DUST AND MENINGITIS IN SUB-SAHARAN AFRICA

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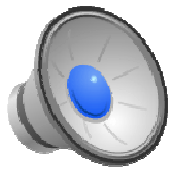
1st AFRICA/MIDDLE-EAST EXPERT MEETING AND WORKSHOP ON THE HEALTH IMPACT OF AIRBORNE DUST

AMMAN, JORDAN, 2-5 NOVEMBER 20

Meningococcal meningitis in North Africa: a climate sensitive disease

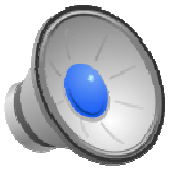
Source: WHO

- Meningococcal Meningitis, bacterial form of meningitis
- Direct transmission, person to person, respiratory droplets
- Average incubation period of 4 days, ranging between 2 and 10 days.
- 1-10% of asymptomatic carriers. Up to 10-25% during epidemics
- Carried in the pharynx
- 12 serogroups. 4 in Africa: A, C, W135, X. Majority of the outbreaks have been due to NmA
- Serious infection of the thin lining that surrounds the brain and spinal cord
- 430 million people at risk. 1 million cases since 1998 (80 % of the global burden)
- 10-50 % fatality rates, 10-20 % of survivors suffer permanent brain damage

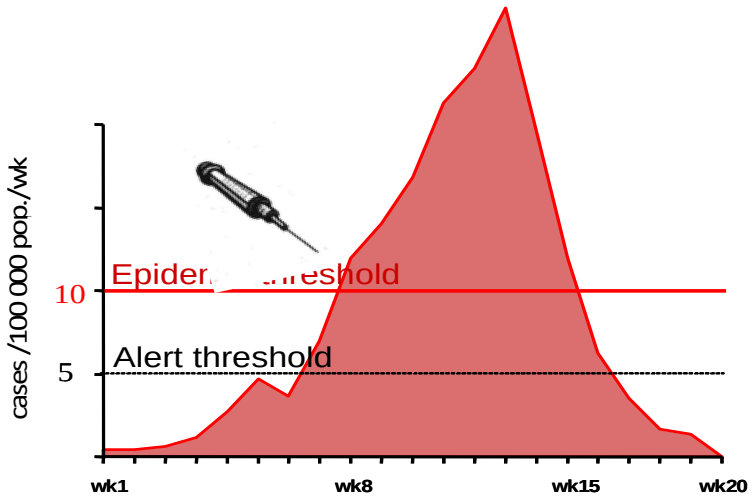


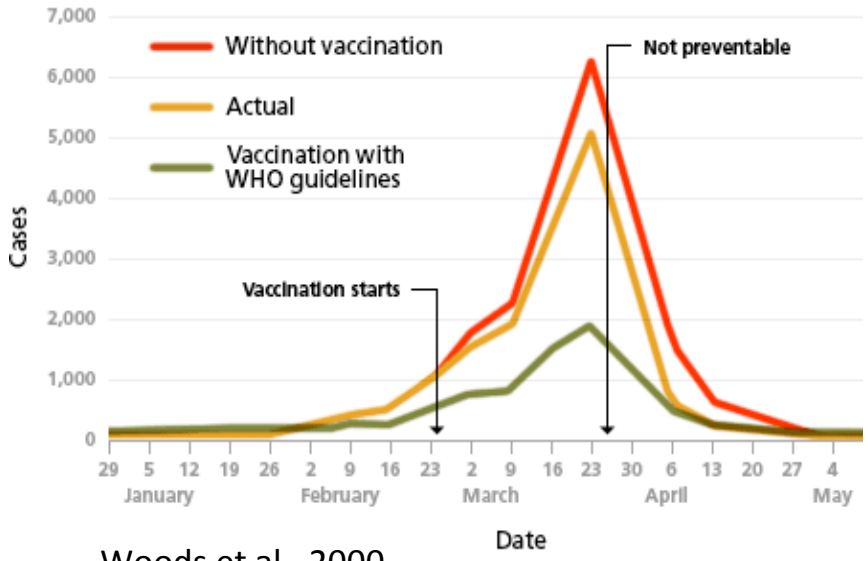
WHO strategy: 4 core components

- Surveillance (district level)
  - Data collection & management + Laboratory support for early detection and confirmation of outbreaks
- Outbreak response (district level)
  - Case management: Oily chloramphenicol / Ceftriaxone
  - Reactive vaccination (against circulating serogroup) with polysaccharide vaccines
- Preventive immunization & vaccine development
  - Introduction of conjugate A vaccine
- Advocacy and partnership



Reactive Vaccination





Woods et al., 2000

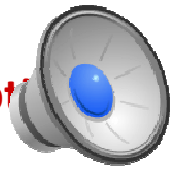
- District level
- With bivalent A/C or trivalent A/C/W135
- Based on incidence thresholds (enhanced weekly surveillance)
- Provides short-term immunity

- Targeting one million persons costs about US$2 million, compromising health budgets in meningitis belt countries

- Epidemics and reactive immunization generates chaos to health systems superseding all other health-related activities

- In theory, prevents 70 % of cases. In practice, at best moderately useful and at worst, ineffective.

- **Need for timely vaccination to opt… the control of the epidemics**



Conjugate Vaccines

Reactive

Polysaccharide vaccines

•Do not protect the very young

•Only two to three years of protection

•Carriage is not decreased (no herd immunity, this not protecting the unvaccinated)

- Still needed for serogroups other than A

Preventive

Conjugate vaccines

•Protect the very young

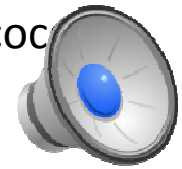
•Longer-lasting protection

•Bacterial carriage decreases

•MenAfriVac®, the meningococcal A conjugate vaccine, since 2010, is strongly reducing serogroup A and is expected to eliminate it

•C, W, Y and X?

•Multivalent conjugate meningococ vaccine?? Cost effective??



Meningitis Environmental Risk Information Technologies:

The MERIT initiative was launched in 2007 as a multi-sectoral partnership led by WHO to enable health specialists (public health specialists, epidemiologists, immunologists, microbiologists, demographers, etc.) and climate and environment specialists to work together to help solve a pressing health problem.

HCF

CERMES

ACMAD

MERIT

IRI

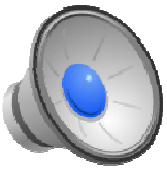
Meningitis Vaccine Project

GEO

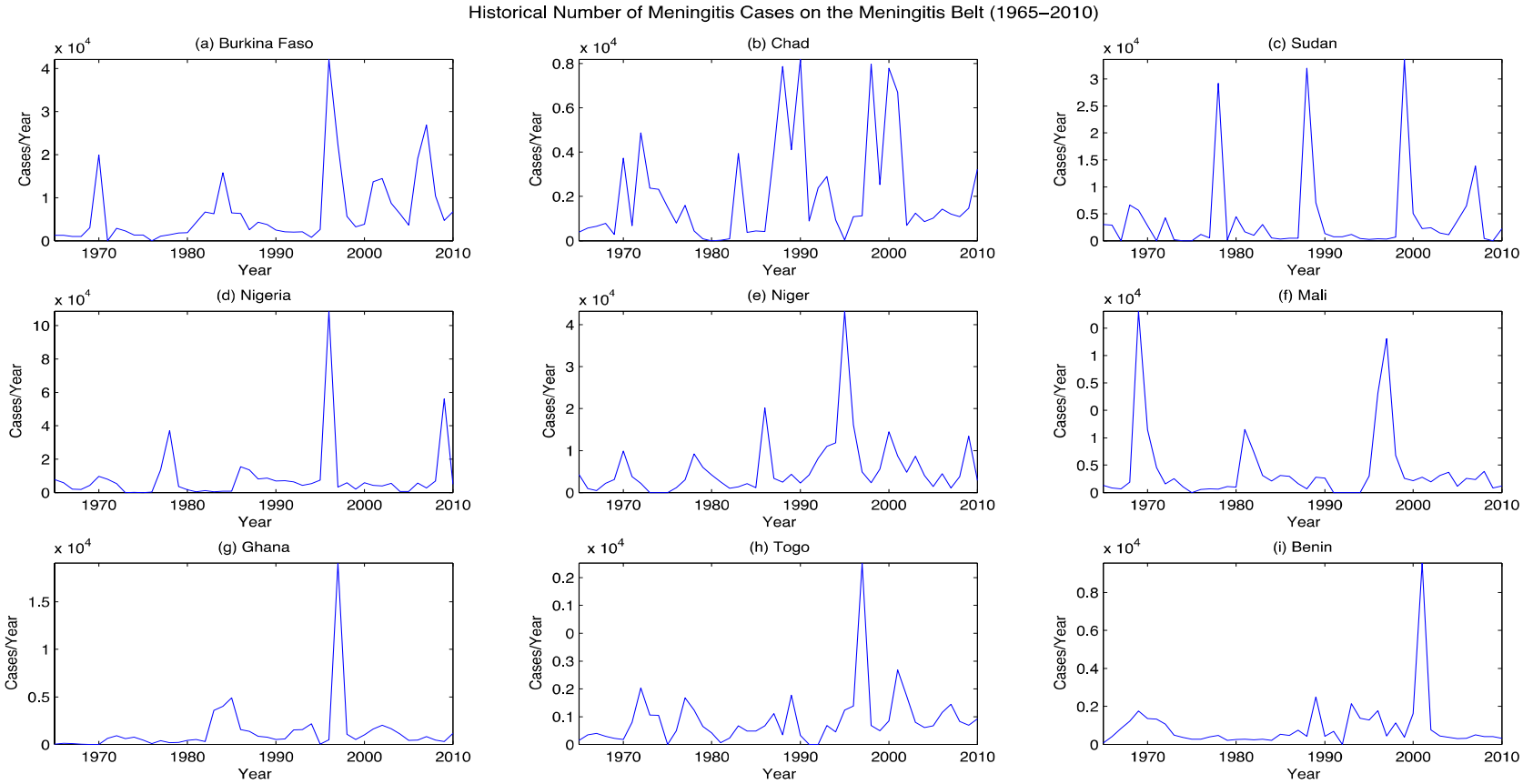
World Health Organization

Outline

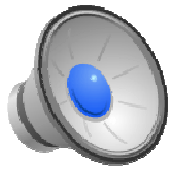
- Spatial and temporal variability of meningitis
- Explanatory models for epidemics
- The role of climate and environment
  - Hypothesis, seasonality and year-to-year variability
- Forecasting to improve epidemic response
- Challenges and future



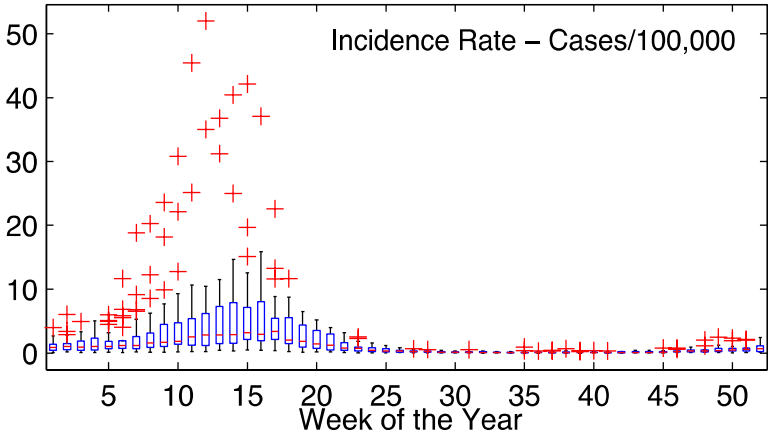
Year-to-year variability at country level



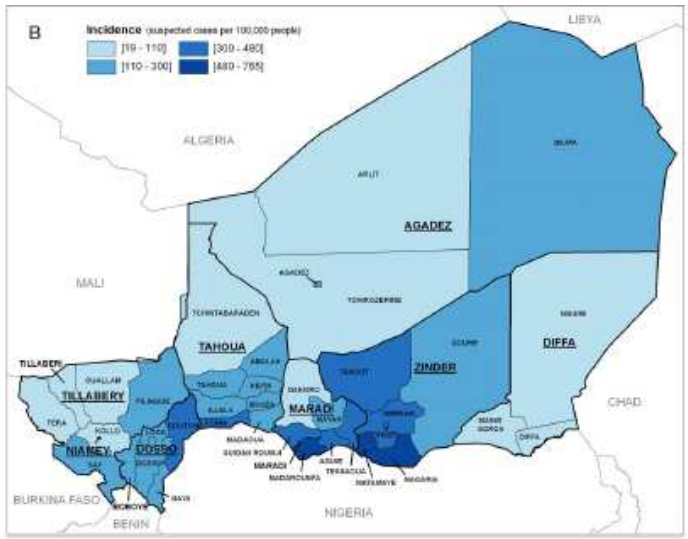
- Epidemic waves following crescendo-decrescendo patterns
- Occurrence every 8 to 14 years
- Significant correlation in meningitis epidemics among countries, although it alternates between perfect or out-of phase synchrony in the majority of comparisons

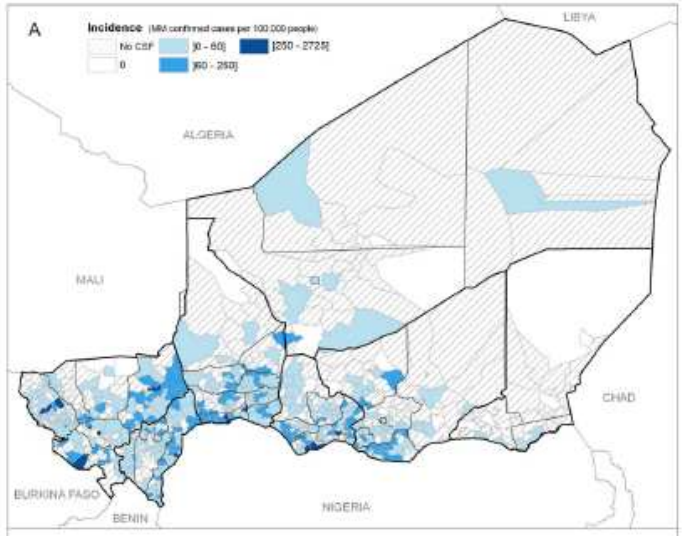


District and sub-district variability

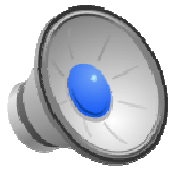


Pérez García-Pando et al. (2014b)

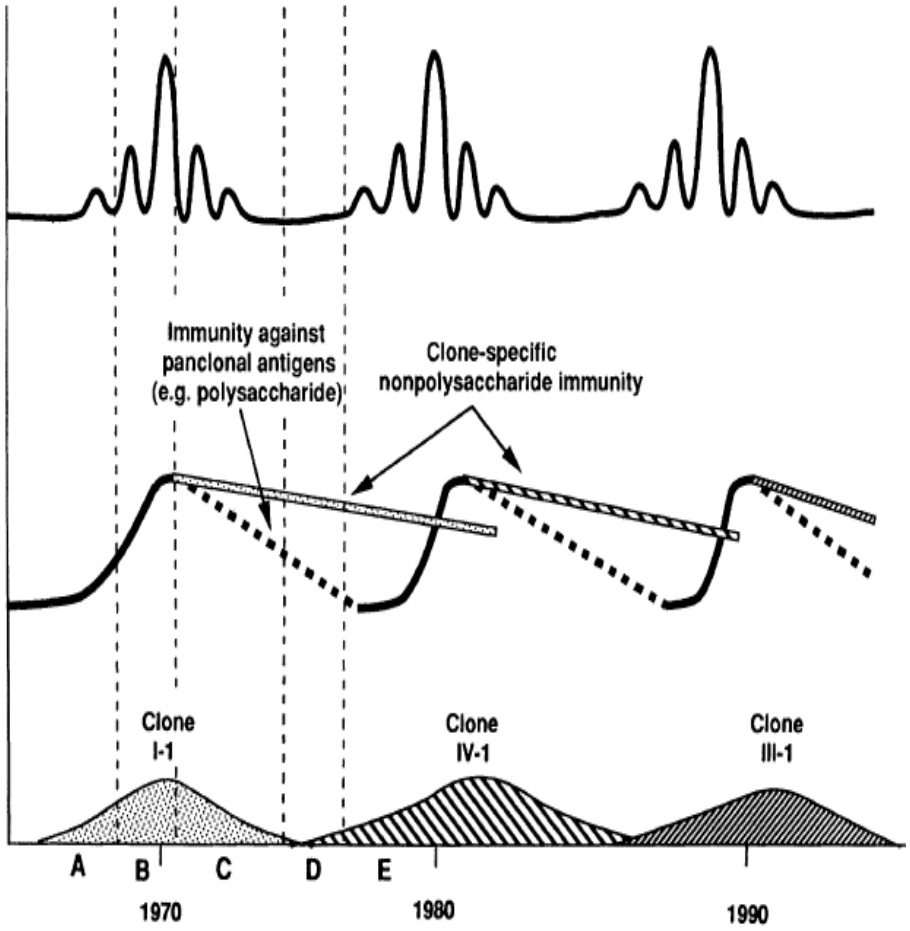




Paireau et al. (2012)

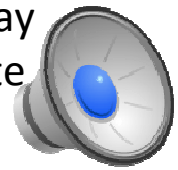


Complex interactions among host, organism and environment

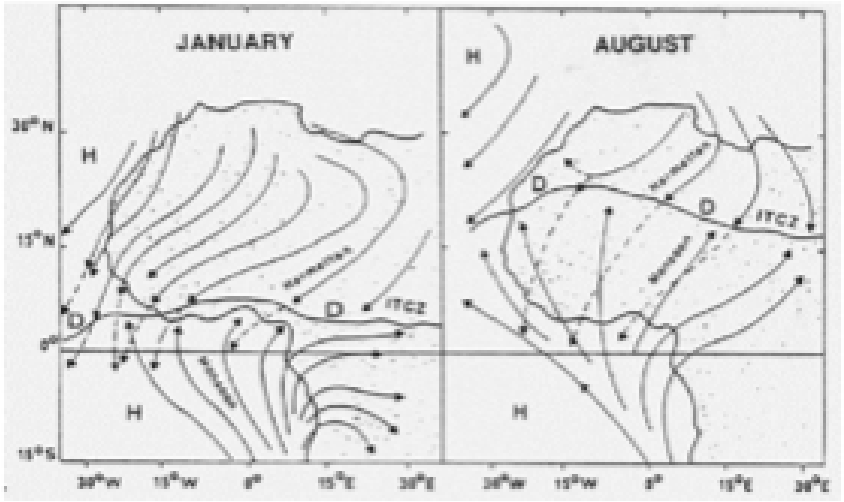


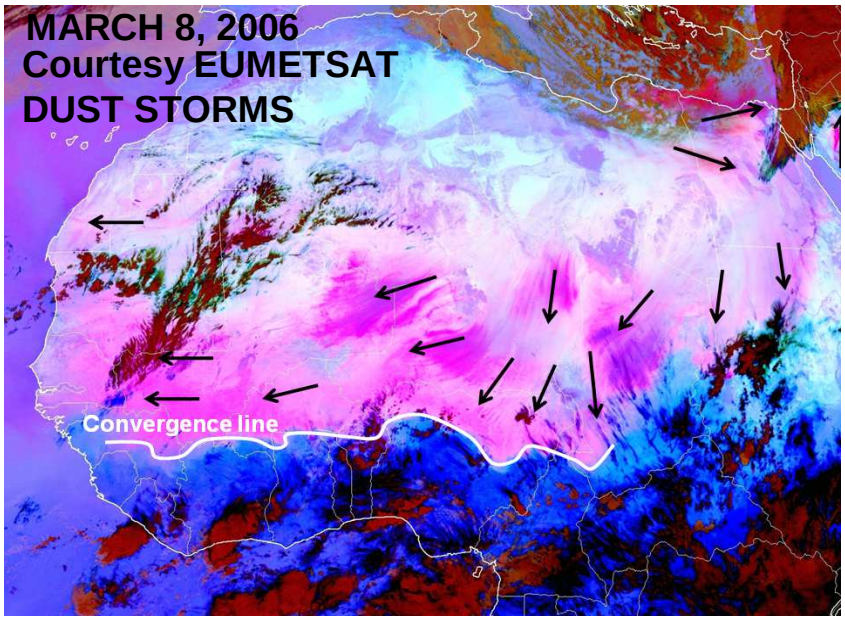
(Moore, 1992)

- Loss of herd immunity to specific strains contribute to the initiation of large-scale epidemic cycles
- Development of herd immunity due to widespread carriage of the epidemic strain during the cycle may have limited transmission ending the epidemic wave
- Dry season epidemics explained by a combination of climatic/dusty conditions and widespread respiratory infections decreasing mucosal protection and thus promoting invasion rather than carriage in a low herd immunity setting
- Upper respiratory tract infections may contribute to the seasonality (Climate involved?)

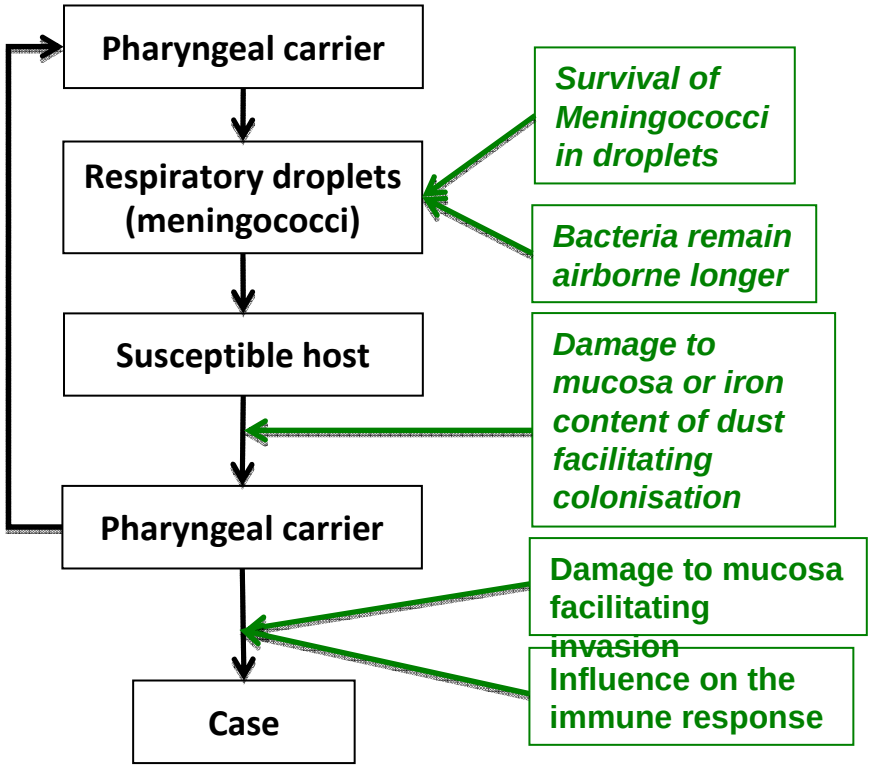


CLIMATE/ENVIRONMENT





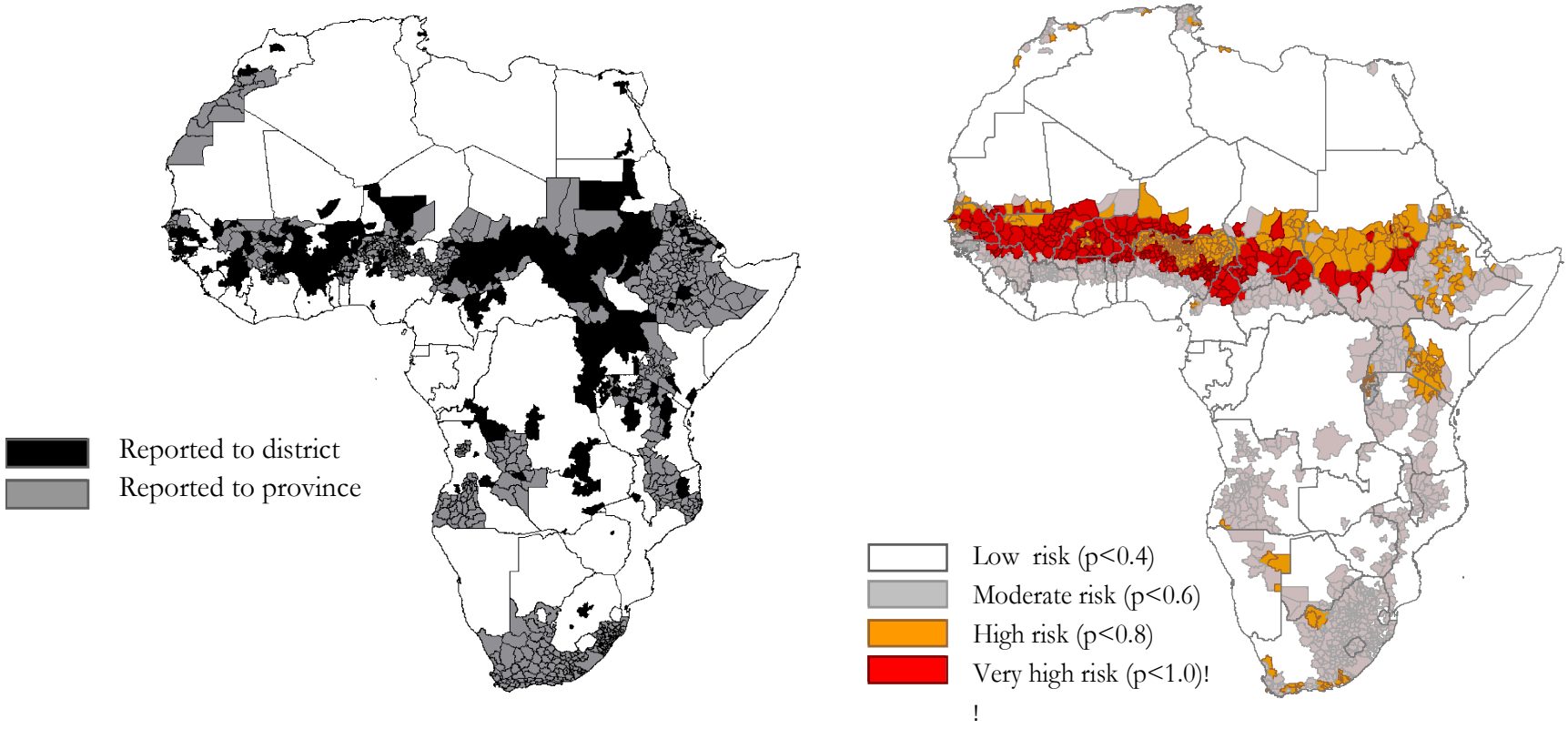
On the pathway of infection



Indirectly

- Enhancing viral epidemics
- Affecting crowding, reduced ventilation
- (More controversially) carriers for bacteri

Broad spatial pattern

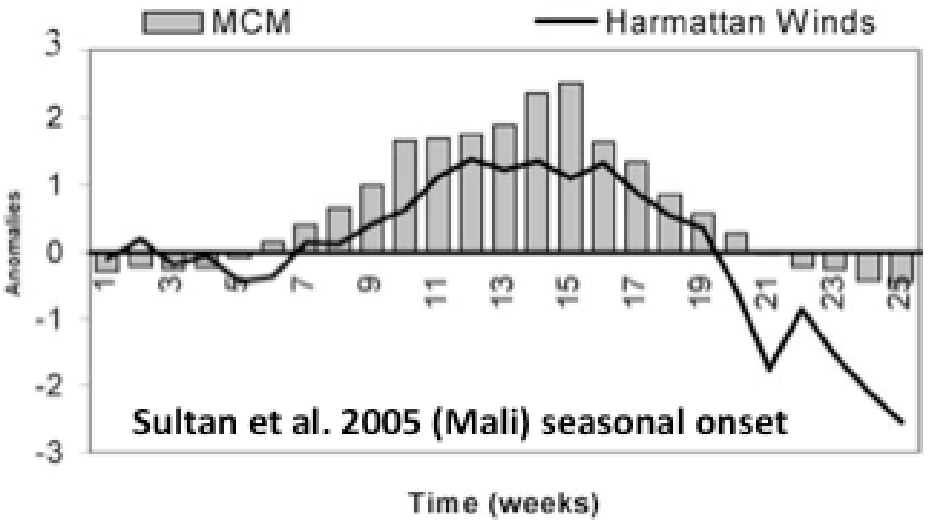


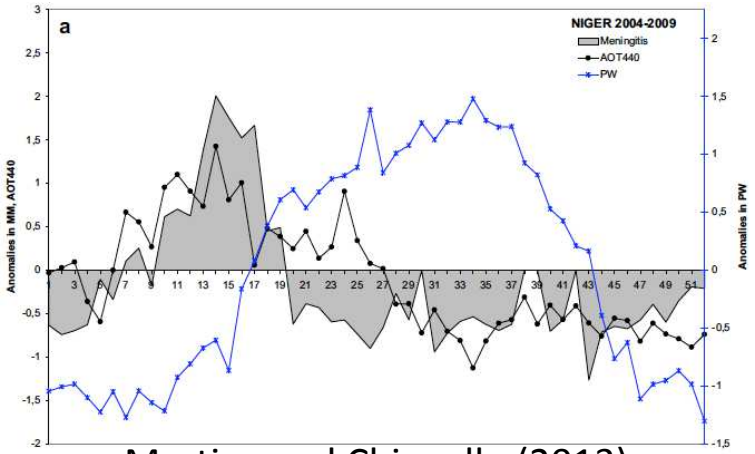
Absolute humidity and land-cover type were found to be the best predictors in a spatial multivariate model of the broad spatial distribution of epidemics
Molesworth et al. (2003)

Seasonality

Seasonality of meningitis epidemics have been related to climate dynamics in the region

Country scale

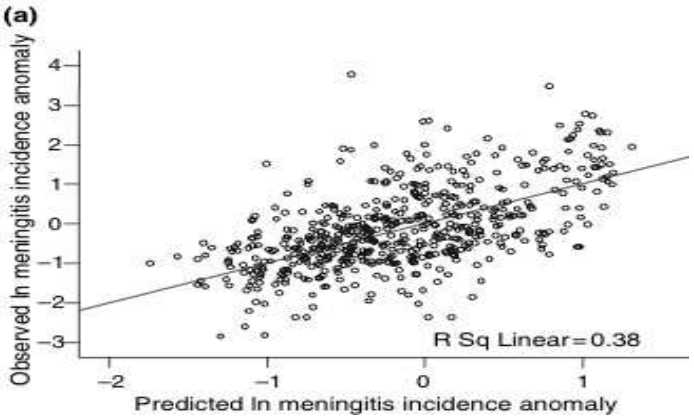


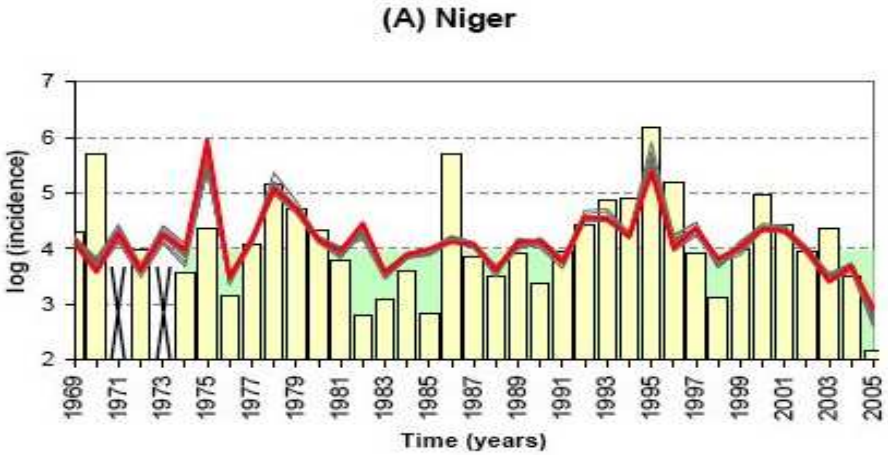


Martiny and Chiapello (2013)

Year-to-year variability

In semi-arid, northern Benin, 14 to 34.5% of the temporal variability of the disease over 28 years was related to low absolute humidity associated with variations of the Harmattan (**Besancenot et al. 1997**)





Thomson at al. (2006)
Rainfall anomalies in January and dust anomalies in October appeared to be the most consistent predictors of anomalies in seasonal incidence at district level in West Africa

Yaka et al. (2008) 25% of the disease variance from year-to-year at national scale can be explained by december climate

Forecasting meningitis today

GOAL
Identify whether an epidemic will occur and predict the magnitude of incidence

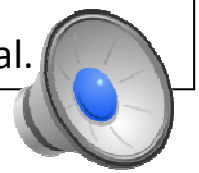
Incomplete understanding
of meningitis epidemics
Lack of data
at the required temporal and spatial scales

Limits the use of mathematical modeling
to forecast epidemics

Magnitude of incidence is of less interest in comparison to whether or not the incidence crosses an action-triggering threshold.

Statistical models based on previous incidence
Beresniak et al. 2012;
Agier et al. 2012;
Stanton et al. 2013

Climate/weather-based models
Pandya et al. 2014
Pérez García-Pando et al.



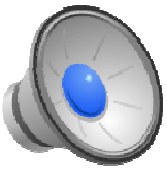
Early season Forecasts in Niger

Pérez García-Pando et al. 2014 EHP

- We modeled the seasonal number of cases (counts), which we defined as cases reported from January through May (the meningitis season).

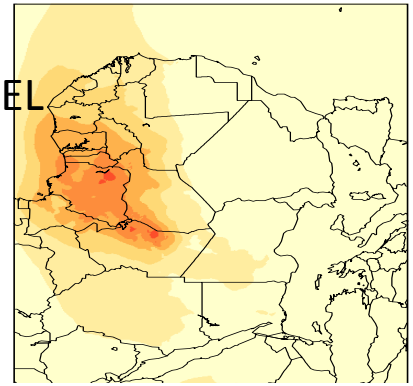
- Data between 1986-2006 were aggregated at both national and district levels for each year.

- We examined whether climate conditions, including dust concentration, could be used to predict the meningitis incidence during January through May.

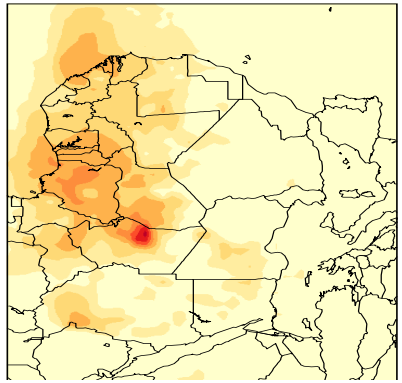


Regional simulations of dust and climate for the Meningitis Belt
NMMb/BSC-Dust model (Pérez et al., 2011)

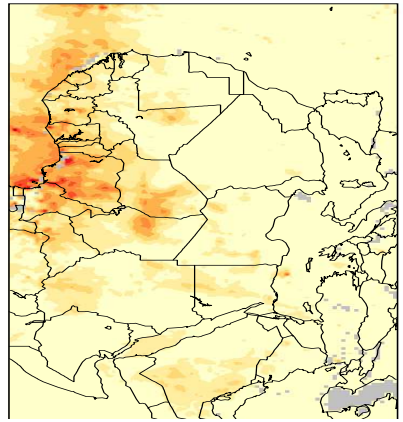
MODEL



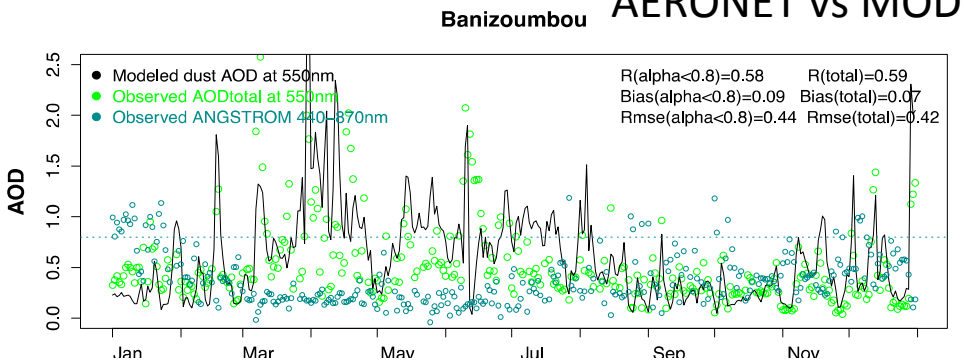
OMI

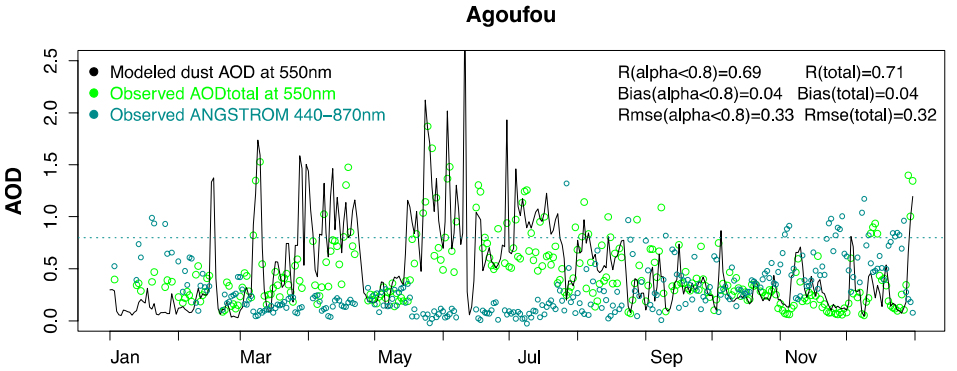


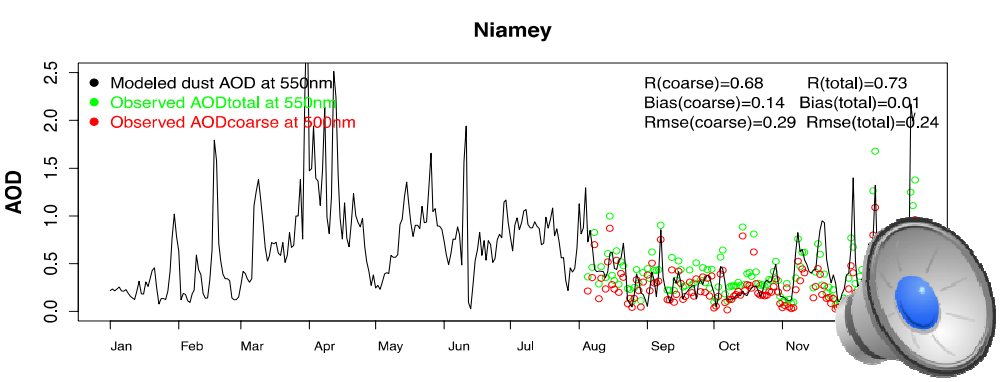
MISR



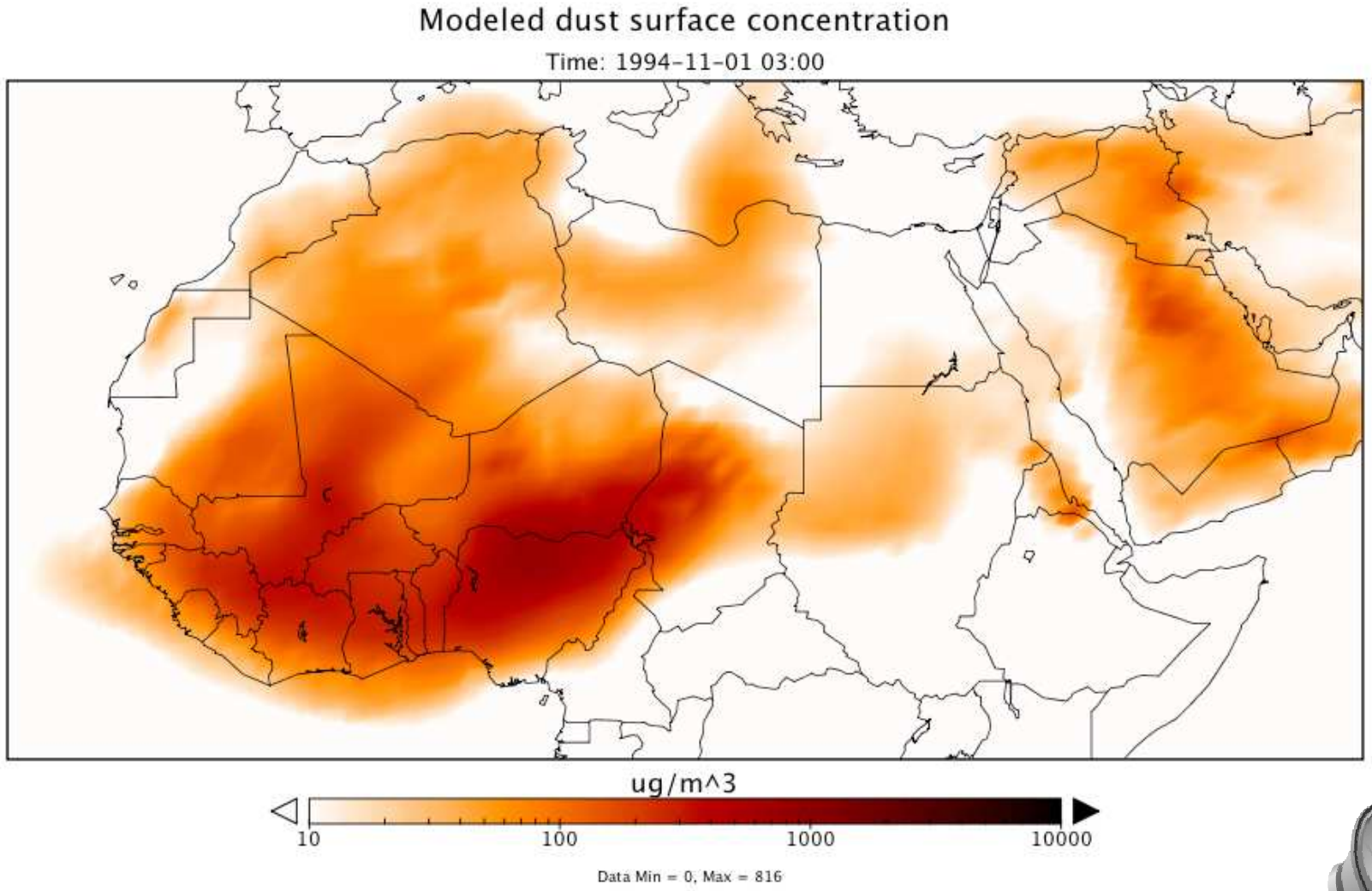
AERONET vs MODEL







Simulated daily dust concentration



National level

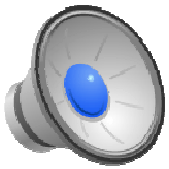
Negative binomial distribution, with mean parameter μ_t, overdispersion parameter θ, and variance $\sigma_t = (\mu_t + \mu_t^2)/\theta_t$

Determined the linear combination of risk factors that best represented the variability in the mean meningitis counts on the ln scale,

$\ln(\mu_t) = \alpha + \beta E_t + \ln(N_t)$ Model based only on early incidence in December

$\ln(\mu_t) = \alpha + \Sigma^K_{k=1} \gamma_k X_{kt} + \ln(N_t)$, Model based only climate/dust variables

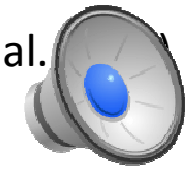
$\ln(\mu_t) = \alpha + \beta E_t + \Sigma^K_{k=1} \gamma_k X_{kt} + \ln(N_t)$. Model based on early incidence and climate/dust variables



Model evaluation

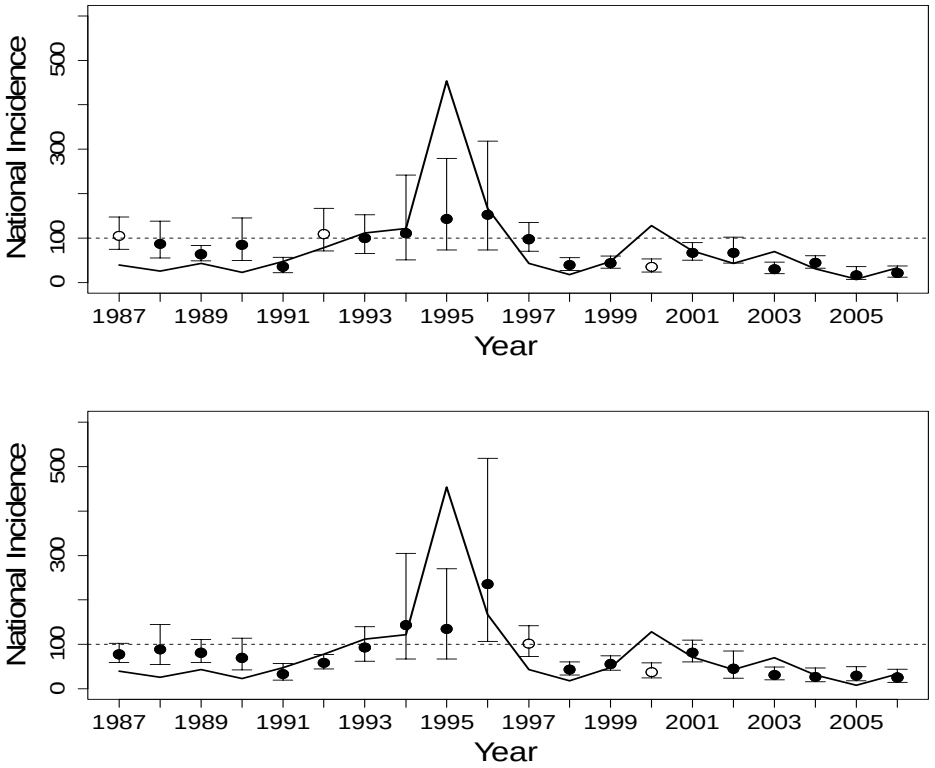
- Akaike Information Criterion (AIC)
- Pseudo-R^2
- Pearson's correlation between the observed data and the resulting cross-validated predictions on the ln-incidence scale (CVC)

- Model's ability to detect whether or not a particular incidence-based threshold had been exceeded:
  - Such that the fitted probability of y_t exceeding a threshold K was greater than some value c (where $0 < c < 1$), then we predict that $y_t > K$
  - calculated sensitivity [SENS = TP / (TP + FN)]
    specificity [SPEC = TN/ (TN + FP)] and
    Hanssen and Kuipers score [HKS = (SENS + SPEC)/2
  - the value of c simultaneously maximized the SENS and SPEC of the model estimates
  - We assumed a threshold K =100 per 100,000 population (de Chabalier et al.



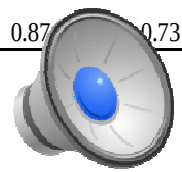
Early season forecasts

Pérez García-Pando et al. 2014 EHP



November-December wind or dust
+ early cases are good predictors

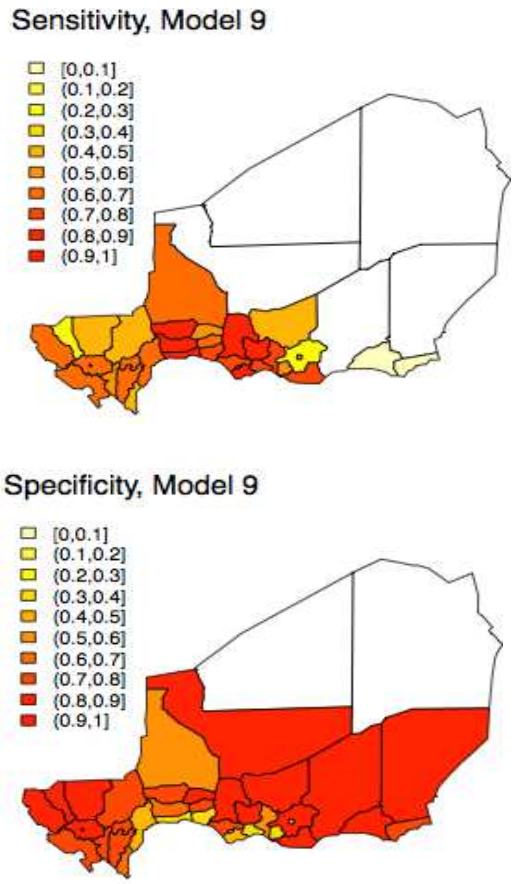
Category	Model	AIC	Pseudo-R2	CVC	SENS (HR)	SPEC (1-FAR)	HKS
1	E	395	0.24	0.38	0.40	1.00	0.70
2*	U_{925}^{ND}	387	0.49	0.51	1.00	0.60	0.80
3*	$U_{925}^{ND}+E$	385	0.57	0.59	0.80	0.87	0.83
2	UV_{925}^{ND}	388	0.47	0.51	1.00	0.53	0.77
3	$UV_{925}^{ND}+E$	385	0.57	0.60	0.80	0.80	0.80
2	$Dust_{10m}^{OD}$	388	0.47	0.46	1.00	0.60	0.80
3	$Dust_{10m}^{OD}+E$	386	0.55	0.56	0.80	0.93	0.87
2	V_{925}^{ND}	394	0.29	0.34	0.60	0.53	0.57
3	$V_{925}^{ND}+E$	392	0.42	0.48	0.60	0.87	0.73



Forecasting Meningitis

Pérez García-Pando et al. 2014

Niger - district scale



- Early-season zonal wind and dust, along with the number of early cases and population density represented the spatio-temporal variability of the disease with pseudo-R2=0.41 and CVC=0.55.
- The inclusion of zonal wind and dust information substantially increased our skill at predicting which districts exceed a particular threshold as it improves the sensitivity and/or PPV depending on optimization criteria.
- District specific intercepts improved the models' performance due to the lack of information to explain additional between-district variability.

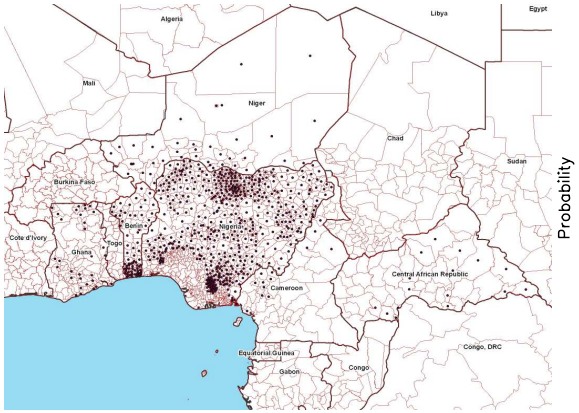
Weekly forecasts

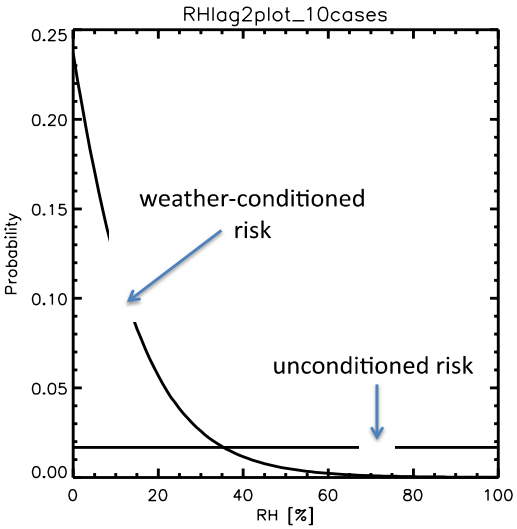
Pandya et al. 2014

$$\frac{dI_t}{dt} = (1-c_1)\beta_1 S_t I_t + (1-c_2)\beta_2 S_t C_t + \alpha C_t - r_2 I_t - r_3 I_t$$

$$I_t^{+\Delta} = \gamma_1(met)PI_t + \gamma_2(met)P^2 + \gamma_3(met)P$$

Probability of an epidemic (10 cases per 100,000) versus Relative Humidity over Africa's Meningitis Belt





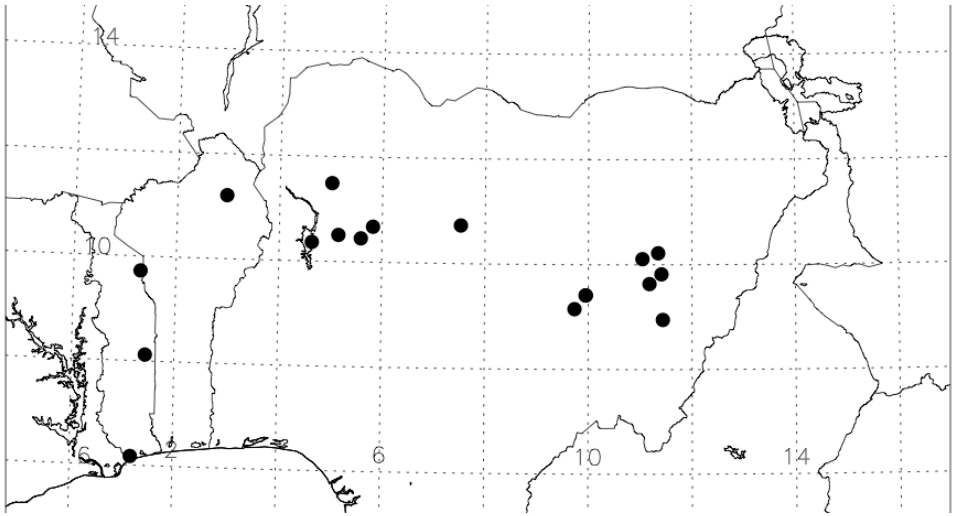
- Niger, Burkina Faso, Benin, Togo and Tchad (2006-2011) (until conjugate vaccine introduction)
- Simplified differential equation disease model based on known transmission dynamics
- Knowing the RH two weeks before improves accuracy in predicting an epidemic by ~25%
- Coupled with a two week weather forecast, this indicates an improved ability to anticipate a roll-off in epidemic 4 weeks in advance
- Other variables (air temp, winds, NE winds) also help, but l han relative humidity (dust n tested)

Locations where end-of-season forecasts would have saved vaccine

(provided by Tom Hopson NCAR/UCAR)

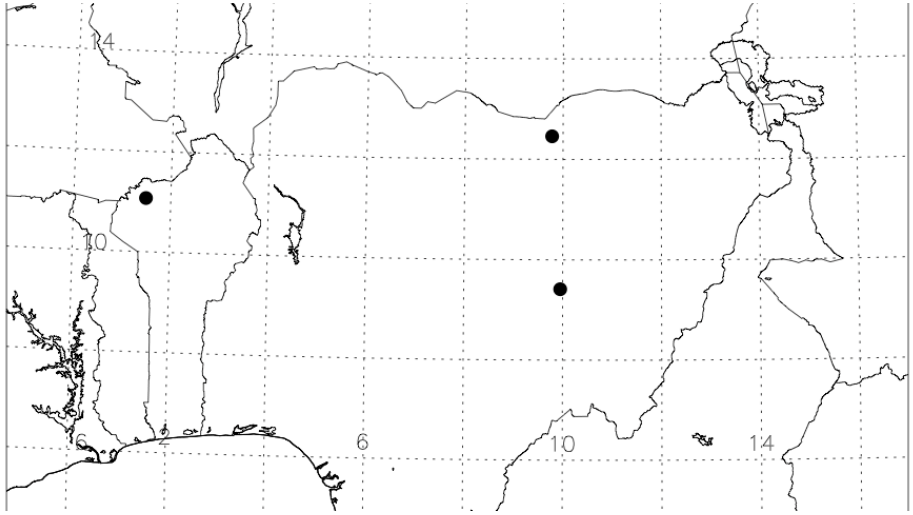
Using "Perfect" Forecasts

- 18 epidemics identified



Using Climatological Information

-- 3 epidemics identified



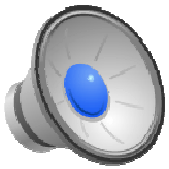
- Calculation based on the approach of Leake et al. (2002)
- Based on relative humidity forecasts only
- Identified whose cumulative probability of being below "background" risk threshold during weeks 3-6
- WHO districts where end-of-season forecasts predict no need for follow-up vaccination campaign due to changing weather conditions
- ~2.6 million doses of vaccine used elsewhere more effectively (prevent as many as 24[illegible] cases of meningitis and 2400 fatalities)

Outlook

- Geographic location, seasonality and year-to-year variability of meningococcal meningitis are associated in part with climatic and environmental factors.

- Determination of the specific seasonal climate drivers including dust are difficult to identify

- Current models that incorporate environmental data, previous incidence, and/or other risk factors have shown some skill for forecasting and are expected to improve as fine-scale surveillance and other sources of data on risk factors (e.g. carriage, vaccination) become available in the Meningitis Belt



Challenges

- Likely elimination of large NmA
- Next step: multivalent conjugate vaccine
- In the meantime:
  Continue outbreak detection-response

Knowledge
Data
Institutional Alignment

Surveillance system for meningococcal disease, carriage
Vacccination data
Sub-district scale

Understanding vaccine-induced meningococcal immunity

Climate/dust data and forecasts

Host and environmental factors

Improve reactive vaccination through forecasting

How and where to implement operational forecasts? WHO, Ministries of Health

laboratory-based research using new animal or cell culture models

Limited funding for translational research

Mathematical modeling