., and C. F. Data acquisition, analysis, or interpretation: M. S., C. M., and P. S. Manuscript drafting and critical revision for important intellectual content: M. S., C. M., P. S., and C. F. Statistical analysis: M. S. Supervision: P. S. and C. F.

Patient consent. This study used publicly available, de-identified survey data from the Uganda Demographic and Health Survey (2016). Therefore, patient consent was not required. The study conforms to ethical standards for secondary data analysis in the United States and Uganda.

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