Relating climate information to meningitis incidence in sub-Saharan Africa: The impact of scale

Michelle Stanton, Carlos Perez, Sylwia Trzaska, Peter Diggle and Madeleine Thomson

Division of Health and Medicine, Lancaster University
and
International Research Institute for Climate and Society, Columbia University

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Outline

1. Introduction to Meningococcal Meningitis in sub-Saharan Africa
2. Summary of research into the relationship between climate and meningitis
3. Meningitis Environmental Risk Information Technologies Project
4. Exploring the relationship between meningitis and climate at various spatial and temporal scales
   - Temporal scale: Weekly and Annually
   - Spatial scale: National and District

Introduction to Meningococcal Meningitis

What is Meningitis?

- Most common form of meningococcal disease (95% of cases)
- Caused by the bacteria *N. meningitidis*
- Public health concern due to its rapid onset and high case fatality rate (10-50%)
- The bacteria itself is contagious, but asymptomatic carriage is common
- Bacteria is transmitted from person to person via respiratory droplets or saliva
- In developed countries, approx 10% - 25% are carriers of the bacteria
- This varies according to certain risk factors
- Factors which facilitate the invasive disease are not well understood

Introduction to Meningococcal Meningitis

Meningitis symptoms and risk factors

Symptoms

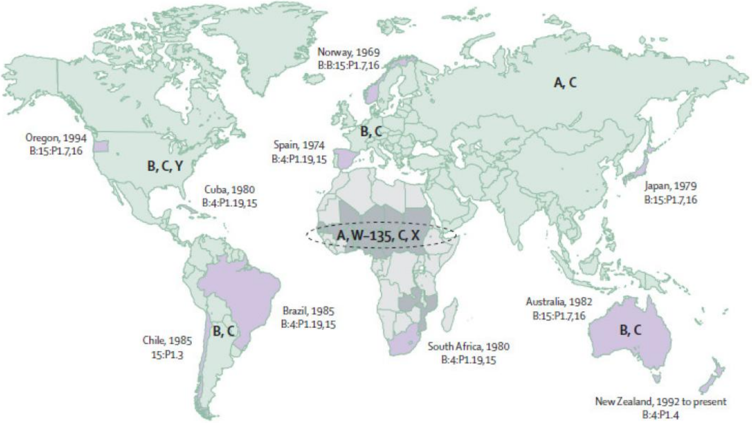
- Infection of the lining of brain
- Stiff neck
- Fever
- Sensitivity to light
- Rapid onset

Risk Factors

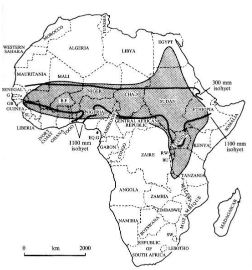
- Age
- Socio-economic conditions
- Pre-existing conditions
- Vaccination coverage

Introduction to Meningococcal Meningitis

Global distribution of meningitis



- Serogroups B & C result in *sporadic cases* (Europe & Americas)
- Serogroup A results in *epidemic meningitis* (Asia, Africa)



Cheesbrough *et al.* (1995)

Characteristics of the belt

- Mean annual rainfall 300mm to 1100mm
- Prolonged dry season of low humidity
- Affected by Harmattan winds during dry season

Meningitis within the belt

- 21 countries, and an at-risk population of 300 million
- 700,000 cases in the past 10 years
- Seasonality - peak in March, few cases during the wet season
- Early cases ⇒ high incidence

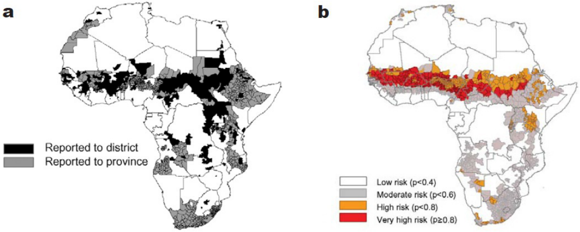
Introduction to Meningococcal Meningitis

Summary of climate-related research

Despite the link between meningitis and climate being recognised almost 50 years ago, relatively little research has been undertaken to explore (and exploit) this relationship.

Previous research has focused on both the **spatial** (*where*)and **spatio-temporal** (*where and when*) distribution of meningitis epidemics

Spatial: Using climate to determine which geographical areas are likely to be affected by meningitis epidemics (Molesworth *et al.* (2003))



Introduction to Meningococcal Meningitis

Summary of climate-related research

Spatio-temporal: Using climate to predict when and where epidemic will occur

Variable	Location
Abs. Humidity	**Zaire**, *sub-national, monthly* (Cheesbrough *et al.*, 1995), **Benin**, *district, monthly* (Besancenot *et al.*, 1997), **Burkina Faso**, **Niger**, *national, annual* (Yaka et al, 2008)
Wind	**Mali**, *national, weekly* (Sultan *et al.*, 1997) **Benin**, *district, monthly* (Besancenot *et al.*, 1997)
Rainfall	**Burkina Faso, Mali, Niger, Togo**, *district, monthly* (Thomson *et al.*, 2006)
Dust	**Burkina Faso, Mali, Niger, Togo**, *district, monthly* (Thomson *et al.*, 2006)

Can this be used to assist in epidemic preparedness and control?

Introduction to Meningococcal Meningitis

How do we explain these relationships?

The mechanisms responsible for these observed relationships are currently unknown.

Hypothesis 1: *Climate conditions facilitate the bacteria entering the blood stream by irritating the lining of the throat*

Hypothesis 2: *Climate influences carriage rates i.e modifies the transmission of the bacteria*

Further social determinants may have an influence, as colder nights result in more overcrowded conditions occurring during the evenings.

Introduction to Meningococcal Meningitis

Current epidemic control strategy

Epidemics within the meningitis belt are controlled via a *reactive* vaccination strategy operated at the district-level on a weekly time scale.

The process

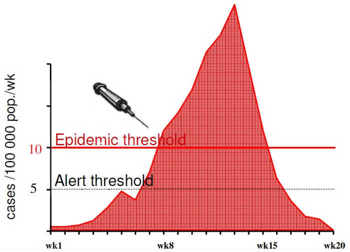
1. Routine surveillance is initiated at the beginning of the dry season, with weekly reports being collated at the district-level by the WHO
2. If incidence > 5 cases per 100,000 population, precautionary measures are implemented, and vaccine supplies are requested
3. If incidence > 10 cases per 100,000 population, mass-vaccination campaigns are initiated throughout the specific district

In practise

- It is likely that only part of a district is targeted for vaccination
- District borders are unlikely to be adhered to

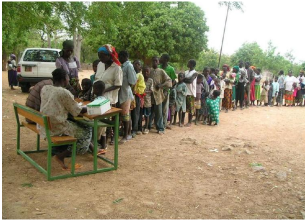
Problems associated with this strategy:

- Weaknesses of the currently used vaccine (no effect on carriage, short-term immunity, not suitable for children < 2yrs)
- Relies heavily on timely surveillance
- Often substantial delays between requesting the vaccine, and delivery of the vaccine (11m doses delivered in 4-23 days, 2009)
- If vaccine is administered between 2-4 weeks of epidemic onset, at most 70% of cases are prevented
- Campaigns begin this quickly only 60% of the time.



MenAfriVac - A new meningitis A vaccine

- Affordable at $\approx$ 30p per dose
- Induces long-term immunity
- Induces herd immunity
- Is safe to use in children $<$ 2yrs



Mass Vaccination Campaign

- Between 2010-2015 administer to 250m 1-29 year olds
- Initially target Niger, Mali & Burkina Faso
- Need to continue using the reactive vaccination strategy until entire at-risk population is immunised
- Epidemics may still occur following the mass vaccination campaign ($<$100% coverage, different serogroups)

MERIT project

Utilising the relationships between climate and meningitis

Meningitis Environmental Risk Information Technologies

A collaborative project involving WHO and members of the environmental, public health and epidemiological communities.

Aim:

1. Improve the understanding of the relationship between meningitis and environmental/climate parameters
2. Use this knowledge to improve the efficacy of meningitis prevention and control strategies

MERIT project

Utilising the relationships between climate and meningitis

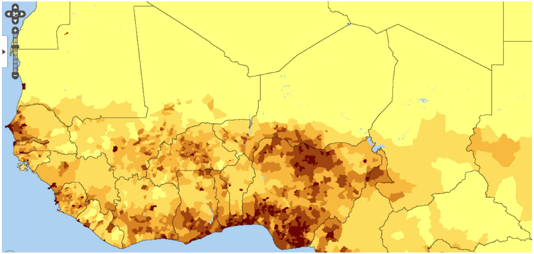
How can climate information improve this process?

1. **Pre-season**: Use climate forecasts to determine the risk of an epidemic in the coming season, and request vaccine supplies accordingly
2. **During the season**: Monitor incidence levels and climate conditions throughout the season, and use this information to predict the probability that the alert/epidemic threshold will be exceeded in future weeks, and hence inform a decision support tool

Therefore, we need to examine the relationship at two different time scales

1. **Annual scale** approach followed that introduced by Yaka (*2008*), who looked at the relationship between monthly averaged climate variables and annual incidence of meningitis in Burkina Faso and Niger
2. **Weekly scale** approach was an extension of PhD work during which short-term forecasting models were developed using previous incidence alone as predictors

A Case Study: Niger

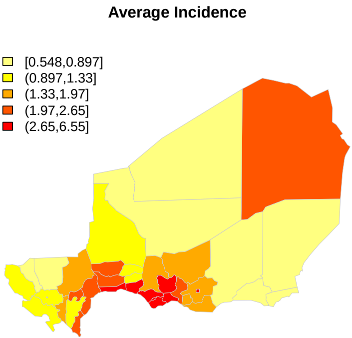


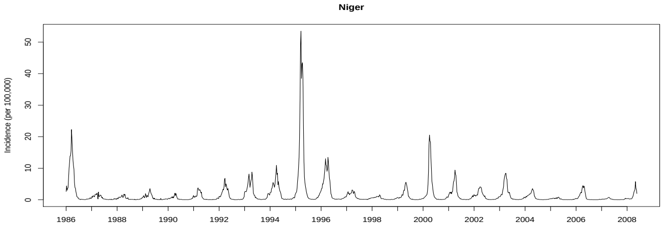
CIESIN: Gridded Population of the World

- Population ≈ 15m
- 42 administrative districts
- One of the most affect countries within the belt
- Weekly surveillance data from 1986

A Case Study: Niger

Incidence Data





A Case Study: Niger

Climate and Dust Data

- Regional Reanalysis
- Long-term simulation were performed with a regional atmospheric dust model
- Resolution was set to 1° by 1°
- The simulation was reinitialized every 24 hours and the boundary conditions we taken from
  - Global NCEP Reanalysis-I pressure level data
  - GLDAS for soil moisture and temperature
- Data were aggregated to the appropriate spatial resolution using the IRI Data Library (`http://iridl.ldeo.columbia.edu/`)
- Variables considered included
  - **Surface**
    - Specific, Absolute and Relative Humidity
    - Temperature
    - Zonal and meridional wind components, plus wind speed
    - Dust concentration and dust optical depth
  - **Atmosphere (925hPa $\approx$ 800m above sea level)**
    - Specific humidity
    - Temperature
    - Zonal and meridional wind components

A Case Study: Niger

Temporal scale: Annual

Modelling approach

- Examine the relationship between *January-March* incidence, and averaged climate variables
- Climate variables were averaged over a range of consecutive months from *September-March* e.g *September-October*, *September-November*, *October-November* etc.

National-level analysis

- For each climate variable at the national level, initially restricted the variables under consideration by examining the correlation between log(Jan-March incidence) and climate variables.

A Case Study: Niger

Temporal scale: Annual

Meridional Wind 10m

Speed	Sep	Oct	Nov	Dec	Jan	Feb	Mar
Sep	-0.1997	0.0545	0.3277	0.5211	0.4351	0.2722	0.1255
Oct	NA	0.1528	0.3749	0.5253	0.4320	0.2870	0.1498
Nov	NA	NA	0.4901	**0.5738**	0.4573	0.2660	0.1091
Dec	NA	NA	NA	0.5229	0.3468	0.1457	-0.0317
Jan	NA	NA	NA	NA	0.0284	-0.0588	-0.2293
Feb	NA	NA	NA	NA	NA	-0.1011	-0.2796
Mar	NA	NA	NA	NA	NA	NA	0.5229

- Selected the two monthly averages with the largest correlations (one surface, one atmosphere if available). Further variables we considered included:
  - Specific Humidity (*Jan-Feb 2m, Feb 925hPa*)
  - Temperature (*Sep-Dec 2m, Sep-Dec 925hPa*)
  - Meridional wind (*Nov-Dec 2m, Nov-Dec 925hPa*)
  - Zonal wind (*Nov-Jan 2m, Nov-Jan 925hPa*)
  - Dust Concentration (*Nov-Dec, Oct-Dec*)

A Case Study: Niger

Temporal scale: Annual

- Fitted a Negative Binomial model to the count data, and modelled the mean μ_t as

$$\log(\mu_t) = \alpha + \beta X_t + \log(N_t)$$

  A Poisson model restricts *variance* $=$ *mean*, whereas a Negative Binomial model allows *variance* $>$ *mean*

- Model selection was then used to determine which combination of parameters was able to explain the temporal variation in meningitis incidence most fully.

Additional (missing) risk factors:
A key influence which needs to be considered is **immunity**. By not accounting for a measure of immunity in a model, the effects of climate on meningitis incidence will be difficult to disentangle.

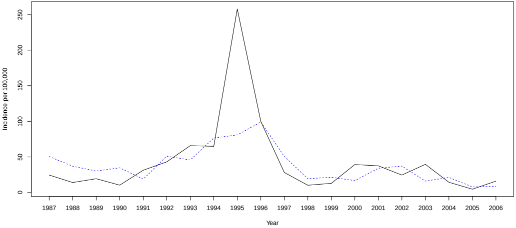
A Case Study: Niger

Temporal scale: Annual

How to incorporate a measure of immunity?

- Vaccination data not currently available
- A susceptibility measure based on epidemic history is currently under consideration
- Used December incidence as a crude proxy. Early cases ⇒ high susceptibility?

Final model: December incidence plus Meridional wind component at 925hPa for November-December.



How to evaluate this model? RMSE$=30.16$ (CV$=42.42$), $R^2 = 0.69$

District-level analysis

Is it possible to detect the effects of climate/early cases at the district level? Consider the following models:

1. Cases = National climate effect + (National-District) climate effect
   Including the difference between the national and district averages allows us to determine whether the effects differ on different spatial scales
2. Cases = National early cases + District early cases
   Include national early cases as a measure of large-scale susceptibility, and district early cases to account for the effects of small scale interventions
3. Combined climate and early cases
4. Included a population density effect
5. Considered allowing each district to have its own intercept, to account for differences in overall levels of meningitis

A Case Study: Niger

Temporal scale: Annual

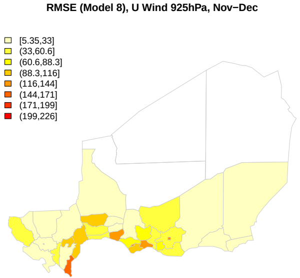
District-level results

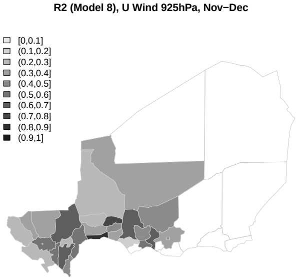
- So far, each climate variable has been considered independently
- We have assumed the effects of climate/early cases and population density are the same in each district
- Two northern districts were removed from the analysis due to small numbers of cases in these areas.
- Detected both National and National-District climate effects, and both National and District early case effects
- The model is not a very good fit overall using any of the climate variables when using all districts to evaluate the model
- However, the fit varies substantially between districts

A Case Study: Niger

Temporal scale: Annual, Spatial scale: District

Meridional wind at 925hPa November-December





- RMSE compares observed and predicted incidence
- Low numbers $\Rightarrow$ better fit
- NW-SE gradient in RMSE observed

- $R^2 = 1 - (\text{RSS}/\text{TSS})$
- Measure usually reserved for goodness-of-fit of linear models
- Indicates % of temporal variation explained by model

A Case Study: Niger

Temporal scale: Annual

Future work

- Consider multiple climate variables in the model
- Investigate spatial dependence, and incorporate if necessary
- Explore additional methods of measuring immunity e.g. a susceptibility measure based on whether or not the district-level epidemic threshold was crossed in previous years.
- Continue to discuss how to evaluate the models with collaborators
    - Consider probability maps (low, medium, high risk?)
    - Interpret results into some form of cost-benefit measure?

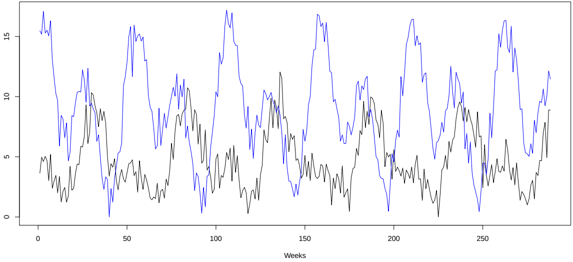
A Case Study: Niger

Temporal scale: Weekly

Models developed on the weekly time scale have the potential to complement a decision support tool developed to determine *where* and *when* the reactive vaccine should be distributed.

Key point

When looking at the relationship between two variables which exhibit a seasonal trend, this trend needs to be taken into consideration e.g.



Large correlation (≈ 0.8) between independent time series.

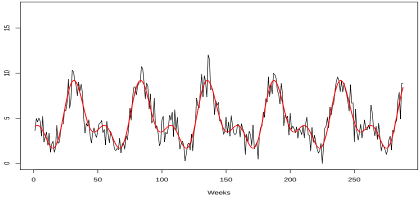
Modelling approach

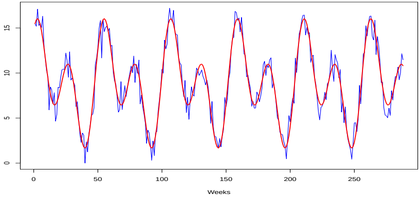
Extension of previous work, where we consider log-transformed incidence, and fit (dynamic) linear models to the transformed data.

1. *log(incidence) = Seasonal cycle + noise*
2. *log(incidence) = Seasonal cycle + climate effect + noise*
3. *log(incidence) = Seasonal cycle + previous incidence effect + climate effect + noise*

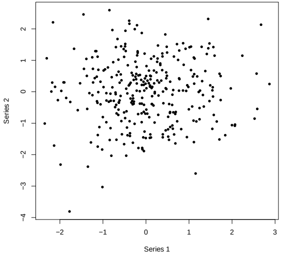
Climate effect: Residuals from a fitted seasonal cycle (similar to climatology) averaged over previous weeks

Fitted seasonal cycle





Residual 1 vs Residual 2



Non-significant correlation

National-level analysis

- National scale models mainly developed to provide a framework for the district-level models, with no practical implementation
- Although including climate variables significantly improved the model fit, in practice no improvement was made the model's forecasting ability
  1. Calculated $\mathbb{P}$(Incidence in week t+k $> C|$data up to time t)
  2. If $\mathbb{P}(\cdot|\cdot) > d$, predict that the threshold C will be exceeded in week $t+k$
  3. Using this information and the observed incidence, obtain

		Observed $> C$ Yes	Observed $> C$ No	
Predicted $> C$	Yes	TP	FP	$PPV = \frac{TP}{TP+FP}$
	No	FN	TN	$NPV = \frac{TN}{FN+TN}$
		Sensitivity $= \frac{TP}{TP+FN}$	Specificity $= \frac{TN}{FP+TN}$	

A Case Study: Niger

Temporal scale: Weekly

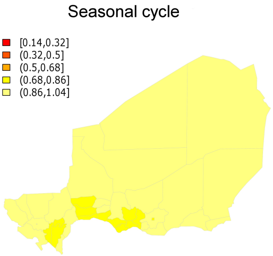
- Select the value of d which simultaneously minimises all four quantities i.e.

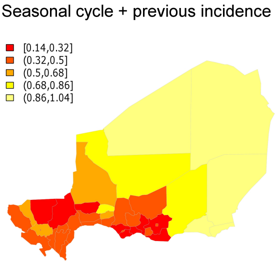
$$\alpha = \sqrt{(\text{Sens.} - 1)^2 + (\text{Spec.} - 1)^2 + (\text{PPV} - 1)^2 + (\text{NPV} - 1)^2}$$

  and used the resulting values to evaluate the model.
- Zonal wind and dust concentration made modest improvements in forecasting ability, but majority of temporal variation could be explained using a seasonal trend and previous incidence.
- Typical values were *Specificity*, *NPV* $\approx 100\%$, *Sensitivity* $\approx 90\%$, *PPV* $\approx 85 - 90\%$.

District-level analysis (Independent Models)

The inclusion of climate variables made no real difference to the models' forecasting performance (as summarised by α), and the majority of temporal variation could be explain using a seasonal cycle and previous incidence.





Also noted that there was a spatial pattern to the performance of the independent district level models

Conclusions

- As yet, there is no evidence that climate can contribute to improving meningitis forecasts at the weekly time scale.
- Data may be too noisy at this temporal scale
    - Epidemiological data: Under-reporting, reporting delays
    - Climate data: Not well enough calibrated with ground truth?
- The impact of climate on meningitis incidence may not be detectable at this temporal scale. Supports Mueller *et al.*(2010).

- Fill in the gaps by considering intermediate spatial and temporal scales.

		Spatial Scale		
		District	Sub-national	National
Temporal Scale	Weekly	✓	?	✓
	Monthly	?	?	?
	Annually	✓	?	✓

- Conduct an analysis at the fringes of the belt?

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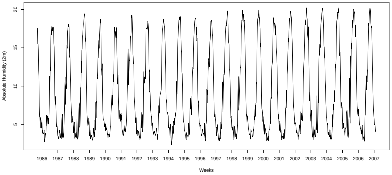

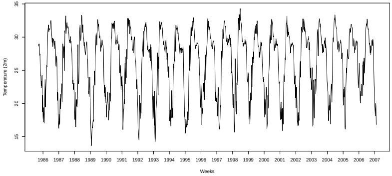

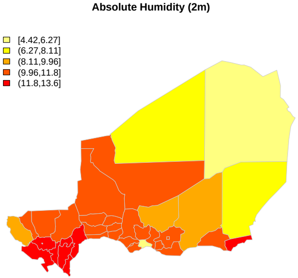

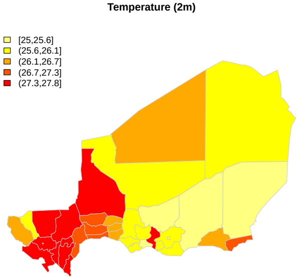

Inter-annual climate variability among the districts at the seasonal scale is low in comparison to the variability of meningitis