AXA Research Fund
Through Research, Protection

Climate services and infectious disease: The case of meningococcal meningitis epidemics

Carlos Pérez García-Pando

Climateurope webinar

15 November 2016

15/11/2016

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

AEMet Agencia Estatal de Meteorología

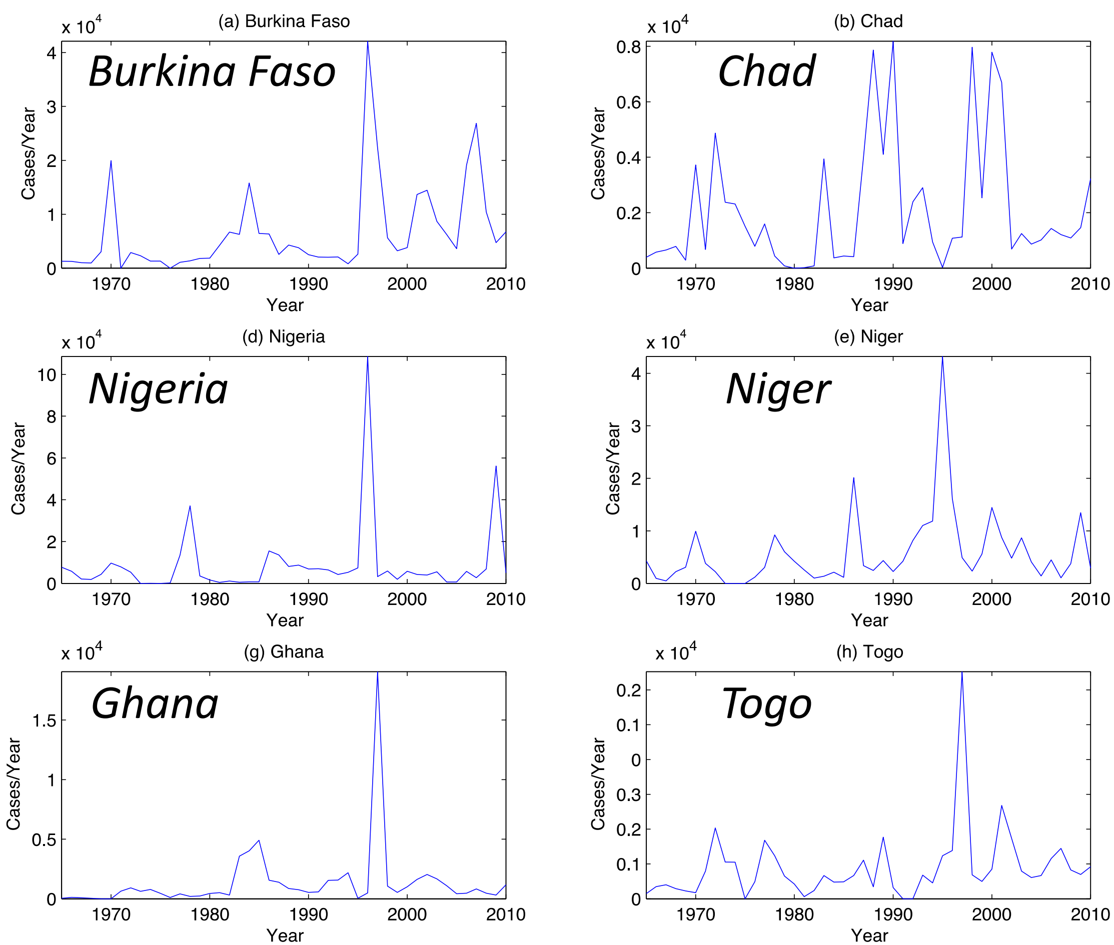
Meningitis Belt

- Serious infection of the thin lining that surrounds the brain and spinal cord
- Bacterial form of meningitis
- Direct transmission, person to person
- 1-10% of asymptomatic carriers - up to 10-20% during epidemics
- Serogroups A, C, W135, X - Historically, majority of the outbreaks have been due to A
- More than 1 million cases since 1998 (80 % of the global)
- 10 % fatality rates (when treated) - 10-20 % of survivors suffer permanent brain damage

Barcelona Supercomputing Center
Centro Nacional de Supercomputación

Year-to-year variability

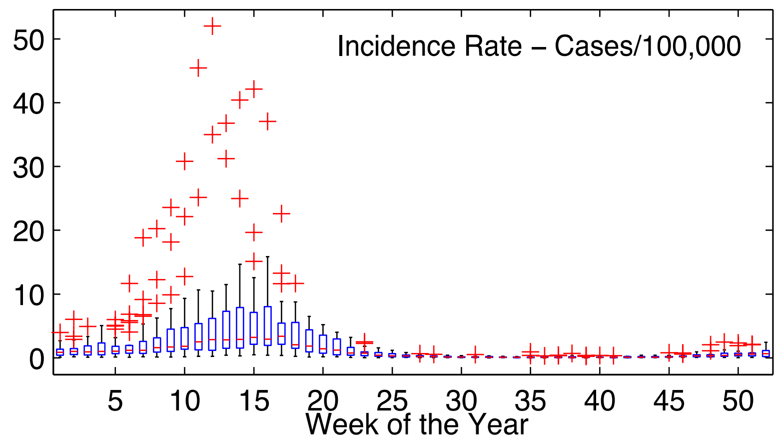
Interactions among host, organism and environment



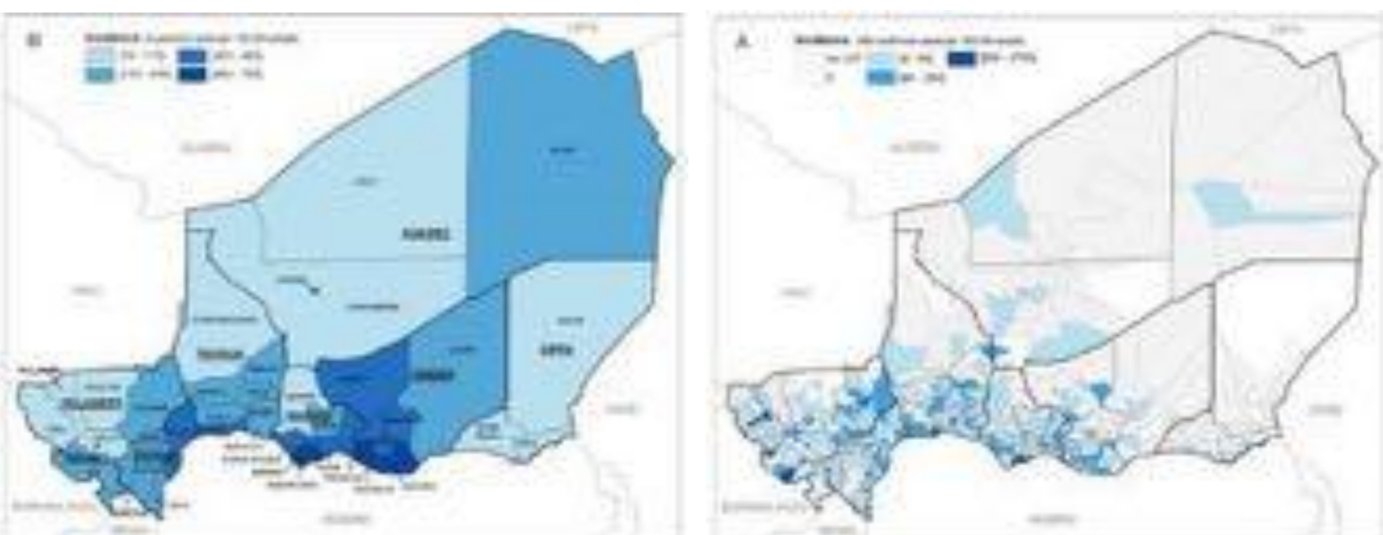
- Loss of herd immunity to specific strains ➔ initiation of large-scale epidemic cycles
- Development of herd immunity due to widespread carriage ➔ limits transmission ending the epidemic wave
- Dry season epidemics ➔ combination of climatic/dusty conditions and widespread respiratory infections decreasing mucosal protection promoting invasion rather than carriage
- Upper respiratory tract infections may contribute to the seasonality (Climate involved?)

Barcelona Supercomputing Center
Centro Nacional de Supercomputación

District and sub-district variability

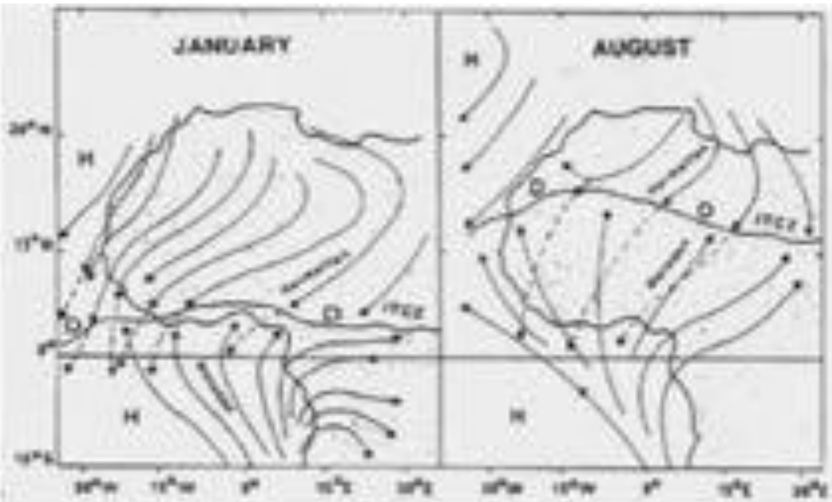


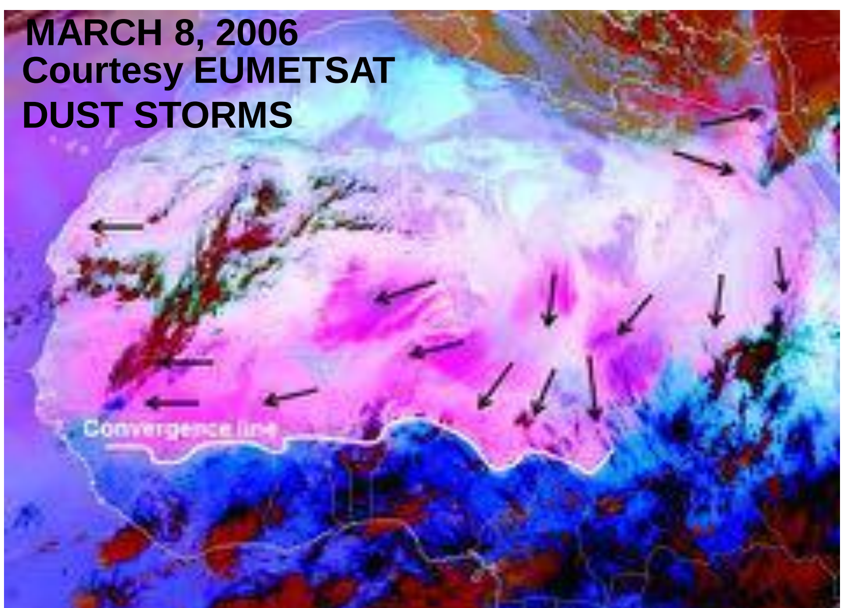
Pérez García-Pando et al. (2014b)



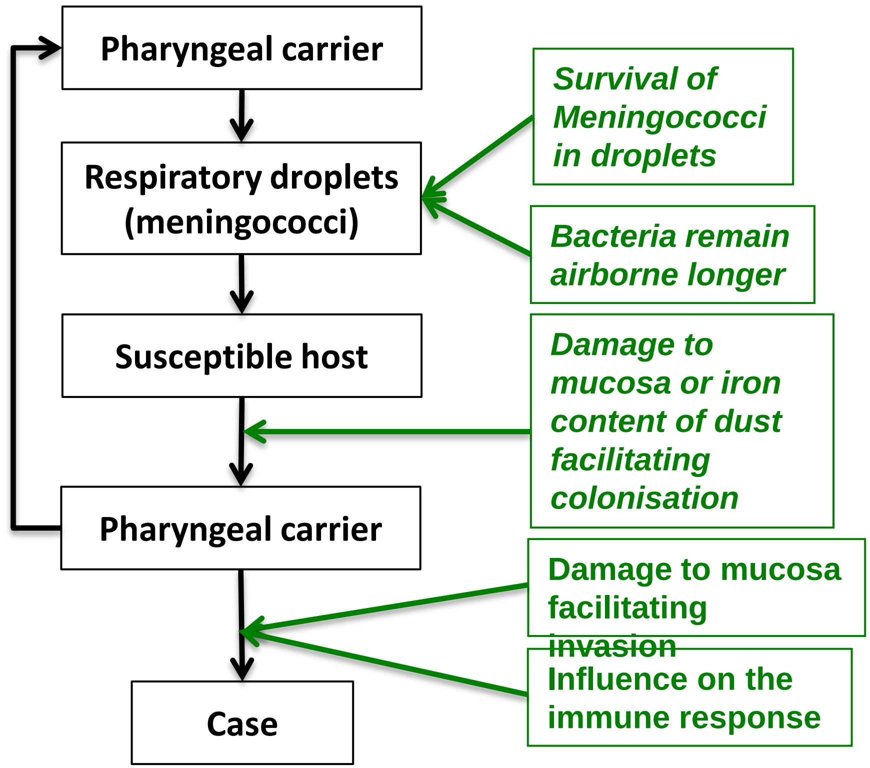
Paireau et al. (2012)

CLIMATE/ENVIRONMENT



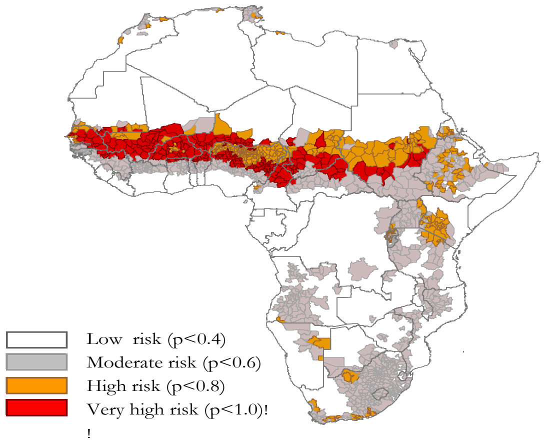


On the pathway of infection



Indirectly

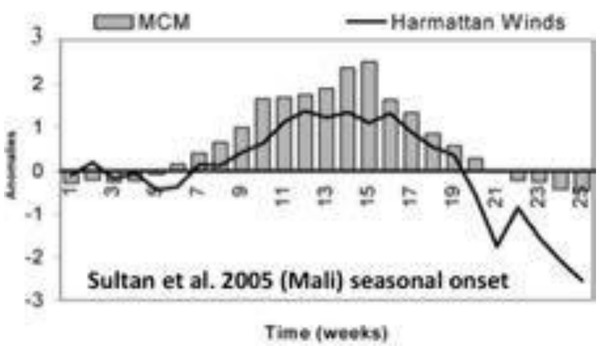
- Enhancing viral epidemics
- Affecting crowding, reduced ventilation
- (More controversially) carriers for bacteria



Broad Spatial Pattern

Absolute humidity and land-cover type

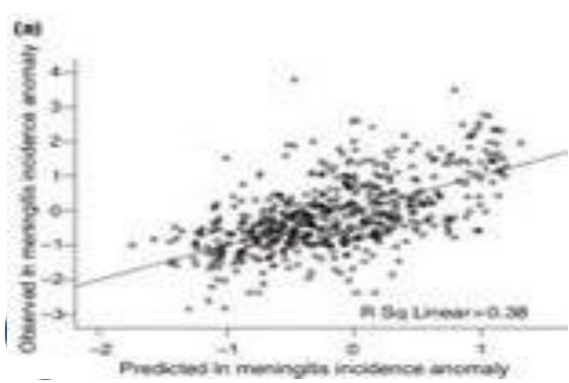
Molesworth et al. (2003)



Seasonality

Wind *Sultan et al. (2005)*

Dust *Martiny and Chiapello (2013)*
Agier et al. (2013)



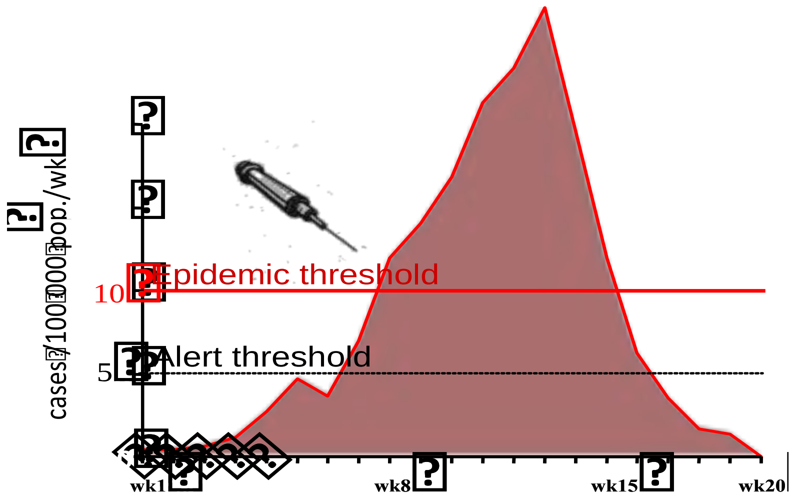
Year-to-year variability

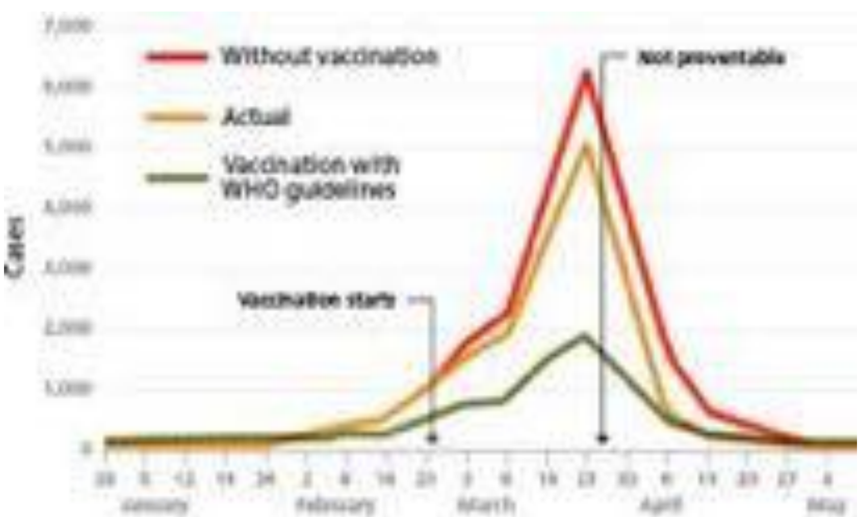
Humidity *Besancenot et al. (1997)*

Rainfall and dust *Thomson et al. (2006)*

Wind *Yaka et al. (2008)*

Reactive Vaccination





Woods et al., 2000

- District level
- With bivalent A/C or trivalent A/C/W135
- 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.

MERIT

Near term climate change predictions

- *Expansion of the Meningitis Belt to other areas?*

➢ Skill likely to be very low
➢ Other factors more relevant (circulating serogroup, conjugate vaccines)

Seasonal climate prediction

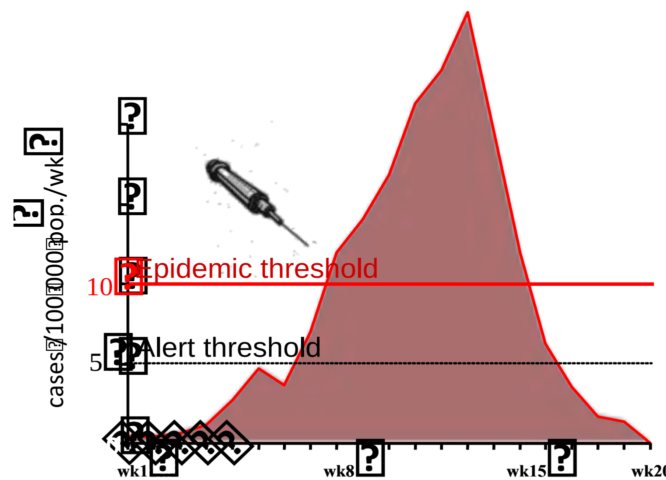
- *Estimates for vaccine production?*

➢ To date predictability during the dry season is low (poorly studied)

Short-term

- *Risk of epidemic during the season?*
- *Above epidemic threshold in the next 1-4 weeks?*
- *End of the season?*

➢ Availability of observed/forecasted weather/dust data
➢ District scale
➢ Lack of data and other factors (in near-real time)



Barcelona Supercomputing Center
Centro Nacional de Supercomputación

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. 2014a

Barcelona Supercomputing Center
Centro Nacional de Supercomputación

Early season Forecasts in Niger

Pérez García-Pando et al. 2014 EHP

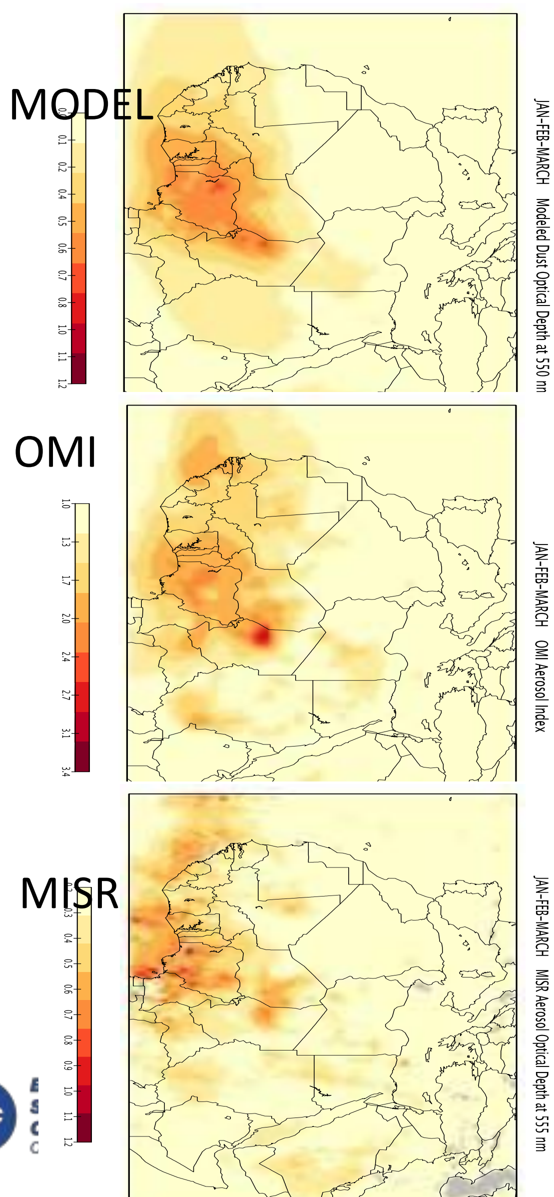
- We modeled the seasonal number of cases (counts), which we defined as cases reported from January through May (the meningitis season).

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

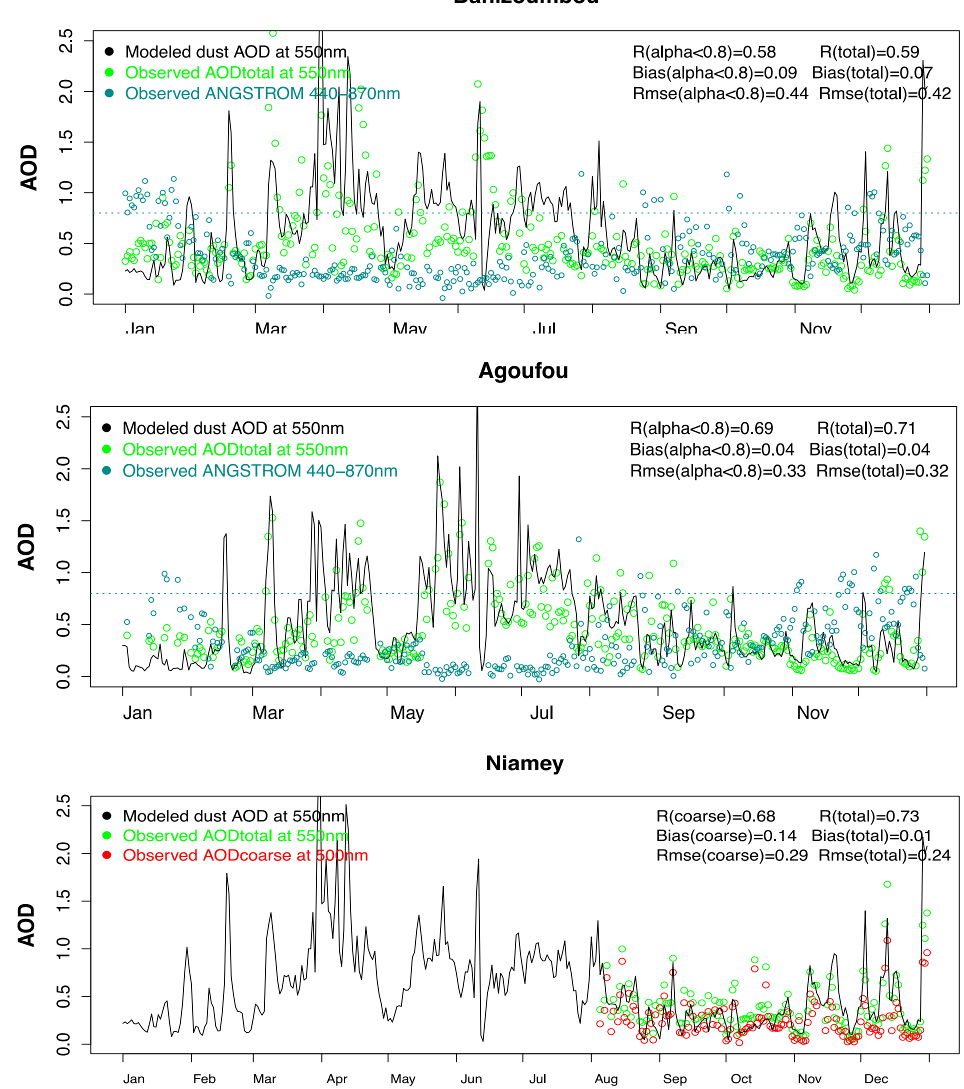
- We examined whether climate conditions, including dust concentration, could be used to predict the meningitis incidence during January through May.

Barcelona Supercomputing Center
Centro Nacional de Supercomputación

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



AERONET vs MODEL



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

Barcelona Supercomputing Center
Centro Nacional de Supercomputación

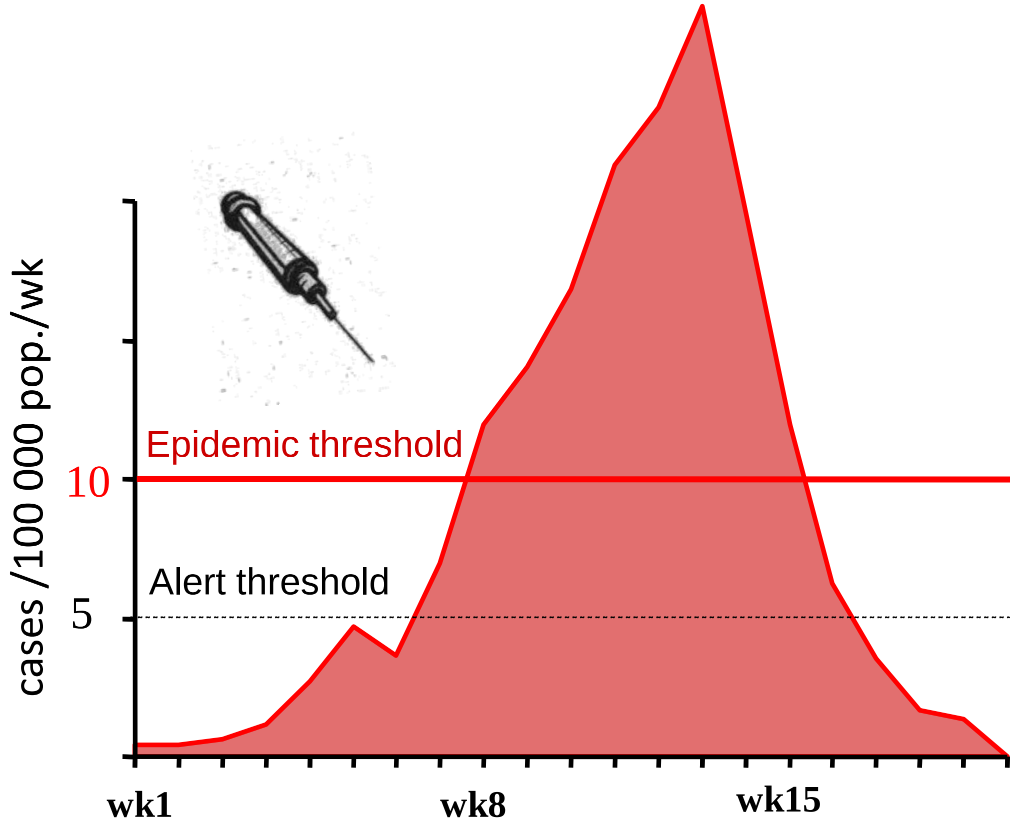
Sensitivity and Specificity

Is it feasible to vaccinate a large number of people unnecessarily if it means that a large proportion of cases are prevented?

-> High sensitivity

Vaccine stock is limited

-> High specificity

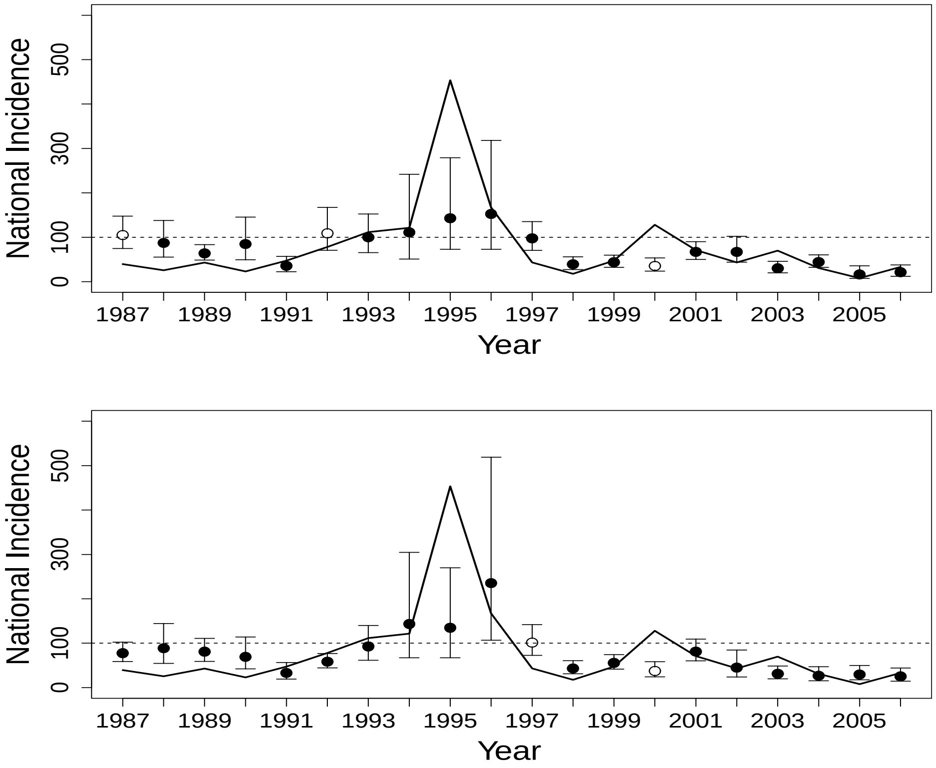


Barcelona Supercomputing Center
Centro Nacional de Supercomputación

Early season forecasts

Pérez García-Pando et al. 2014 EHP

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



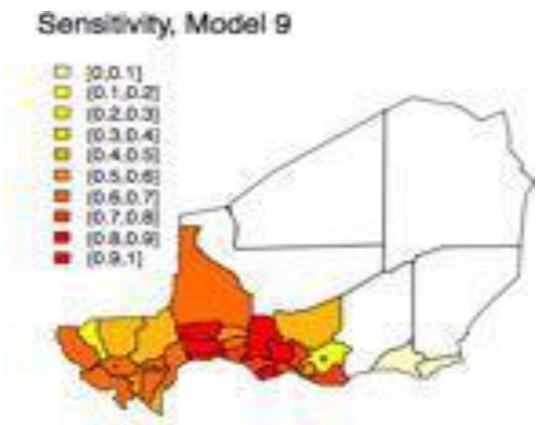
Category	Model	AIC	Pseudo-R2	CVC	SENS (HR)	SPEC (1-FAR)	HKS
1	E	395	0.24	0.38	0.40	1.00	0.70
2*	U_{925}^{ND}	387	0.49	0.51	1.00	0.60	0.80
3*	$U_{925}^{ND}+E$	385	0.57	0.59	0.80	0.87	0.83
2	UV_{925}^{ND}	388	0.47	0.51	1.00	0.53	0.77
3	$UV_{925}^{ND}+E$	385	0.57	0.60	0.80	0.80	0.80
2	$Dust_{10m}^{OD}$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

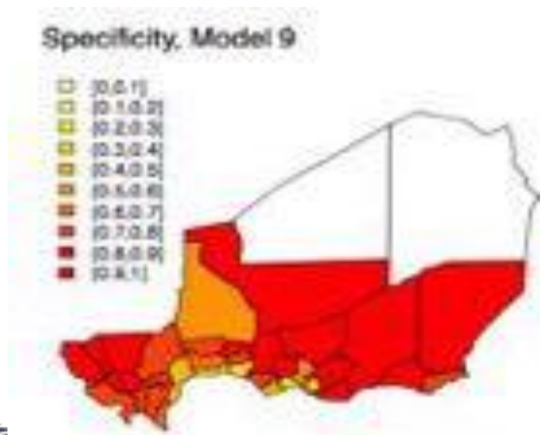
Barcelona Supercomputing Center
Centro Nacional de Supercomputación

Forecasting Meningitis

Pérez García-Pando et al. 2014

Niger - district scale





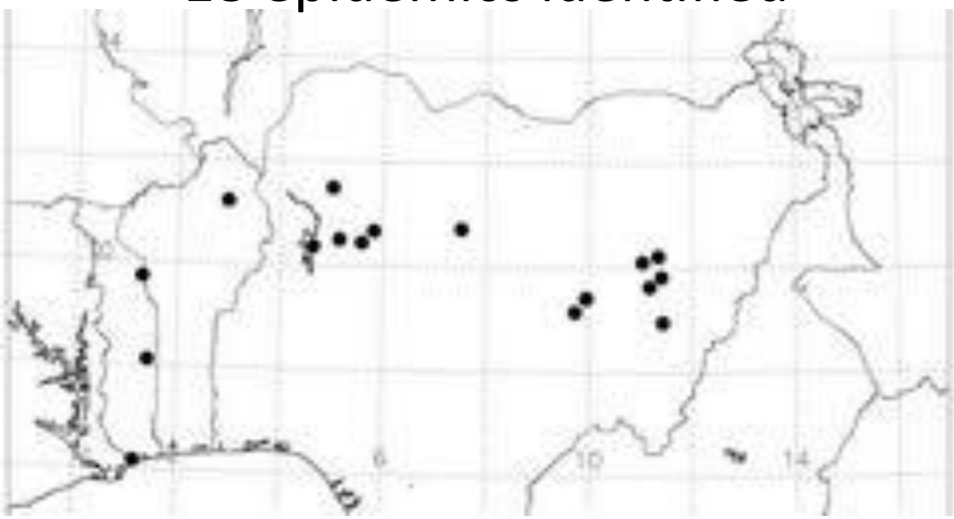
- Early-season zonal wind and dust, along with the number of early cases and population density represented the spatio-temporal variability of the disease with pseudo-R2=0.41 and CVC=0.55.

- 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.

Locations where end-of-season forecasts would have saved vaccine (provided by Tom Hopson NCAR/UCAR)

<u>Using "Perfect" Forecasts</u>
- 18 epidemics identified



<u>Using Climatological Information</u>
-- 3 epidemics identified

- 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 24,000 cases of meningitis and 2400 fatalities)

Challenges

Knowledge
Data
Institutional Alignment

- Likely elimination of large NmA
- Next step: multivalent conjugate vaccine
- In the meantime:

Continue outbreak detection-response

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

Barcelona Supercomputing Center
Centro Nacional de Supercomputación

AXA Research Fund
Through Research, Protection

Thanks

carlos.perez@bsc.es