Climate Influences on Meningitis Incidence in Northwest Nigeria

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ABSTRACT
Northwest Nigeria is a region with a high risk of meningitis. In this study, the influence of climate on monthly meningitis incidence was examined. Monthly counts of clinically diagnosed hospital-reported cases of meningitis were collected from three hospitals in northwest Nigeria for the 22-yr period spanning 1990–2011. Generalized additive models and generalized linear models were fitted to aggregated monthly meningitis counts. Explanatory variables included monthly time series of maximum and minimum temperature, humidity, rainfall, wind speed, sunshine, and dustiness from weather stations nearest to the hospitals, and the number of cases in the previous month. The effects of other unobserved seasonally varying climatic and nonclimatic risk factors that may be related to the disease were collectively accounted for as a flexible monthly varying smooth function of time in the generalized additive models, \( s(t) \). Results reveal that the most important explanatory climatic variables are the monthly means of daily maximum temperature, relative humidity, and sunshine with no lag; and dustiness with a 1-month lag. Accounting for \( s(t) \) in the generalized additive models explains more of the monthly variability of meningitis compared to those generalized linear models that do not account for the unobserved factors that \( s(t) \) represents. The skill score statistics of a model version with all explanatory variables lagged by 1 month suggest the potential to predict meningitis cases in northwest Nigeria up to a month in advance to aid decision makers.

1. Introduction

The strictly human pathogen *Neisseria meningitidis* is a gram-negative *diplococcus* that mainly causes meningitis (Rosenstein et al. 2001; Schuchat et al. 1997). Despite the existence of several bacteria that can cause meningitis, this bacterium is responsible for causing large epidemics [World Health Organization (WHO) 2012].
The associated symptoms of meningitis may include headache, fever, vomiting, and a stiff neck. The disease is a major public health burden in several countries around the world (Peltola 1983), but its magnitude is more profound in Africa, in an area mainly in the Sahelian region recognized as the meningitis belt by Lapeyssonnie (1963) and acknowledged by many (e.g., Greenwood 2006; Harrison et al. 2009; Molesworth et al. 2002).

Although the mechanisms by which climatic factors influence meningitis are still not well understood, it is believed that increased concentrations of dust, high winds, elevated temperatures, and low humidity may cause damage to the nasopharyngeal mucosa (WHO 2012), thereby increasing meningitis risk. Outbreaks have been associated with climatic and environmental factors in the meningitis belt (e.g., Besancenot et al. 1997; Mueller et al. 2008; Sultan 2005; Thomson et al. 2006; Yaka et al. 2008). The annual peak incidence of meningitis has been found to correlate significantly with the highest mean temperatures, and to correlate inversely with absolute humidity and rainfall (Dukić et al. 2012). Although some studies have concluded that prevalence of carriage does not vary with season (Greenwood et al. 1984; Trotter and Greenwood 2007), others have found a statistically significant link with seasonal and spatial climatic variability (Kristiansen et al. 2011). In the Sahel, the hypothesis that meteorological factors influence the seasonality of disease transmission (e.g., Jandarov et al. 2012) and the development of invasive disease is supported by the idea that the prolonged dry season, which normally starts in the “cold dry” months (November–January), may facilitate the occurrence of precursory diseases that increase meningitis risk in the subsequent “hot dry” months (e.g., Cartwright 1995). These previous efforts connecting climatic conditions to meningitis incidence suggest the possibility of predicting meningitis outbreaks using environmental information.

Other nonclimatic factors may also play important roles in the risk of meningitis transmission. Among these factors are socioeconomic, cultural, and behavioral practices; and migration. Previous studies have established the association between nonclimatic factors and meningitis risk—for example, previous incidents of other upper respiratory tract infections (URTIs), such as pneumococcal pneumonia (Moore et al. 1990), exposure to smoke from cooking fires (Hodgson et al. 2001), overcrowding (Brundage and Zollinger 1987), disco patronage (Cookson et al. 1998), and smoking (Fischer et al. 1997). To attain precision in simulating and possibly predicting any kind of climate-related disease epidemic, if possible, climatic variables should be jointly used with other nonclimatic factors as explanatory variables (Thomson et al. 2006; Palmgren 2009).

An extensive part of Nigeria lies within the meningitis belt (see appendix A). The disease primarily affects the country during the dry months, beginning with the Harmattan (a dry and dusty northerly wind) in November and continuing through May with peak incidence during the hottest months of March and April. During the 1996 epidemic, Nigeria alone reported over 100,000 cases and 11,000 deaths to the World Health Organization (WHO) (Mohammed et al. 2000), which is almost half of the total cases reported from the 25 countries within the belt. Most of these cases and deaths were reported from the northern part of the country, where there is a more pronounced dry season than in the south, and where the disease mainly occurs each year. Meningitis in northern Nigeria is known in the native Hausa language as “Sankarau,” literally meaning “the disease of stiffness,” obviously named because of the stiff neck often associated with the disease, caused by inflammation of tissues that surround the brain and the spinal cord. Anecdotal evidence suggests that many people in northern Nigeria believe that the disease is caused by the intense heat usually experienced during outbreaks. In Nigeria, meningitis transmission and invasion may be influenced by many factors apart from climate, such as socioeconomic and cultural practices. In the cities, areas mostly occupied by low-income earners are densely populated with many people per household, and most use wood as their source of cooking fuel. Based on previous studies such as Hodgson et al. (2001), people living in these areas are likely at higher risk and more vulnerable to the development, carriage, and transmission of invasive meningitis.

For the past 30 years, meningitis in Africa and Nigeria, in particular, has been occurring in sporadic cases, outbreaks, or even in large epidemics (Greenwood 2006) mainly caused by serogroup A (Greenwood and Stuart 2012; Riou et al. 1996). Until recently the only strategy for controlling the disease has been through reactive mass vaccination campaigns after crossing a certain case threshold (WHO Working Group 1998), using polysaccharide A vaccine, and sometimes through special campaigns intended for religious pilgrims. Although the efficacy of this vaccine has been established, it is expensive and has a short period of effectiveness (Wahdan et al. 1973). The introduction of the conjugate vaccine (WHO 2012) brings hope for controlling the disease. The new vaccine will not only provide longer protection but also prevent the disease (WHO 2012); that is, a whole population can be vaccinated proactively before meningitis epidemics are detected. Another advantage of the conjugate vaccine is carriage prevention (Maiden et al. 2008; Vestrheim et al. 2010). Despite these advantages, since the conjugate vaccine is serogroup A specific (Greenwood and Stuart 2012), other serogroups like

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W135 (Decosas and Koama 2002) and C (Broome et al. 1983) might continue to circulate, increasing the risk of epidemics (Koumare et al. 1993). These other strains could be introduced by travelers from outside regions (Lingappa et al. 2003).

The new conjugate A vaccine was recently administered in Nigeria in 2011 (O. Kale et al. 2011, unpublished manuscript). The vaccine was administered between 5 and 14 December 2011 during phase 1 (out of 3) of the campaign, which focused on the population group spanning 1–29 years of age in five northern Nigerian states: Bauchi, Gombe, Jigawa, Katsina, and Zamfara. The campaign did not influence the results of this study because the peak of our final year of meningitis case data had already ceased before the administration of the vaccine.

The current study aims to statistically model the influence of climate on monthly meningitis incidence in northwest Nigeria while collectively accounting for the effects of all unobserved climatic and nonclimatic factors that may be related to meningitis, such as social and behavioral practices, and migration. Our paper is the first to report a relationship between meteorological conditions (reflected by variables from station observations) and meningitis in Nigeria since the study by Greenwood et al. (1984); since that time, a much longer case record has been established. The model development and results are based on 22 years (1990–2011) of clinically diagnosed hospital-reported cases of meningitis.

2. Materials and methods

a. Study site and regional meteorological conditions

Northwest Nigeria is located in the African Sahel savannah region (see appendix A), and currently has an estimated population of over 41 million people based on the 2006 census. The regional climate (Fig. 1) is characterized by two seasons, a short wet season from June to September and a prolonged dry season for the remainder of the year. Daytime maximum temperatures remain consistently high throughout the year with maxima during March–May (up to 47°C), while relative humidity is low during the dry season and increases during the wet season. These mean regional climate conditions are mainly a consequence of the West African monsoon (WAM) system, which exhibits large spatiotemporal variability (e.g., Cornforth 2012), especially with respect to regional rainfall distributions. The WAM is a large-scale wind system characterized by moist northward flow from the Gulf of Guinea during the wet season and a dry and dusty southward flow (Harmattan) during the dry season. As meningitis is known to decrease with the onset of the monsoon, from a seasonal perspective, the variability of meteorological conditions should relate to the variability of incidence in specific regions such as northwest Nigeria.

b. Epidemiological data

Monthly counts of clinically diagnosed meningitis cases reported between 1990 and 2011 were collected in situ from selected hospitals in the region; see Fig. 2. The selection of hospitals was based on three criteria: (i) proximity to meteorological stations with long-term records of measurements, (ii) similar climatic patterns, and (iii) consistently reported records of infectious disease cases. In Nigeria, the Federal Ministry of Health (FMoH) classifies four categories of hospitals based on ownership status: federal, state, and local public hospitals, and private hospitals. Personal communication with FMoH staff prior to the data collection indicated that the state-owned hospitals best suited the above-mentioned criteria because most of the infectious disease cases are treated at these hospitals. Four hospitals in major regional cities met the first two requirements: Kaduna, Kano, Sokoto, and Gusau. Kaduna was not included in the model because it lies farther southward and has a distinct climatology, but the city was later used for testing the regional model. We also briefly summarize the results of a separate model developed for Kaduna in the discussion. In addition to the monthly case data from these three hospitals (1990–2011), we also obtained weekly records of suspected meningitis cases at the district level (from all hospitals in a district) in Nigeria for the years 2007–11, from the WHO. The proportion of cases between WHO and hospital records was rather constant across the study period, providing evidence that the records are of sufficient quality and that the hospital records are regionally representative (see appendix B).

It is noteworthy, for the sake of interpreting the results, that the collected meningitis cases are suspected cases clinically diagnosed based on the WHO recommended definition: as a person with sudden onset of fever (>38.5°C rectal or 38.0°C axillary) with one or more of following symptoms: neck stiffness, meningeal sign, or altered consciousness (WHO 2010).

c. Meteorological data

Digital records of seven variables from airport-based meteorological stations in each of the three cities were obtained from the Nigerian Meteorological Agency (Table 1). Daily precipitation and maximum and minimum temperatures were quality controlled using the software tool RClmDex.r (1.0), which has been developed and maintained by the Climate Research Division (2008) of the Meteorological Service of Canada on behalf of the Expert Team on Climate Change Detection...
and Indices. Other variables were manually quality controlled by removing obvious spurious values based on expert knowledge of the regional climate; too few values were removed to affect the overall quality and continuity of the meteorological data. Monthly averages, totals, or percentages were then computed from the quality controlled daily values.

In addition to meteorological records, monthly total estimates of carbon monoxide (CO) emissions (Tg month$^{-1}$) for the subperiod from 1997 to 2009 were produced for northwest Nigeria by version 3.1 of the Global Fire Emissions Database (GFEDv3.1) model (van der Werf et al. 2010). These emissions estimates are driven by satellite observations of active fires, burn area, and modeled vegetation information.

Both lag zero and 1-month lagged meteorological data were included as explanatory variables in the development of the models, while CO was only used for a sensitivity test because the data spans too short a period for inclusion in the final model development.

d. Demographic and vaccination campaign data

District-level population census data as of 2006 were obtained from the National Population Commission in Abuja, Nigeria. Annual population estimates for each city were calculated forward and backward from 2006 using the Nigerian population growth rate index (World Bank 2012). As vaccination campaigns will influence the number of meningitis cases that would occur in the absence of vaccination and thus can confound the model.

FIG. 1. Annual cycle of selected monthly meteorological variables, averaged over stations Kano, Sokoto, and Gusau in northwest Nigeria between 1990 and 2010. The vertical bars represent the ±1 standard deviation from the monthly mean, and the gray shading represents the range of monthly means over the 21-yr record.
results, we obtained information from FMoH on the specific years that reactive mass vaccination campaigns were carried out in the selected cities. Using an established methodology described below, this information was used to estimate the expected number of meningitis cases that would have occurred had there been no vaccination campaign. An additional model was then developed using these expected cases as predictands, and compared to the models that used the actual (unadjusted) cases as predictands.

e. Model overview

For statistical model development, monthly meningitis counts for the three hospitals in Kano, Sokoto, and Gusau were aggregated, and variables of the corresponding three meteorological stations were averaged. Distances between meteorological stations and the respective hospitals range between 3 and 6 mi. Monthly meningitis counts were aggregated in order to minimize the effect of bias in reporting to individual hospitals, and as well to have a regional perspective, which is the intent of this study. Generalized additive model (GAM) and generalized linear model (GLM) approaches were used. GAMs are a flexible extension of GLMs and are comprehensively described by Hastie and Tibshirani (1999). Because of the additive smoothing function within the GAM (cf. below), we can collectively account (albeit not specifically) for the effects of all unobserved
climatic and nonclimatic factors that may be related to meningitis.

Both GAM and simpler GLM frameworks were subsequently applied to model the influence of climatic conditions on the monthly variability of clinically diagnosed hospital-reported cases of meningitis. During model development, collinearity diagnostics and autocorrelation variables were performed, and explanatory variables were selected through a process of manually entering and removing variables from the model in a stepwise selection process, with a criterion of elimination being a p value \( \leq 0.05 \) when testing the significance of the coefficient estimate. The explanatory variables include meteorological variables aggregated monthly between the three selected stations (Table 1), as well as the previous incidence of meningitis in some models. Additionally, all other unobserved seasonally varying climatic and nonclimatic factors that may influence the disease were represented in GAMs by a smooth function of time, \( s(t) \), which was modeled as a low-degree cubic spline that changes monthly over the course of the annual cycle (Dukić et al. 2012). The variable \( s(t) \) is the so-called additive function characteristic of GAMs, and it captures the seasonality effect in a way that can be viewed as a smoothed analog of the month-specific effects. It is assumed that \( s(t) \) is common to all years (i.e., that there is no intercept that can be applied to adjust the function for a specific year). We assume that the clinically diagnosed hospital meningitis counts \( y_{i,t} \) follow independent Poisson distributions (thus, we use a log link function; Cameron and Trivedi 1998), with mean \( \mu_{i,t} \), where \( i = 1, \ldots, 22 \) denotes the years, and \( t = 1, \ldots, 12 \) denotes the month within each year. The GAM formulation is thus

\[
\log(\mu_{i,t}) = s(t) + X_{i,t}\beta.
\]

The expected meningitis count \( [E(y_{i,t}) = \mu_{i,t}] \) in year \( i \) in month \( t \) therefore depends upon the vector of coefficients \( \beta \), which contains the effects of climate variables collected in the covariate matrix \( X_{i,t} \), and upon the effects of the unobserved seasonally varying factors, \( s(t) \). The GAM is fitted and \( \beta \) and the parameters for \( s(t) \) are estimated. For the simpler GLMs, the equation is identical except that the additive function \( s(t) \) is removed if compared to the GAM.

f. Model fitting

To understand the sensitivity of models to a variety of a priori model choices, we fit three GAMs (denoted as models A, B, C) and a simpler GLM (denoted as model D). Model A was fitted with the combination of both 1-month lagged and nonlagged climatic variables and cases from the previous month; model B, with only the 1-month lagged explanatory climatic variables and cases from the previous month; and model C is the same as GAM A, except previous cases were excluded. All three GAMs were tested for a variety of degrees of freedom (DOF) for the fit of \( s(t) \), but it was found that those models in which \( s(t) \) has four DOF have the best fit. Model D, which is a GLM, has the same composition as model A but without the smooth component \( s(t) \). In summary, model A is intended to be the optimal explanatory model of meningitis cases, whereas model B by using only lagged variables is intended to be the optimal predictive model (with 1-month lead time). Model C, which does not include previous cases, is intended to be used for future climate change studies (since the number of cases in the previous month is unknown in the future). Model D is meant to test whether adding a smooth function of time \( s(t) \) improves the model fit. All models were fit within R statistical software (R Core Team 2009).

The best models were selected by minimizing the Bayesian information criteria (BIC). Variable selections were made separately for each model, although the same variables were retained in all models but variables were all lagged by 1 month in model B, while previous cases were not included in model C. The retained variables in models A and D include the current mean monthly maximum and minimum temperatures; precipitation totals; average relative humidity, sunshine, and the 1-month lag of wind speed; dustiness; and cases (i.e., cases in the previous month).

A population offset term (to account for population growth) was not included in our models because estimating the changes to the population served by a single hospital, the source of our records, is highly uncertain. For example, as population grows, new hospitals and other treatment facilities are built to accommodate more patients, so the population served by a given hospital does not fluctuate linearly with regional population growth.

g. Model validation

The robustness and accuracy of models were assessed using a threefold cross-validation technique, the root-mean-square error (RMSE), and the skill score (Murphy 1988). All three statistics were computed for observed versus predicted values for each model. To perform the cross validation, we partitioned the data into three consecutive subsets of equal length. We successively excluded one of these subsets, fitted the model on the remaining data and computed the fitted values for the excluded subset. We then combined the fitted values that were obtained into one time series for ease of comparison with the “full model” (i.e., based on all 22 years of
The skill score provides a measure of the prediction accuracy of the models by comparing the models’ predicted RMSE, $E_{\text{pre}}$, with that of a reference model $E_{\text{ref}}$, written as

$$\text{Skill score} = 1 - \left( \frac{E_{\text{pre}}}{E_{\text{ref}}} \right).$$

In this case, $E_{\text{pre}}$ represents the RMSE of the monthly model-predicted cases compared to the observed cases, while $E_{\text{ref}}$ represents the RMSE of the long-term monthly mean of the observed meningitis cases, also compared to the observed cases for each month and year. The reference model is thus a persistence model: if one did not have a model, then they could predict cases for a given year and month by assuming that they will equal the long-term average of cases for that month, based on observations from other years. The skill score is the percentage of improvement or deterioration of a given model’s RMSE with respect to the reference model.

To gain a perspective on the average comparative importance of each covariate for a given month, we compute the relative influence (RI) by estimating the effect of each covariate with respect to all the covariates in the model, based on the long-term monthly means of each covariate over the 22-yr period, as well as the monthly value of $s(t)$. The RI for a GAM is calculated as a percentage of all terms for a given month as follows:

$$RI = 100 \left\{ \frac{\overline{X}_{t,\vartheta} \beta_{\vartheta}}{|s(t)| + \sum_{v=1}^{n} \overline{X}_{t,v} |\beta_{v}|} \right\},$$

where in the numerator $\overline{X}_{t,\vartheta}$ is the long-term mean of $X$ for a given month, $t$, and $\vartheta$ denotes a particular variable within the vector of $X$ (e.g., $\text{Tmin}$), and $\beta_{\vartheta}$ is the coefficient that corresponds to that particular variable. In the denominator $s(t)$ is the month-specific additive function (which does not vary by year) and $\sum_{v=1}^{n} \overline{X}_{t,v} |\beta_{v}|$ is the sum of all other model terms $\overline{X}\beta$ over all variables from $v = 1$ to $n$ (maximum and minimum temperatures, relative humidity, dust, etc.), for a given month $t$. The absolute values are taken for the coefficients, $\beta$ and $s(t)$ in the denominator, in order to omit negative terms in the equation; otherwise, the RI of a given term may be inflated due to cancellation of negative and positive terms.

### h. Sensitivity tests

We performed three tests of model sensitivity to 1) the influence of accounting for vaccination campaigns in the case data, 2) the influence of including CO emissions as an explanatory variable, and 3) whether the model can...
be applied outside our immediate study area. The first test requires greater description here.

We could not account for vaccination efficacy carried out within the study period directly in our models because we do not have a reliable record of the number of people vaccinated and the time of administration for any of the four campaigns. However, to test the sensitivity of the model fit and accuracy to the influence of vaccination, we refit the model to an adjusted case dataset that accounts for vaccinations. The proportion of cases assumed to be mitigated during epidemic years by the polysaccharide A vaccine were estimated based on information collected from the FMoH indicating the years and districts in which vaccination campaigns were conducted. The month in which the vaccination campaign began was estimated to be the first month during an FMoH-indicated vaccination year in which the average case rate exceeded 20 per 100 000 persons (this was required because FMoH did not indicate the month in which vaccination was begun). The threshold of 20 cases per 100 000 in a given month was chosen because we were limited to monthly resolved case data, whereas the officially defined threshold for epidemics (which trigger reactive vaccination campaigns) is 10 cases per 100 000 based on weekly data. Considering the strong weekly variability of case counts, it is likely that at least one week in a given month would have epidemic conditions (10 cases per 100 000) if 20 cases per 100 000 or more are reported for a given month.

The proportion of cases mitigated due to vaccination campaigns was estimated by comparing the number of actual cases occurring in a given month with a projection of the number that may have occurred supposing polysaccharide vaccination was not administered, using the following equation (Leake et al. 2002; Pinner et al. 1992):

\[
EC = OC[(1 - VE)(PV) + PNV],
\]

where EC is the monthly estimate of expected cases if vaccination was not carried out, OC is observed cases, VE is vaccine efficacy, PV is the proportion of population vaccinated, and PNV is the proportion of the population not vaccinated; VE is defined to be 85% in the month following vaccination administration (e.g., Reingold et al. 1985), and it decreases linearly to zero over the next 30 months in order to simulate for the development of postvaccination immunity and diminishing effect. The choice of 30 months was made because polysaccharide A vaccine has an efficacy of approximately 2–3 years or even less in children under 4 years of age (e.g., Reingold et al. 1985). Because of uncertainties about PV, we calculated EC for different plausible bounds of PV, 40% and 60%.

### 3. Results

#### a. Model performance

Generally, both the individual and aggregated counts of the monthly hospital-reported meningitis cases exhibit a marked annual cycle, with yearly disease onset and maxima occurring during the beginning of the dry season (November) and the peak of the hottest months (March and April). Also, as in other places in the meningitis belt, cases decrease with the increase of humidity and the onset of the rainy season. See appendix A shows the individual contribution of each hospital.

The shape of \( s(t) \) is shown in Fig. 3 for the best models, A and B. The shape of the estimated function of both models is similar and follows the seasonality of the disease, with the months of February–April having the highest values of \( s(t) \). The model estimates and standard errors for models A and B are presented in Tables 2 and 3, respectively. Models C and D are not shown for brevity, but their estimates are similar (their skill is discussed below). Current maximum and minimum temperatures, sunshine duration, and 1-month lagged dust frequency and wind speed are positively correlated with disease incidence, while relative humidity and precipitation are inversely correlated in all models. Figure 4 shows the 22-yr time series of observed cases versus predicted cases for models A, B, and D (results were similar for model C).

The threefold cross-validation technique gives us a way to verify our results (Table 4), as well as an indication of how sensitive our model fits are to the period we selected for development; for example, if the model fits were substantially different in the early 1990s versus the late 2000s, the “full” versus cross-validated statistics would be notably different. As Table 4 shows, the fit between the observations and both the full and the cross-validated model statistics are remarkably good and almost similar, indicating that the meningitis case dynamics were
similar throughout the 22-yr period. As expected, model A is the best model as measured by cross-validation correlation (CVC) and skill score (0.75 and 0.52, respectively). The skill score indicates that the RMSE of model A is 52% lower than if one assumes the number of cases in a given year and month are equal to the long-term monthly average of observed cases for that month; thus, model A exhibits substantial skill compared to doing no modeling at all. The 1-month lag model B also has similar CVC and skill score statistics (0.73 and 0.45, respectively), suggesting its potential for short-term prediction of cases. Likewise, model C has similar statistics, suggesting it may be useful for exploring how cases may change in the future as a function of climate change. Model D (the GLM) has a lower CVC and skill score (0.62 and 0.40, respectively) compared to the GAMs, suggesting that the GAM additive function $s(t)$ is effective in capturing some of the unobserved seasonally varying factors that may affect meningitis.

The relative influence of each explanatory variable for the four months in which meningitis incidence is generally high is shown in Fig. 5. Overall, the maximum temperature shows a comparatively important influence on the fitted meningitis cases for models A and B.
Regardless of the model, the relative influence of maximum temperature increases from about 30% in January to over 35% in April during the peak of meningitis incidence. The influence of average relative humidity remains almost the same across the months, having an important negative influence of about $-15\%$; this is because humidity usually remains consistently low throughout the dry season. As expected, the dust and wind speed influence is higher in the cold dry months in which the Harmattan is strongest. Rainfall plays a negligible role throughout these months because it rarely rains (Fig. 1). The number of cases in the previous month provides a comparatively modest influence of up to about 10%. The function $s(t)$, which accounts for unobserved seasonally varying explanatory variables, varies in influence from about 6% to 15%, suggesting that unexplained factors are important drivers of meningitis incidence, especially during the annual peak of cases.

### Table 4. Model validation results, given by correlation and skill score. Full and CV stand for full and threefold cross-validated models, respectively.

<table>
<thead>
<tr>
<th>Models</th>
<th>Kendall correlation</th>
<th>Skill score</th>
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<tbody>
<tr>
<td></td>
<td>Full</td>
<td>CV</td>
</tr>
<tr>
<td>A</td>
<td>0.762</td>
<td>0.746</td>
</tr>
<tr>
<td>B</td>
<td>0.740</td>
<td>0.732</td>
</tr>
<tr>
<td>C</td>
<td>0.750</td>
<td>0.736</td>
</tr>
<tr>
<td>D</td>
<td>0.634</td>
<td>0.616</td>
</tr>
</tbody>
</table>

**Fig. 5.** Relative influence of explanatory variables on meningitis in northwest Nigeria for models A and B, for the dry-season months in which the meningitis burden is typically highest: January, February, March, and April.
Model sensitivity

1) EXPERIMENT 1

As described in section 2h, to investigate the influence on our results of the four vaccination campaigns that occurred between 1990 and 2011, we estimated the expected cases that would have occurred in the absence of the campaigns. A model was fit using the expected cases as predictands and retaining all of the explanatory variables used in model A, except the previous month’s cases. We omitted previous cases because we intend to employ this model in a follow-up study to investigate the impacts of climate change on meningitis in the absence of vaccination (because it is impossible to know what vaccine advancements will occur in the future). The new model is therefore identical to model C, except it is trained on the expected case data rather than the actual case data. The new model (with PV = 40%) has a higher CVC and skill score of 0.75 and 0.52, respectively, compared to model C (0.74 and 0.48, respectively). The slightly higher skill score of the new model compared to model C is perhaps expected, since the additional effects of vaccination are at least partially removed, and therefore the explanatory climate variables are targeting a largely expected number of meningitis cases without vaccination. Since the choice of PV is somewhat arbitrary, we also fitted a model assuming a different proportion of the population was vaccinated, PV = 60%, and found that the values and significance of the model coefficients in the GAM are relatively insensitive to the choice of PV (see appendix B), although the best model fit is for the case of PV = 40%.

2) EXPERIMENT 2

Air quality contributes to the risk and incidence of meningitis in northern Ghana (e.g., Hodgson et al. 2001). We investigate this in northwest Nigeria by refitting model A, keeping all of the variables in the model but now including the total regional CO from biomass burning emission estimates (for the 15-yr period from 1997 to 2009, for which we have CO data). Although the previous month’s CO emissions are significant in the model, it does not substantially change the model estimates for other explanatory variables, and it does not appreciably change the model fit (see appendix B). Therefore, biomass burning CO emissions, and presumably other air pollutants released in conjunction with the CO, do not appear to exert much influence on meningitis incidence in northwest Nigeria compared to the other meteorological variables in the model.

3) EXPERIMENT 3

For the purpose of testing the model elsewhere, we use the estimated coefficient of model A to predict cases for Kaduna, and then compare the predicted time series with that observed from Kaduna hospital. Although the fit is not as good as that of model A (CVC = 0.57 and skill score = 0.39), the monthly variability of cases is reasonably captured. We also fitted a completely new GAM with four DOF specifically for Kaduna city, employing the same variables as for model A. The estimates of this model are shown in appendix C. The only difference of this model with model A is that the rain variable is less significant, but the model remains qualitatively similar in terms of predictive power. This suggests that the explanatory variables employed in our models may be relevant for simulating meningitis incidence in other regions of Nigeria, and perhaps the broader Sahelian region [this is supported by the fact that Dukić et al. (2012) found similar explanatory variables when modeling meningitis incidence in northern Ghana].

4. Discussion

In this study, we employed both GAMs and GLMs to model the influence of meteorological conditions on the monthly meningitis incidence from three hospitals in northwest Nigeria, using monthly aggregate counts of clinically diagnosed hospital-reported meningitis cases for 1990–2011. The case data exhibit a marked annual cycle, with yearly disease maxima occurring during the peak of the hot dry season in March and April. Explanatory variables in the models include meteorological variables, cases from the previous month, and $s(t)$ in the GAMs. Model performance was estimated by threefold cross validation, RMSE, and skill score.

The results indicated that both explanatory (fitted with the combination of lagged and nonlagged climatic variables) and predictive (fitted with only 1-month lagged climatic variables) models showed similar capabilities to fit values of meningitis incidence. The best explanatory model (A) had a CVC of 0.75 with the observations and
a skill score of 0.52 out of 1.0. Additionally, the cross-validation version of model A (that was developed by systematically omitting the first, middle, and last 7 years of case data) exhibited nearly identical statistics to the full model that was fit using all 22 years of case data, indicating that the model performance is not sensitive to the period chosen for development. Although the best predictive model B was not as powerful as the best explanatory model A in terms of fitting performance, it has strong potential for short-term disease prediction, having a CVC of 0.73 and a skill score of 0.45. It is noteworthy that all of the most successful models were GAMs, suggesting that model fit is substantially improved by employing the monthly varying $s(t)$. Despite the fact that reliable vaccination data are difficult to obtain, we estimated the expected number of cases that would have occurred assuming the vaccination campaigns were not carried out. We then fit a model to these expected cases and found that the model fit and accuracy changed very little, suggesting the results are reasonably insensitive to whether vaccination is accounted for. Regardless, documentation of vaccination campaigns may improve for future studies, as Nigerian authorities are now keeping detailed records of vaccination campaigns for the ongoing MenAfriVac (the new conjugate A vaccine). The recent change in strategy from reactive to preventive vaccination is a welcome development in the effort of controlling the disease; however, there is need for continual surveillance because other strains not covered by the conjugate vaccine may cause epidemics (e.g., Koumare et al. 1993).

Although, there is no agreed-upon physical explanation for the role of meteorological conditions in the incidence of meningitis (e.g., Cheesbrough et al. 1995), our results support the hypothesis that hot, dry, dusty conditions may facilitate both the transmission and the development of invasive meningitis in northwest Nigeria. For example, these conditions might be playing important role during the cold dry months, aiding in initiating the meningitis season by causing microtrauma to the nasal mucosa (Burgess and Whitelaw 1988). This damage may make it possible for the bacteria to penetrate the nasopharyngeal membrane and subsequently enter the bloodstream, causing invasive disease. This may explain why

Table A1. Experiment 1, showing model estimates for two bounds of PV. Asterisk means that variables lagged by 1 month.

<table>
<thead>
<tr>
<th>Predictors</th>
<th>PV = 40%</th>
<th>PV = 60%</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Coef</td>
<td>Std error</td>
</tr>
<tr>
<td>Monthly-mean Tmax (°C)</td>
<td>0.0827</td>
<td>0.0069</td>
</tr>
<tr>
<td>Monthly-mean Tmin (°C)</td>
<td>0.0576</td>
<td>0.0078</td>
</tr>
<tr>
<td>Rain (mm)</td>
<td>-0.0039</td>
<td>0.0006</td>
</tr>
<tr>
<td>Relative humidity (%)</td>
<td>-0.0403</td>
<td>0.0024</td>
</tr>
<tr>
<td>Wind speed (km h⁻¹)</td>
<td>0.0143</td>
<td>0.0048</td>
</tr>
<tr>
<td>Sunshine (h)</td>
<td>0.0494</td>
<td>0.0124</td>
</tr>
<tr>
<td>Dusty days (%)</td>
<td>0.0166</td>
<td>0.0007</td>
</tr>
</tbody>
</table>

**FIG. B1.** Reported cases of meningitis from three hospitals in Kano, Sokoto, and Gusau (dashed) in comparison with reported cases at the WHO district level from corresponding districts (solid) between 2007 and 2011.
reported meningitis cases are highest during the hot dry period (February–May) that follows the cold dry period. Unobserved seasonally varying nonclimatic factors such as the occurrence of URTIs, and societal and behavioral practices, which are represented in a very basic sense by the function \( S(t) \), are likely to enhance the transmission of the disease in this region. For example, during the cold dry period (which favors diseases such as influenza) people are often overcrowded in rooms and sometimes cluster around wood fires for warming. This overcrowding (e.g., Brundage and Zollinger 1987) might enhance transmission through respiratory droplets, while particulates from wood fires may irritate the lining of the nasal mucosa. Additionally, social gatherings such as marriages and economic activities in market places tend to be more frequent and active during this season.

5. Conclusions

Our results indicate the role of specific meteorological conditions in explaining and predicting monthly meningitis variability in northwest Nigeria, and also emphasize the importance of additional risk factors that are not well understood but may be linked to societal and behavioral practices. With respect to the latter, we are currently limited only to collectively accounting for these unobserved seasonally varying climatic and nonclimatic risk factors via functions such as \( S(t) \). Identifying and quantifying such factors and improving disease surveillance will likely enhance our understanding and ability to predict and reduce meningitis incidence.

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APPENDIX A

Meningitis Belt Map and Vaccination Influence

A map of the African meningitis belt is shown in Fig. A1 Experiment 1 is detailed in Table A1.

![Fig. C1. Distribution of meningitis cases from the three selected hospitals in northwest Nigeria.](image-url)
TABLE C1. Experiment 3, showing model estimates for Kaduna. Asterisk means that variables are lagged by 1 month.

<table>
<thead>
<tr>
<th>Predictors</th>
<th>Coef</th>
<th>Std error</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Monthly-mean Tmax (°C)</td>
<td>0.0872</td>
<td>0.0042</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Monthly-mean Tmin (°C)</td>
<td>0.0613</td>
<td>0.0023</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Rain (mm)</td>
<td>-0.0054</td>
<td>0.0031</td>
<td>&lt;0.050</td>
</tr>
<tr>
<td>Relative humidity (%)</td>
<td>-0.0462</td>
<td>0.0034</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Dusty days (%)*</td>
<td>0.0285</td>
<td>0.0016</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Wind speed (km h⁻¹)*</td>
<td>0.0166</td>
<td>0.0040</td>
<td>&lt;0.010</td>
</tr>
<tr>
<td>Sunshine (h)</td>
<td>0.0327</td>
<td>0.0150</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Previous month cases</td>
<td>0.0116</td>
<td>0.0123</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

APPENDIX B

Meningitis Cases in Northwest Nigeria and the Role of Biomass Burning

The cases of meningitis reported compared with WHO district level cases from the period 2007–11 are shown in Fig. B1. Experiments 2 described in Table B1.

APPENDIX C

Individual Hospital Meningitis Counts and Kaduna Model

The individual counts of meningitis reported from Kano, Sokoto, and Gusau are displayed in Fig. C1. Experiment 3 is described in Table C1.

REFERENCES


