

# PREVENTION OF MENINGOCOCCAL MENINGITIS BY VACCINATION IN THE AFRICAN MENINGITIS BELT

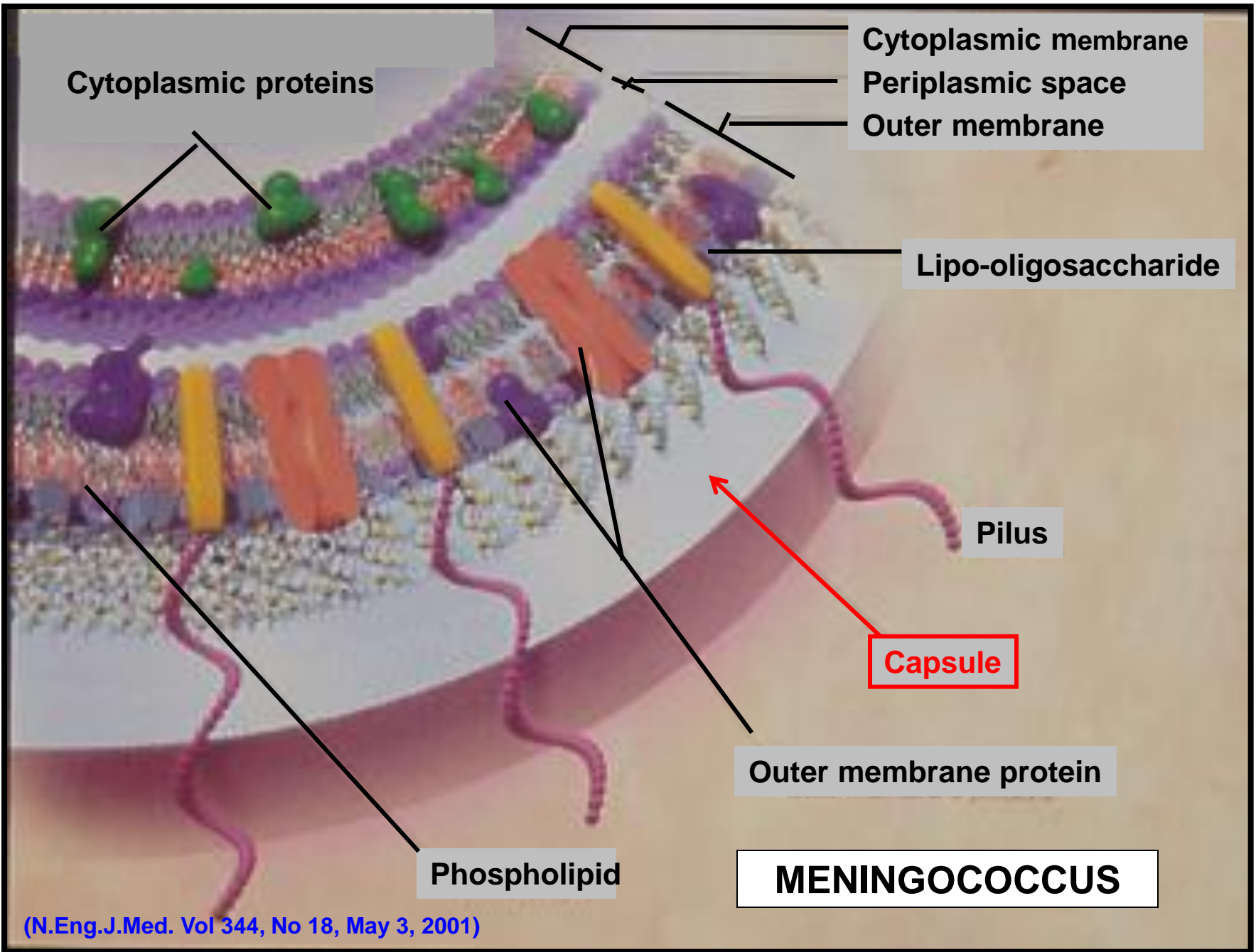


**Brian Greenwood**

**London School of Hygiene  
& Tropical Medicine**

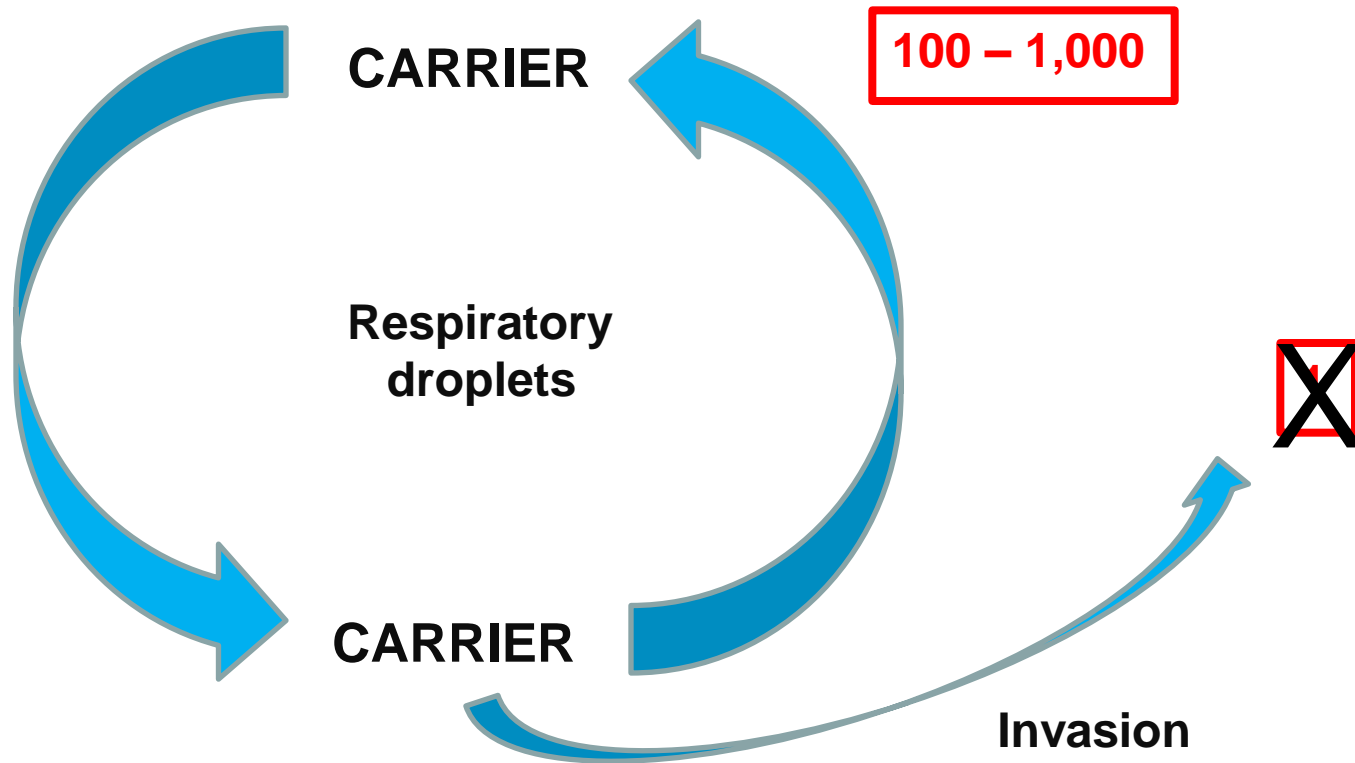
**ADVAC, Annecy  
May 19 th 2014**



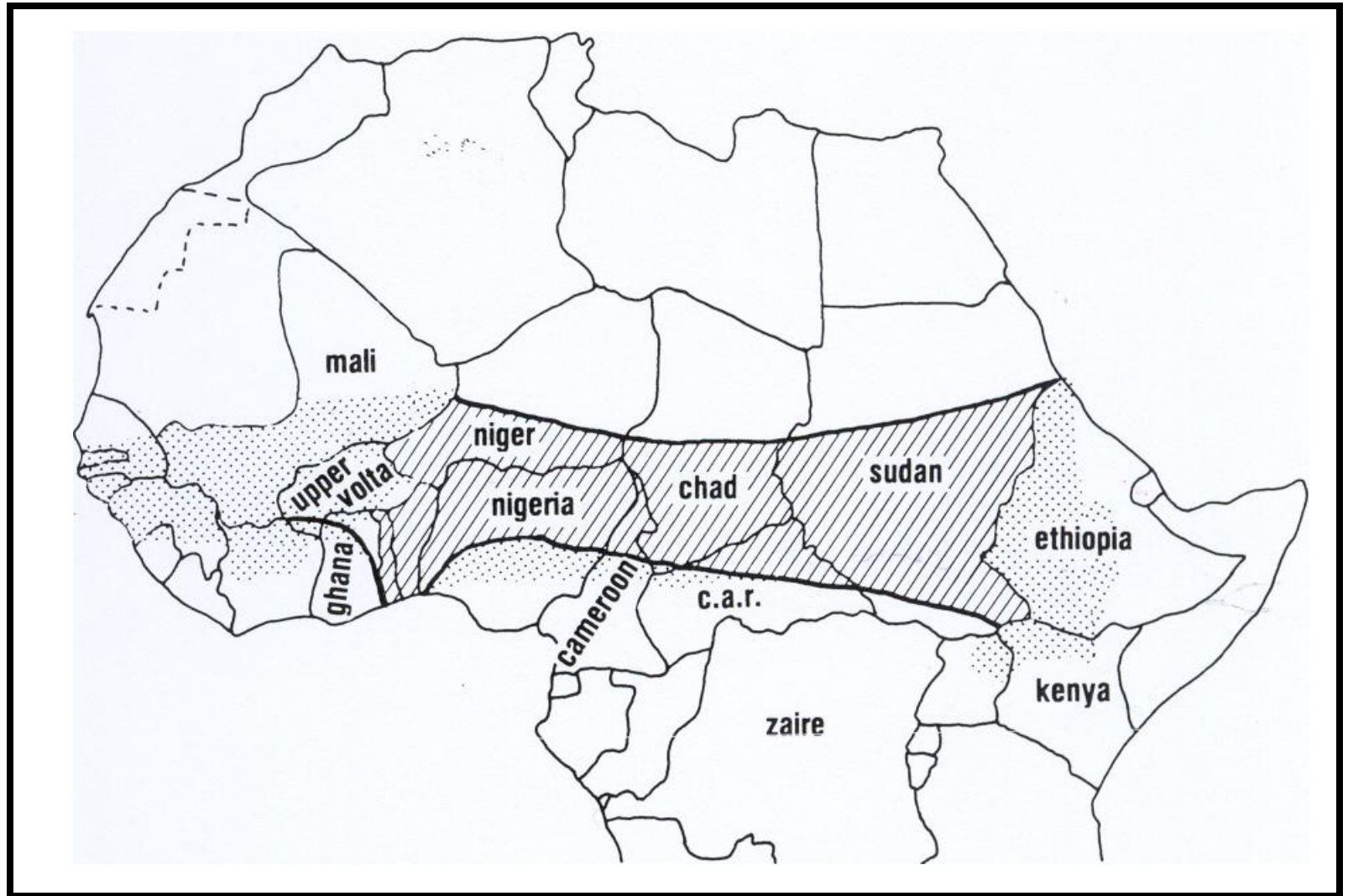


(N.Eng.J.Med. Vol 344, No 18, May 3, 2001)

# MENINGOCOCCAL INFECTION

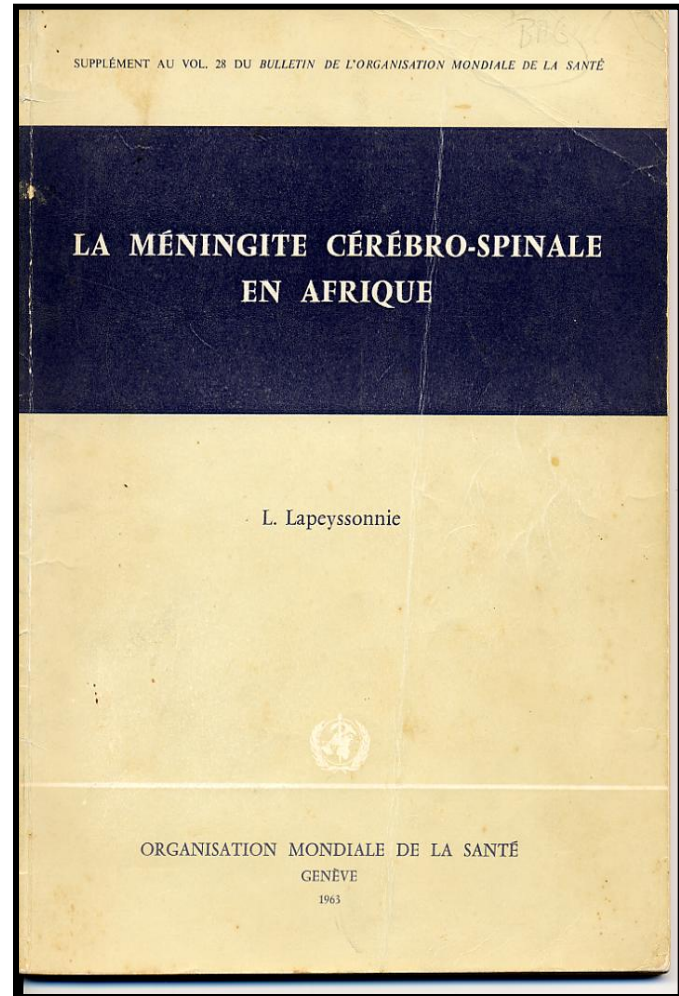


# THE AFRICAN MENINGITIS BELT



(Lapeyssonnie, Bull WHO 1963;28 suppl:3-114)



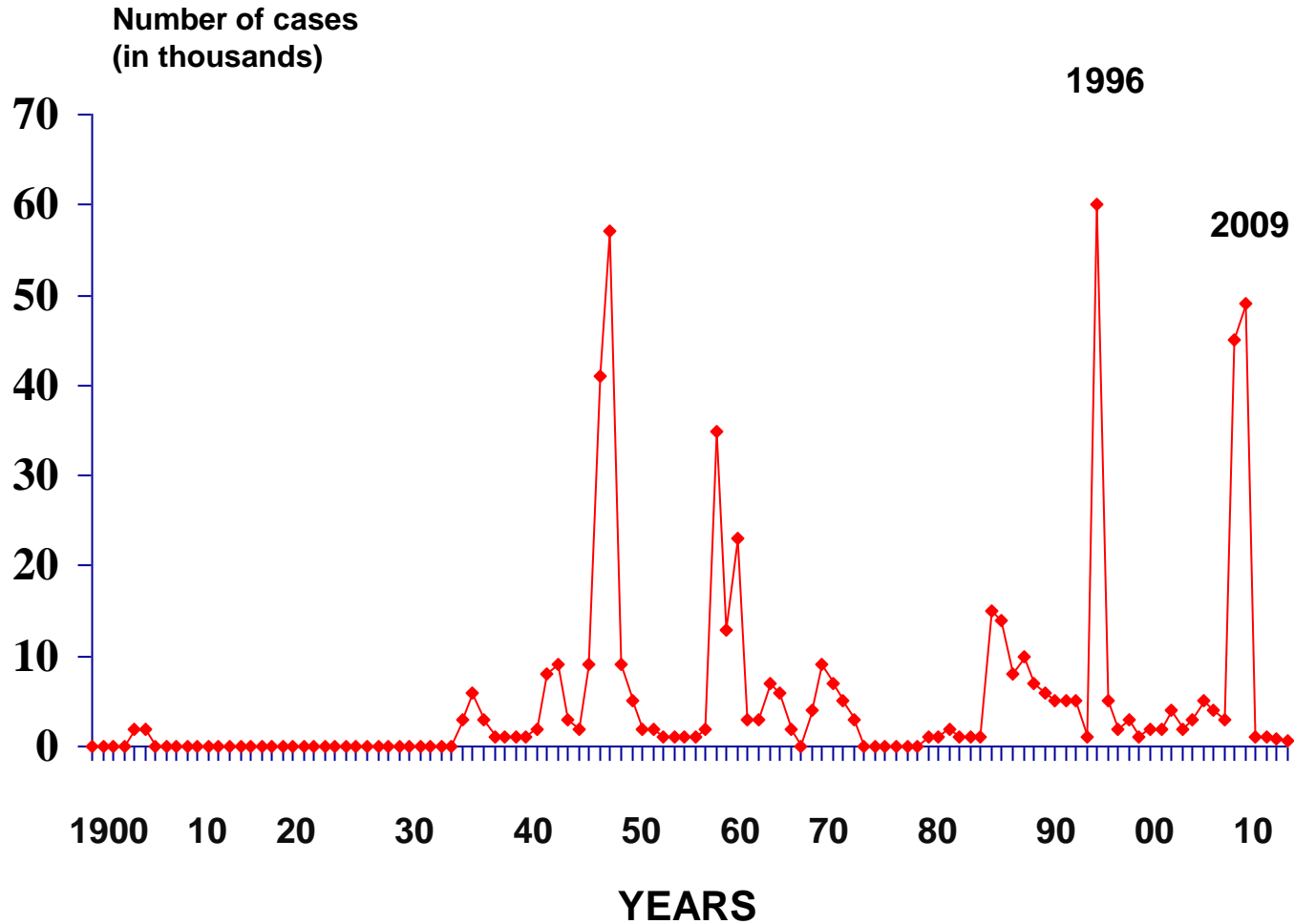


**General Lapeyssonnie**

# **MENINGOCOCCAL DISEASE IN THE AFRICAN MENINGITIS BELT**

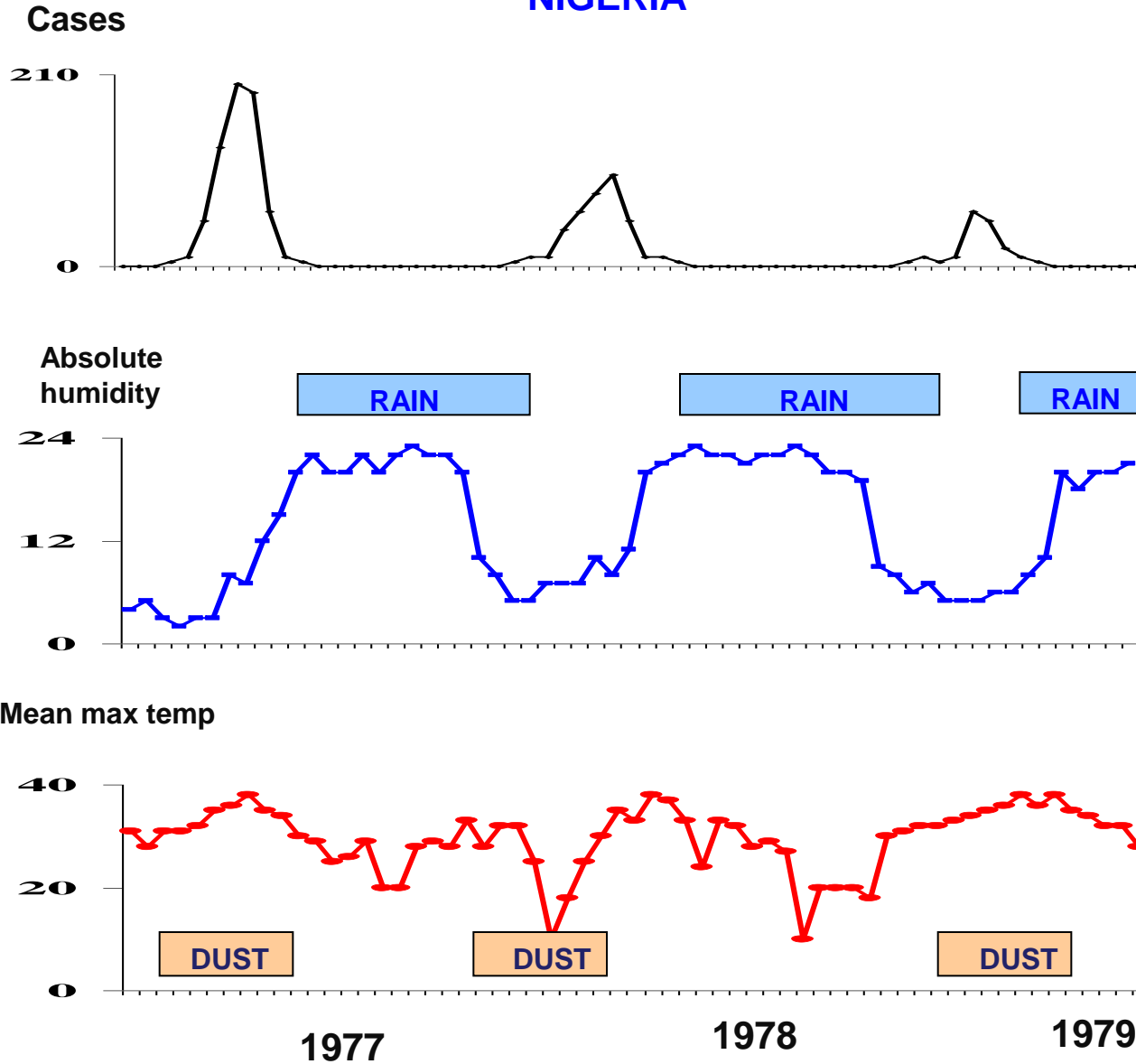
- **High rate of endemic infection**
- **Regular epidemics**
  - **geographically limited**
  - **periodic**
  - **markedly seasonal**
  - **large size**
  - **mainly serogroup A**

# MENINGOCOCCAL MENINGITIS - NIGERIA



# SEASONALITY

## NIGERIA





# THE TOOLS FOR THE PREVENTION OF EPIDEMIC MENINGITIS

- **Improvement in socio-economic conditions.**
- **Quarantine.**
- **Chemoprophylaxis.**
- **Vaccination.**

# MENINGOCOCCAL VACCINES

## 1. WHOLE CELL VACCINES



## 2. POLYSACCHARIDE VACCINES



Polysaccharide

(A+C; A+C+W; A+C+W+Y)

**REACTIVE  
VACCINATION**

## CONJUGATE VACCINES

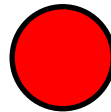
Polysaccharide



Linker



Protein



Conjugate

(A; C; A+C+W+Y)

**PROPHYLACTIC  
VACCINATION**

## 4. PROTEIN VACCINES



Protein

(B)

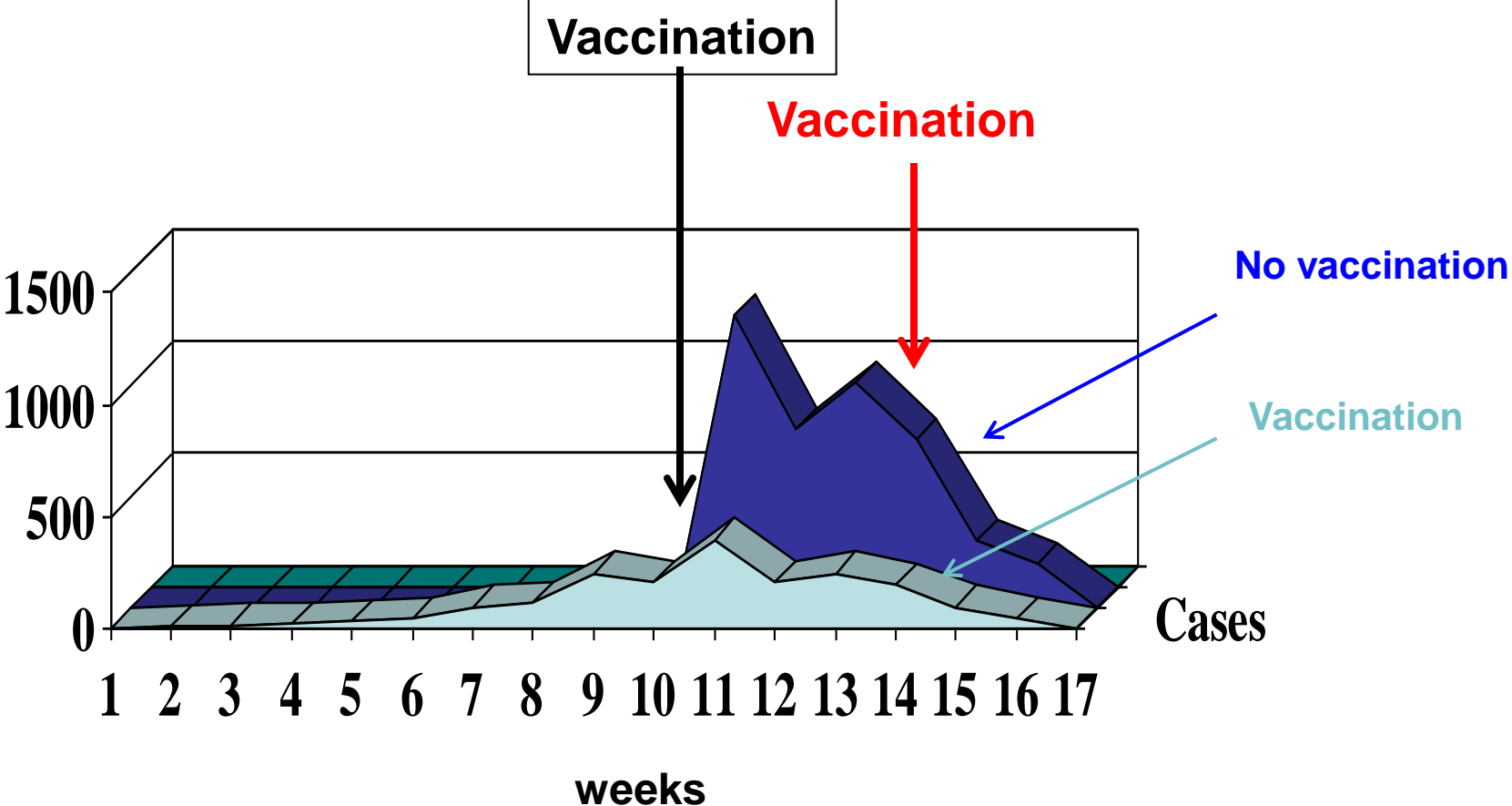
**REACTIVE VACCINATION IN  
RESPONSE TO OUTBREAKS**

# **REACTIVE VACCINATION**

## **Essential requirements**

- **Early detection of a meningitis outbreak**  
**- effective surveillance system.**
- **Rapid determination of the aetiology of the outbreak**  
**- rapid diagnostic tests.**
- **A speedy vaccination response (ICG).**

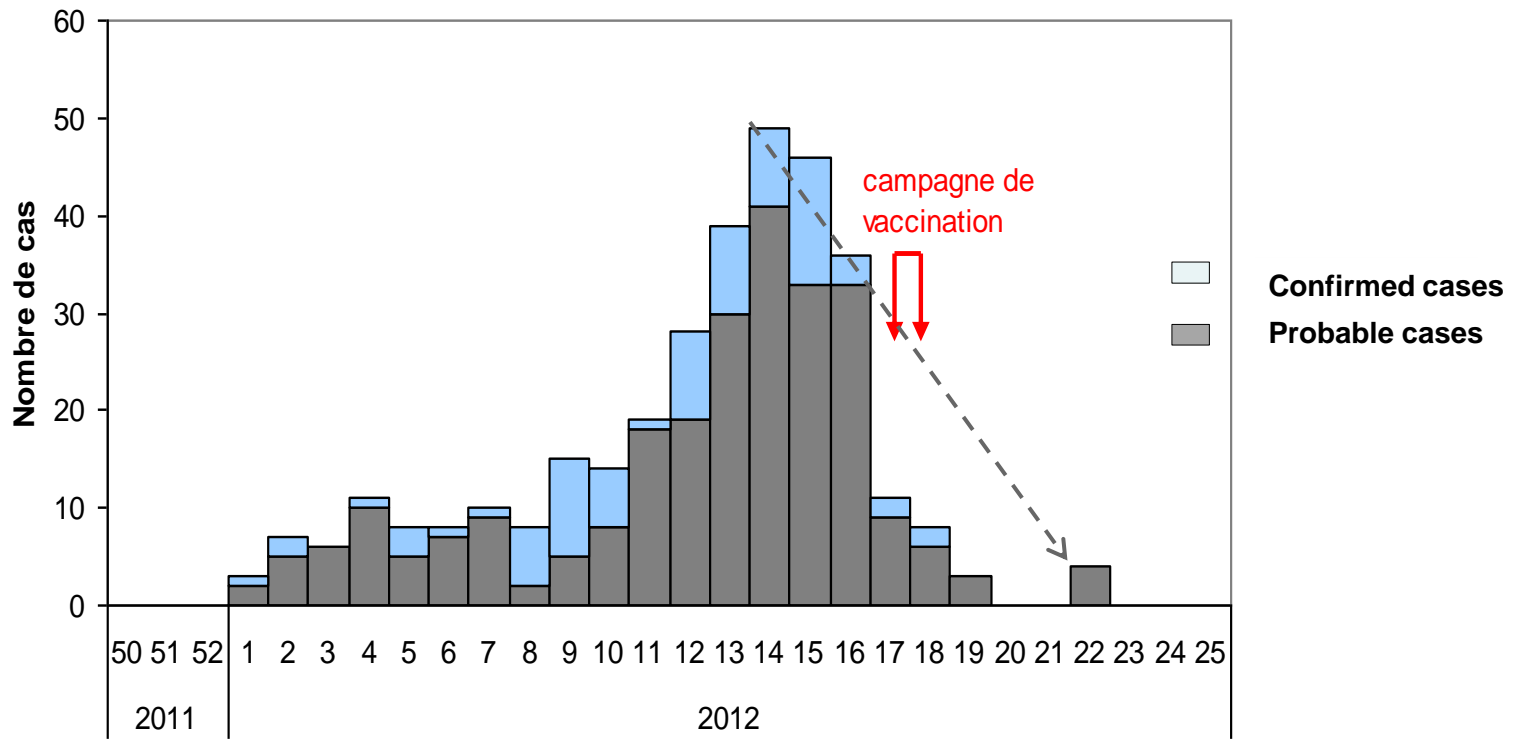
# POTENTIAL OF REACTIVE VACCINATION



(Leake et al. Bull WHO 2002; 80:345)

# REACTIVE VACCINATION IN CHAD

## Cases of meningitis by week of admission Moissala district, Chad, 2012

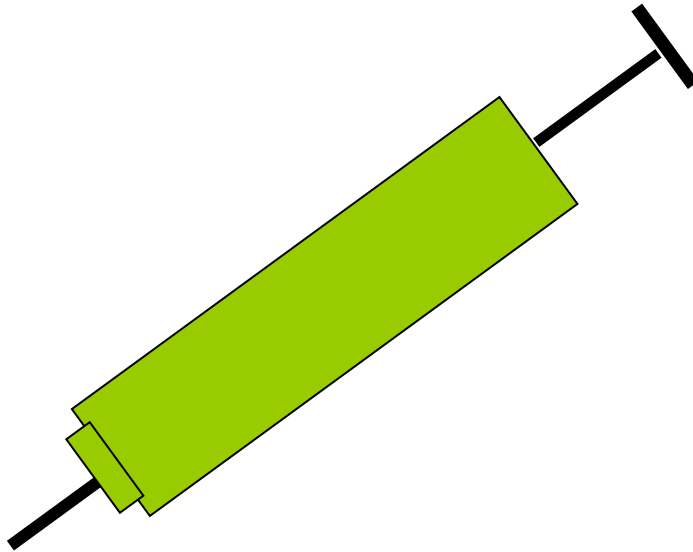




## **DRAWBACKS TO REACTIVE VACCINATION**

- **Vaccination is often undertaken too late.**
- **Polysaccharide vaccination does not induce long-lasting immunity in children.**
- **A policy of reactive vaccination has not reduced the frequency of epidemics.**
- **Difficulties in matching vaccine needs to supply.**

# PROPHYLACTIC VACCINATION WITH CONJUGATE VACCINES



**Group A**

**Group C**

**Group A + C + W + Y**

# DEVELOPMENT OF A SEROGROUP A MENINGOCOCCAL CONJUGATE VACCINE FOR AFRICA

**1992/3**

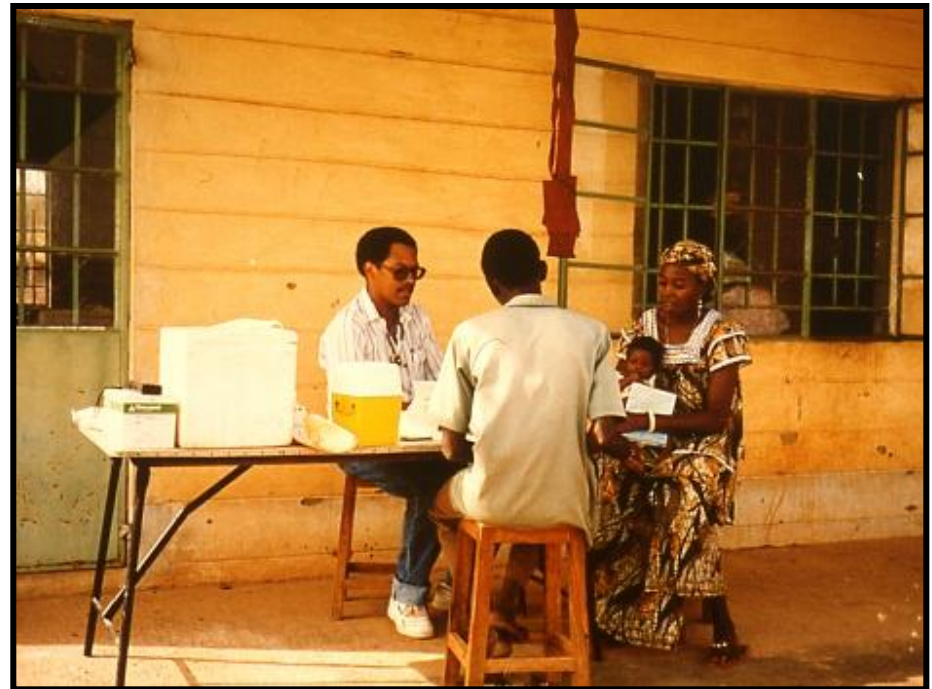
**A + C conjugate vaccine  
(Biocine/Sclavo)**

**Basse, The Gambia**

**1996/7**

**A + C conjugate  
(Pasteur Merieux Connaught)**

**Niamey, Niger**



(Twumasi et al. JID 1995;171:632-8; Campagne et al. PIDJ 200;19:144-50)

# THE MENINGITIS VACCINE PROJECT



## Aim

**Production of an affordable,  
serogroup A  
meningococcal conjugate  
vaccine for use in Africa**

**Established in 2001 with support from  
the Bill and Melinda Gates Foundation**

# **MVP – ACHIEVEMENTS**

- **Efficient conjugation method developed.**
- **Technology transferred successfully to an Indian manufacturer.**
- **Vaccine produced in India at a cost of \$0.40 per dose.**
- **Vaccine is relatively heat stable.**
- **Phase 2 trials (Gambia, Mali) showed the vaccine to be safe and highly immunogenic.**
- **Vaccine shown to be safe and immunogenic in infants (Ghana).**
- **Vaccine prequalified by WHO in 2010.**
- **Mass campaigns commenced in Burkina Faso, Mali and Niger in those aged 2 – 29 years at the end of 2010.**

**10 YEARS FROM VACCINE DEVELOPMENT TO DEPLOYMENT**

# VACCINE MANUFACTURE



**MenAfriVac**

**Serum Institute  
Pune, India**



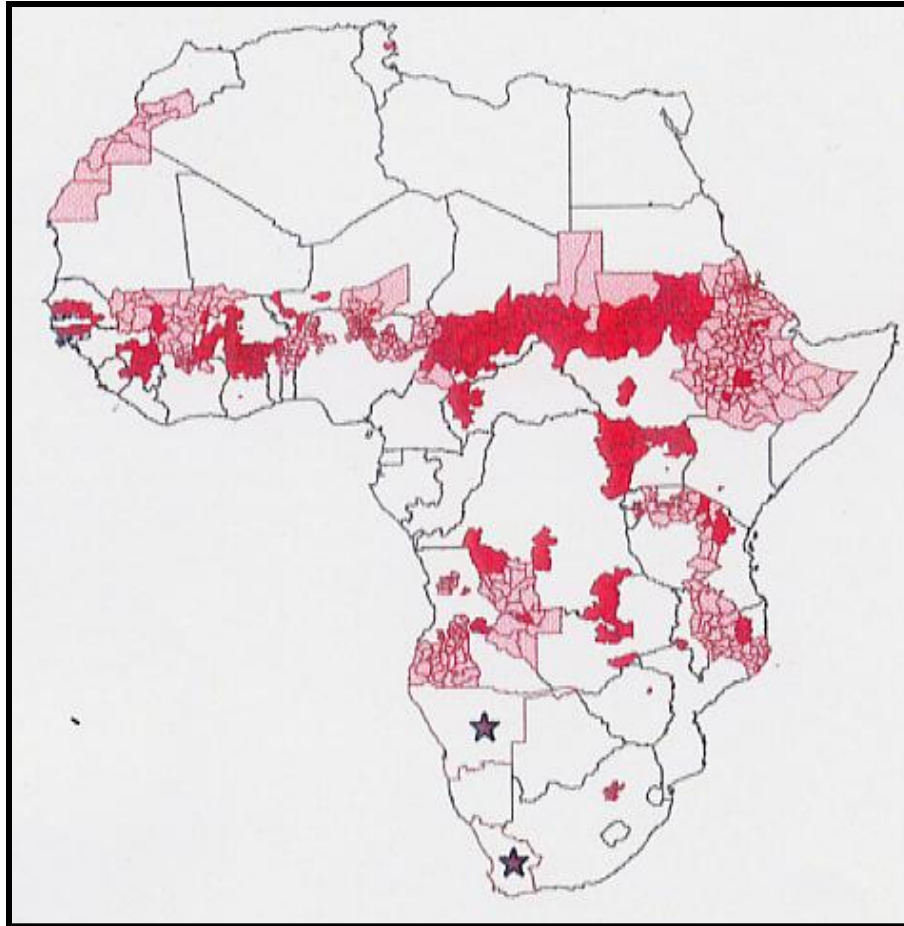


## **DEPLOYMENT OF MENAFRIVAC**

- **Where should the vaccine be deployed ?**
- **Which age group should be vaccinated ?**

# DEPLOYMENT

Where?



## Meningococcal disease

 High incidence

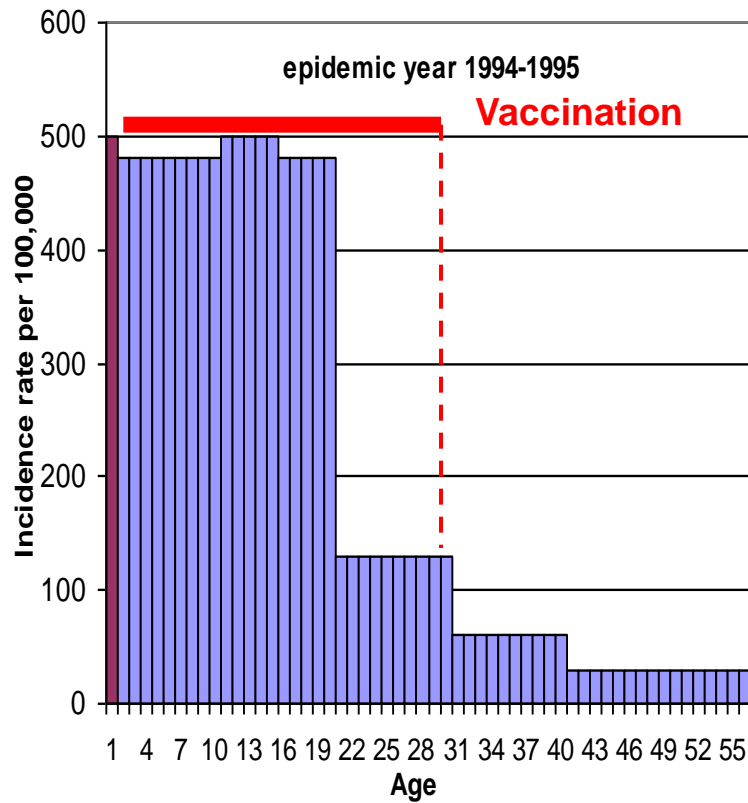
 At risk

(1980 – 1999)

# DEPLOYMENT

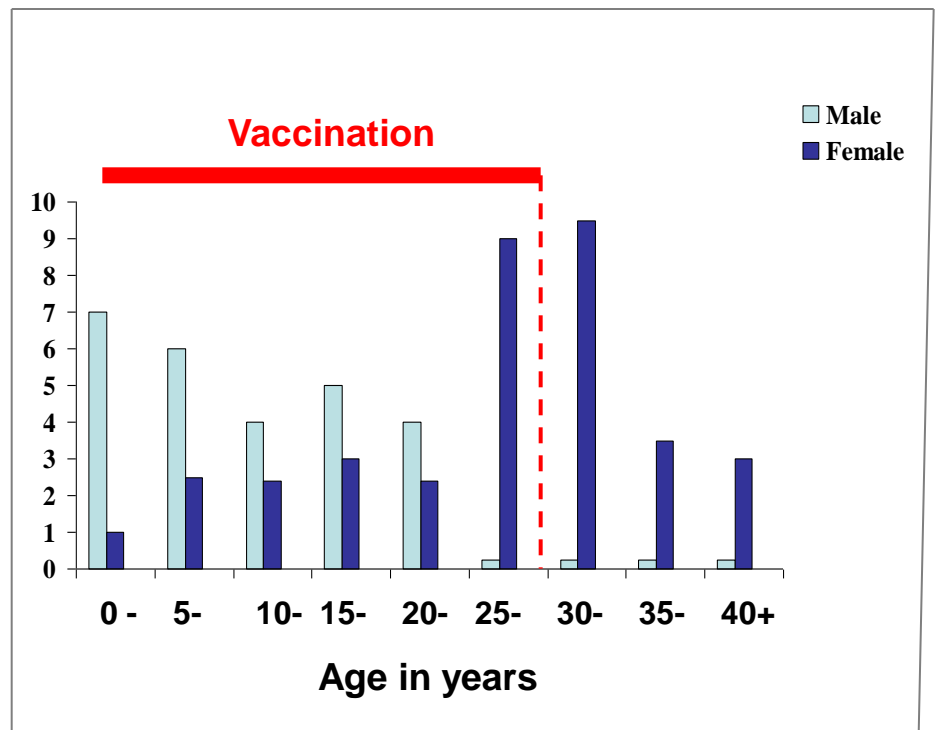
## Who?

### Meningococcal disease - Niger



(Campagne et al. Bull WHO 1999;77:499)

### Meningococcal carriage in Nigeria



(Hassan-King et al. TRSTMH 1979;73:567-73)

# MENAFRIVAC

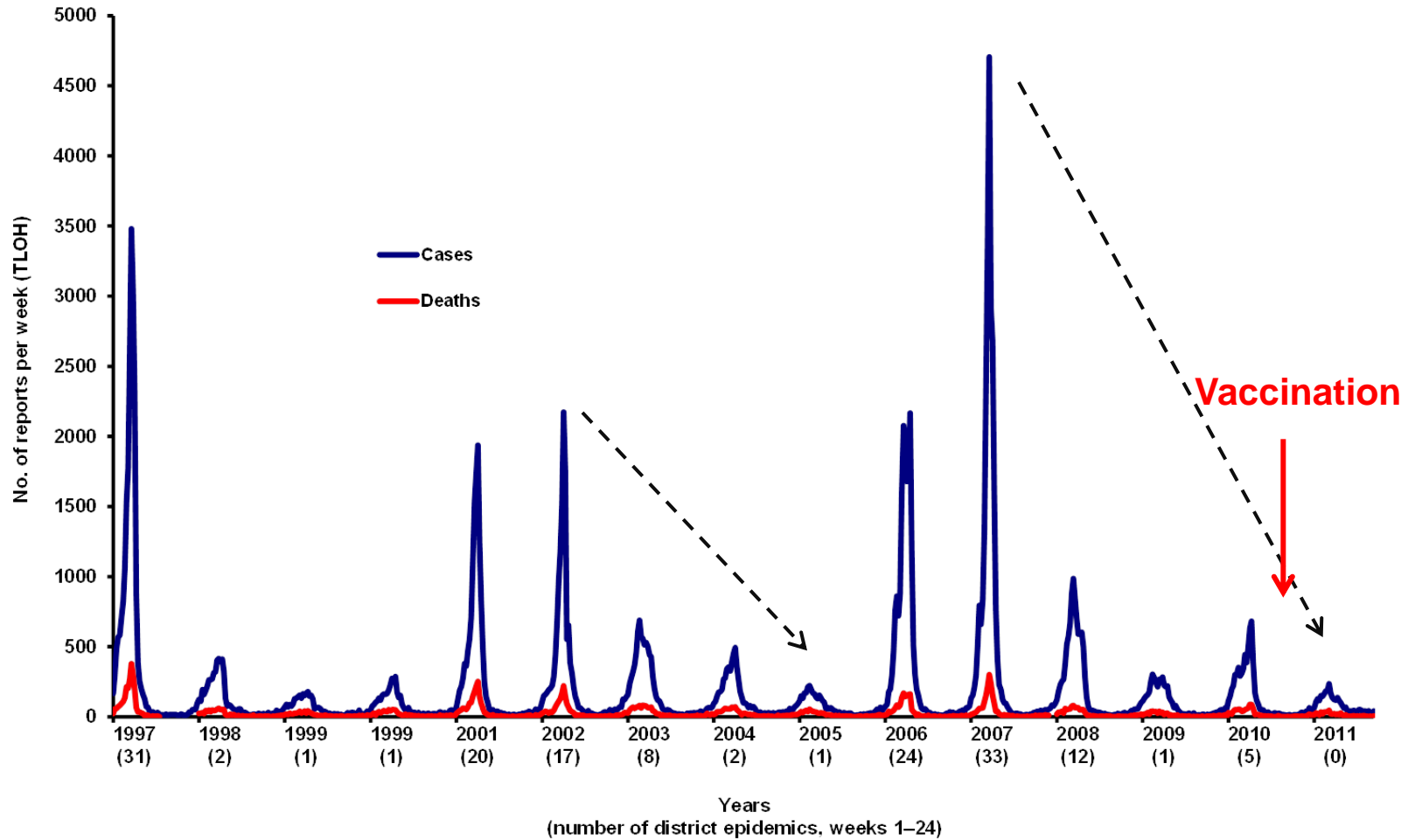
## Roll out plans

MenAfriVac Roll out plan 2012 - 2016	2011	2012	2013	2014	2015	2016
<b>GROUP 1</b>						
Nigeria	X	X	X			
Chad	X	X				
Cameroon	X	X				
North Sudan		X	X			
<b>GROUP 2</b>						
Ghana		X				
Benin		X				
Senegal		X				
<b>GROUP 3</b>						
Ethiopia			X	X	X	
DRC				X		
Southern Sudan				X	X	
Ivory Coast					X	
Togo				X		
Uganda					X	
Guinea				X		
<b>GROUP 4</b>						
Gambia			X			
Central Africa					X	
Erithrea						X
Kenya					X	
Burundi						X
Guinea Bissau						X
Mauritania					X	
Rwanda						X
Tanzania						X

# **DOES MENAFRIVAC WORK ?**

- **Does it prevent cases of meningitis?**
- **Does it prevent pharyngeal carriage?**
- **Can it prevention of epidemics?**

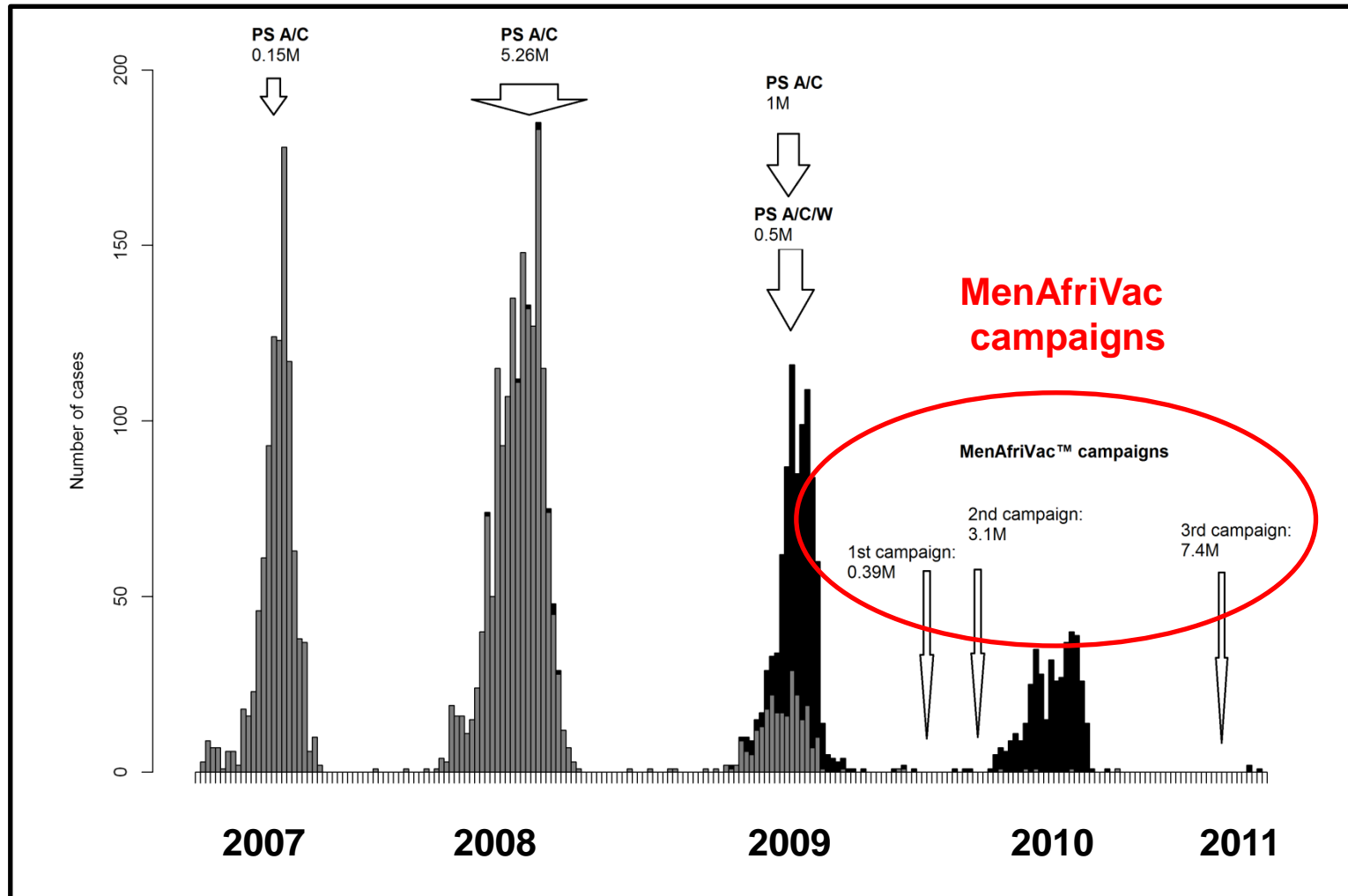
# IMPACT OF MENAFRIVAC ON MENINGITIS BURKINA FASO



(Novak et al. LID 2012; 12 : 757-64)



# IMPACT OF MENINAFRIVAC ON MENINGITIS - NIGER



(Collard et al. 2013;13:576)

Serogroup A meningitis in grey

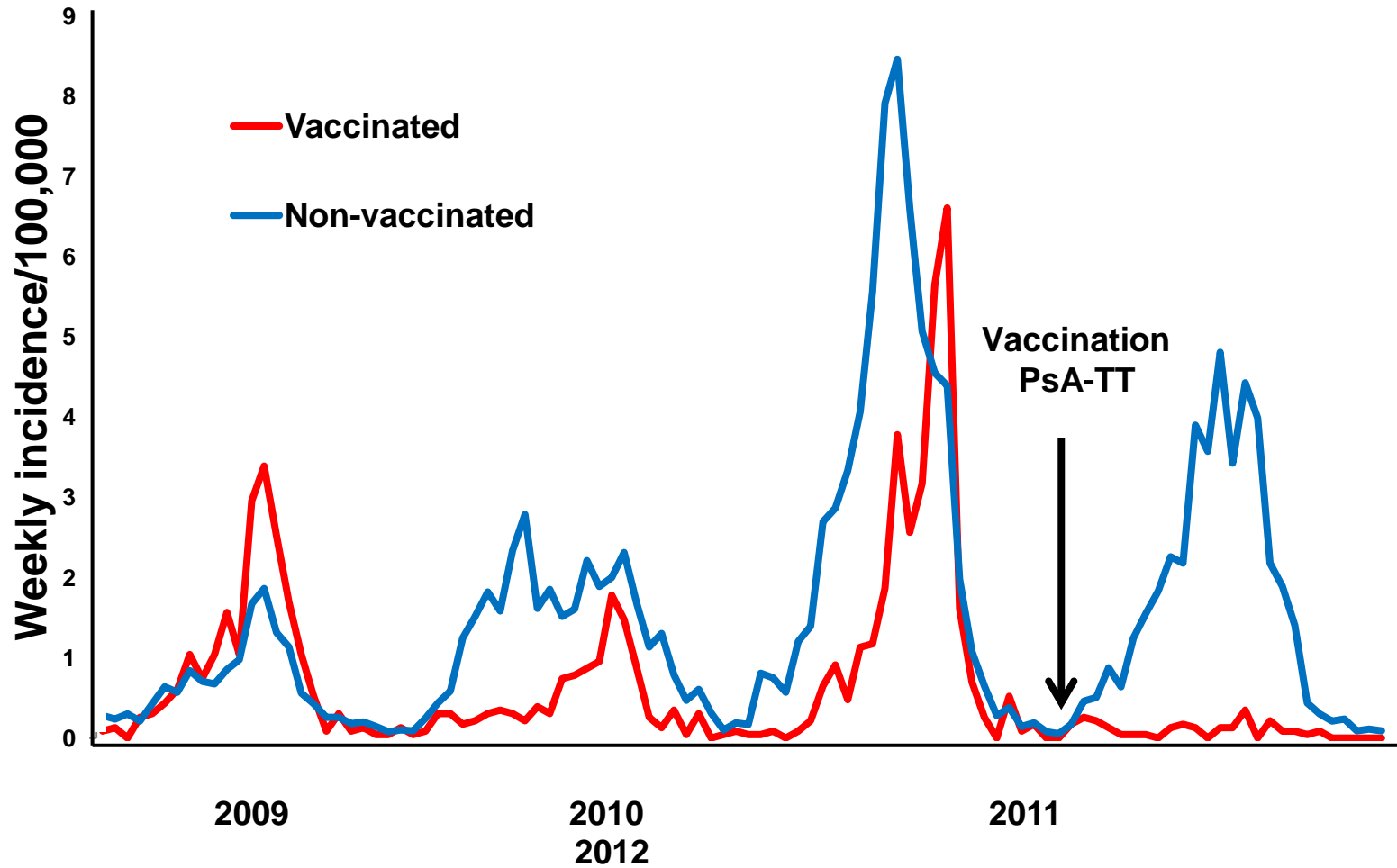
# IMPACT OF MENAFRIVAC ON MENINGITIS IN CHAD



**Dr Kadidja Gamougamand  
Dr Daugla Doumagoum  
(CSSI, N'Djamena)**



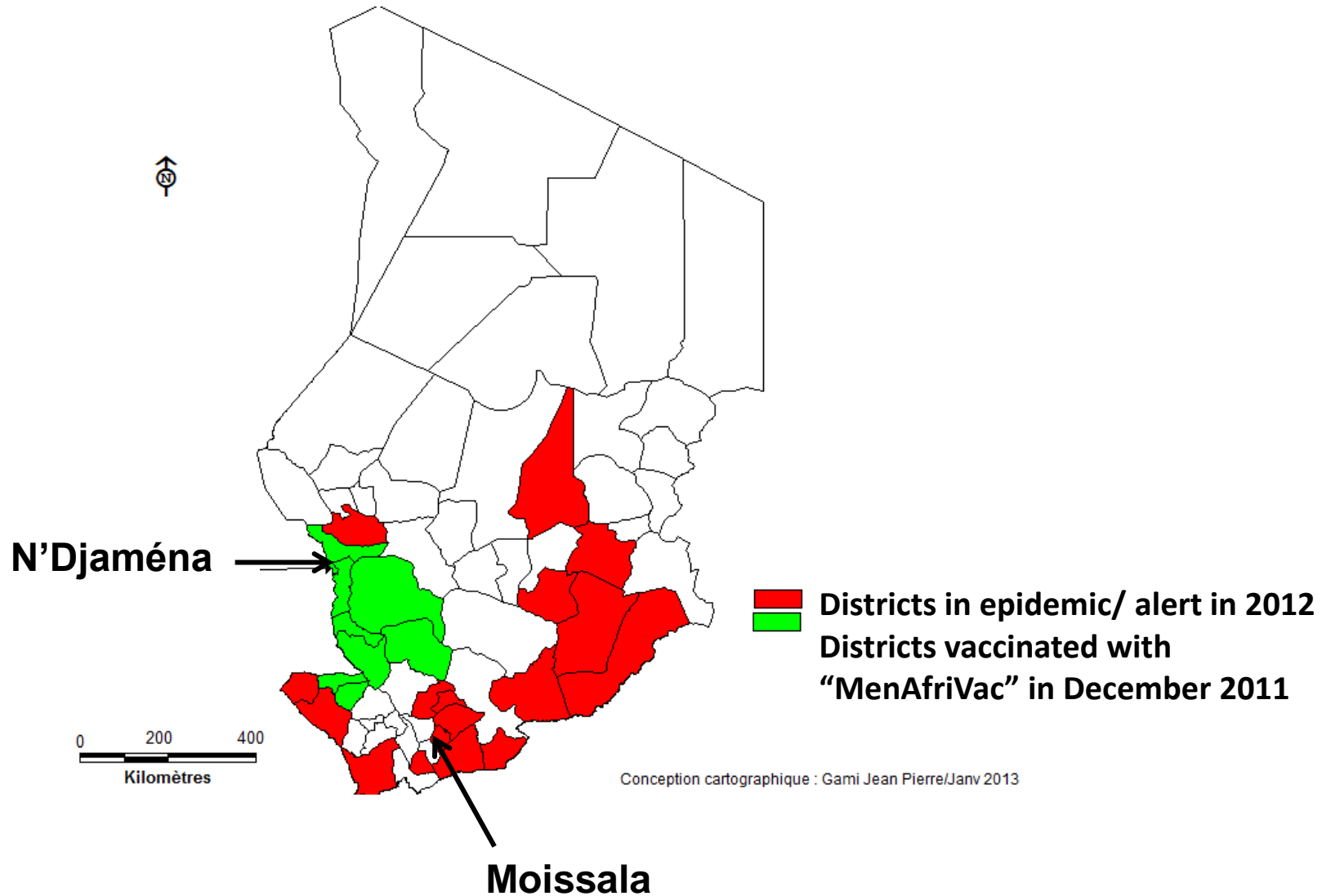
# IMPACT OF MENAFRIVAC ON MENINGITIS CHAD - 2012



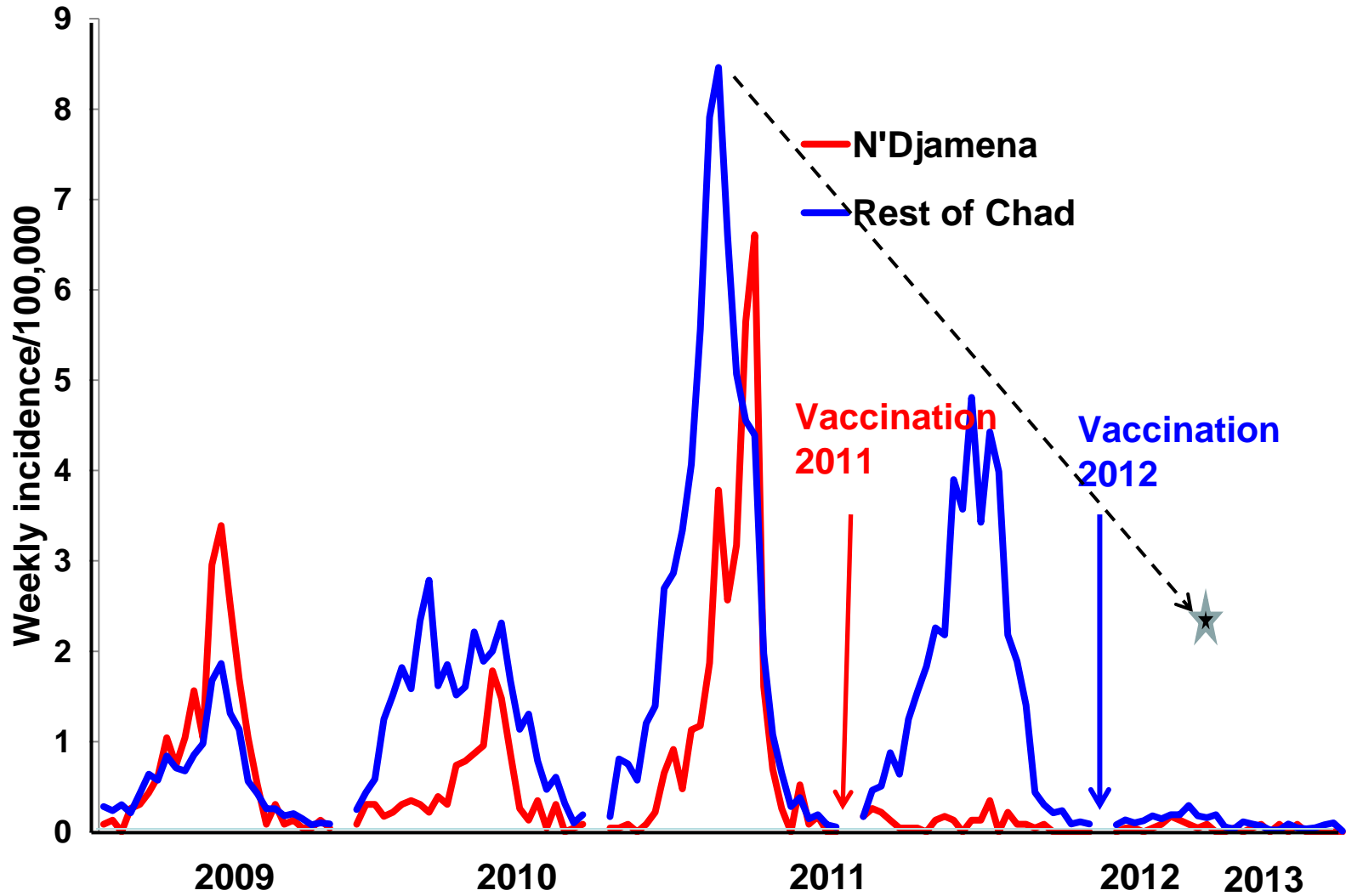
(Daugla et al. Lancet 2014; 383:40-47)

Incidence odds ratio 0.096 (0.05,0.19)

# EPIDEMIC MENINGITIS IN CHAD 2012



# IMPACT OF MENAFRIVAC ON MENINGITIS IN CHAD 2013



## 60 SECONDS

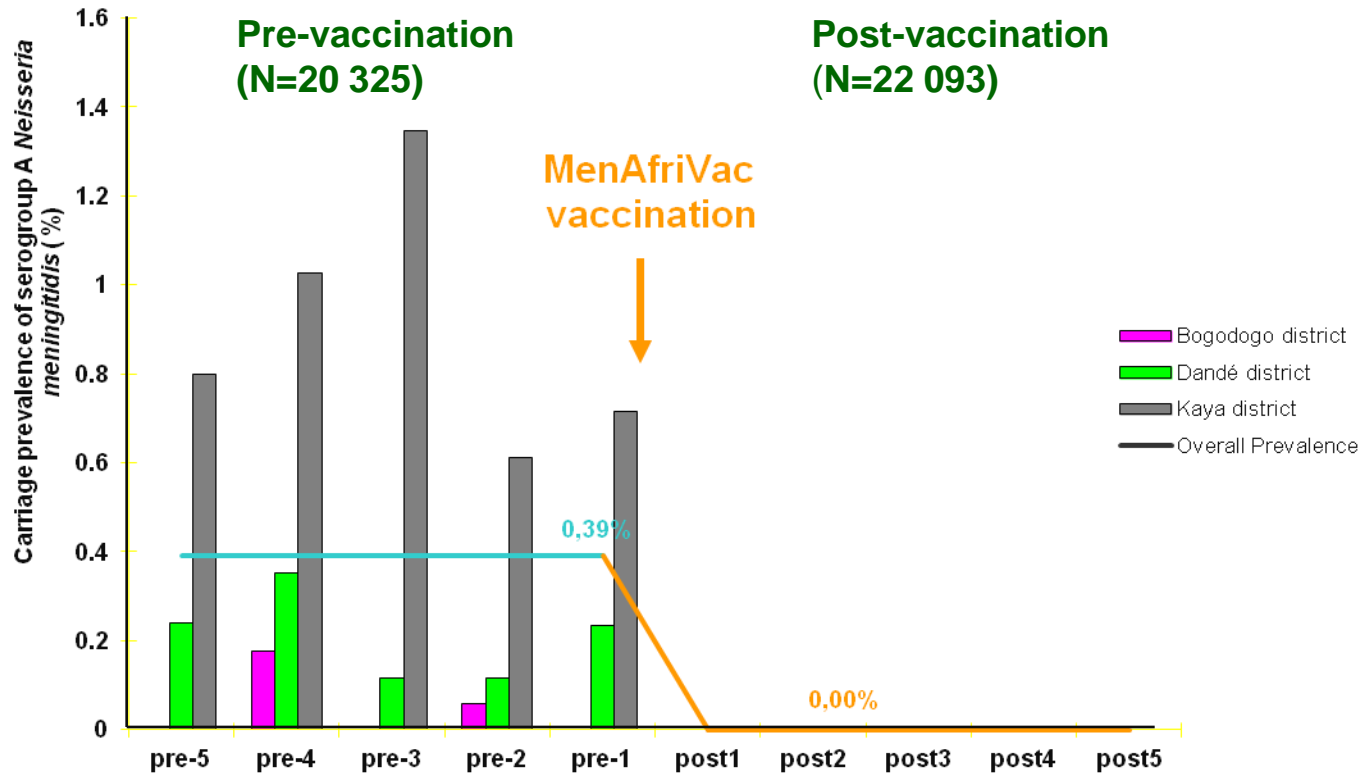
### Meningitis milestone

This week the 100 millionth person will be vaccinated against meningitis with MenAfriVac, which can last four days without a fridge and costs less than 50 cents. In Africa's largest seasonal epidemic in 1996, meningitis A killed 25,000. Very few people now die in the regions where vaccination takes place.

**New Scientist**

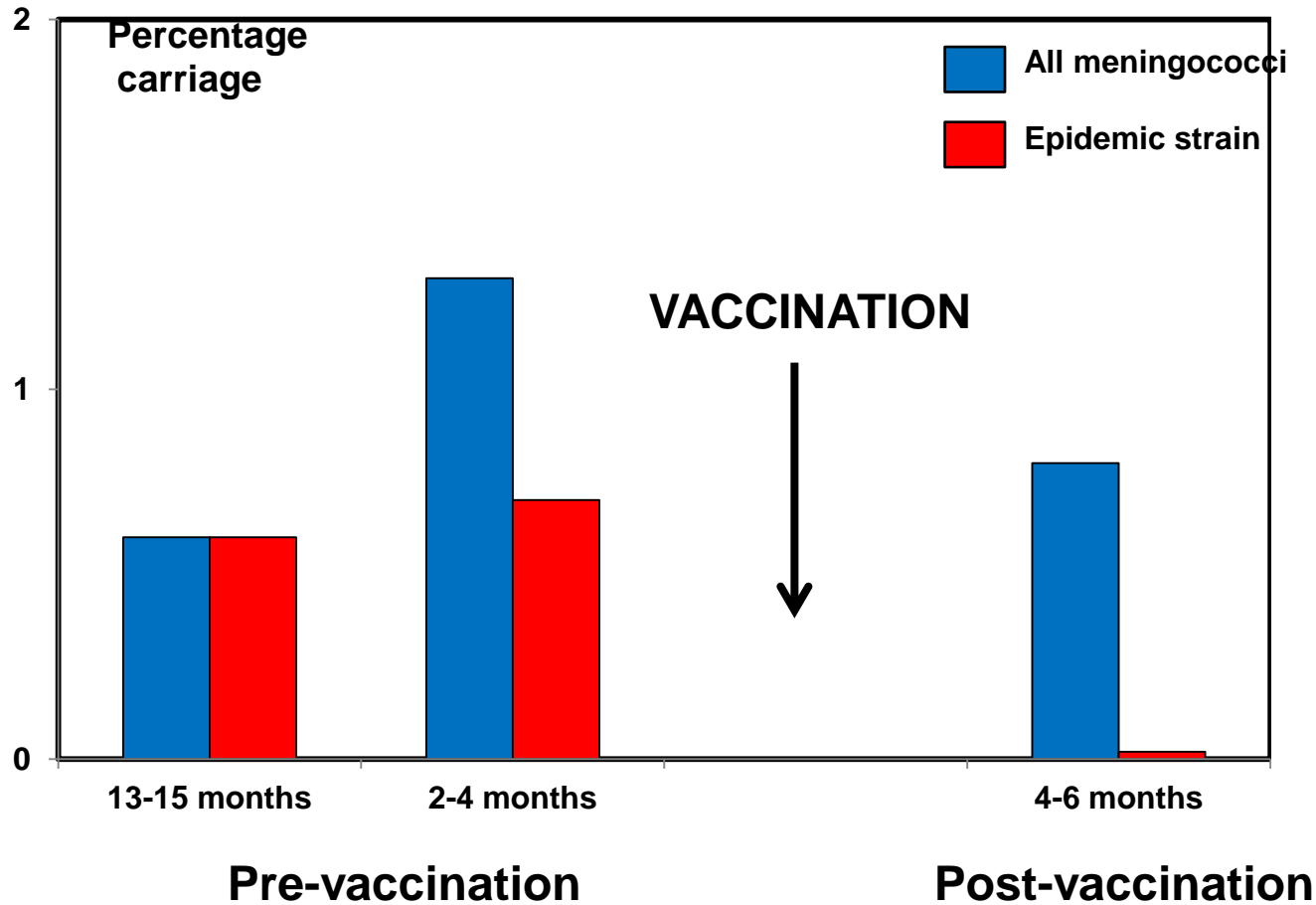
**8<sup>th</sup> December, 2012**

# IMPACT OF MENAFRIVAC ON CARRIAGE BURKINA FASO



(Kristiansen et al. Clin Infect Dis 2012; 56 354-63)

# IMPACT OF MENAFRIVAC ON CARRIAGE CHAD

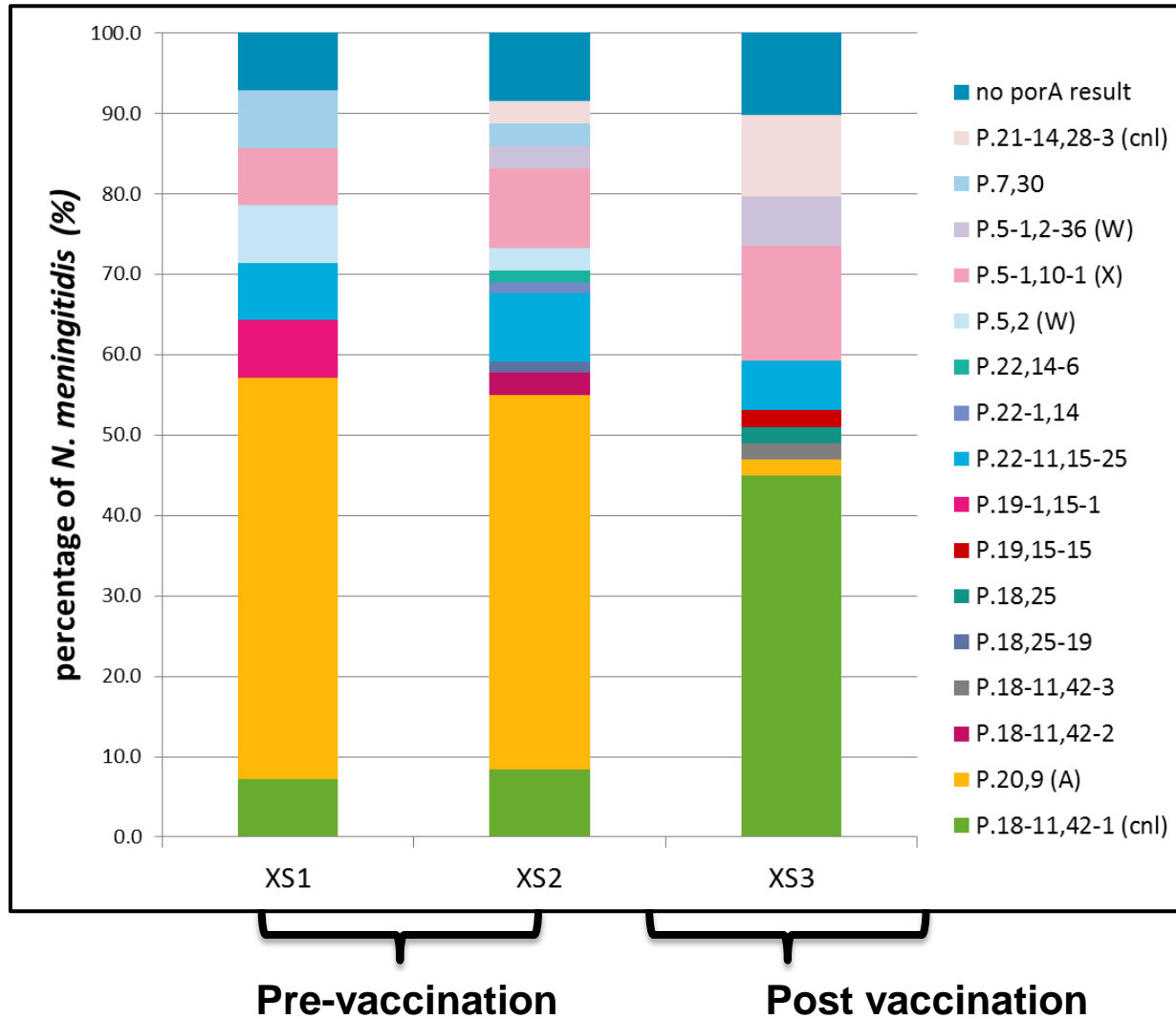


(Daugla et al. Lancet 2014; 383:40-47)

[Adjusted OR = 0.019, 95% CI 0.002, 0.14].

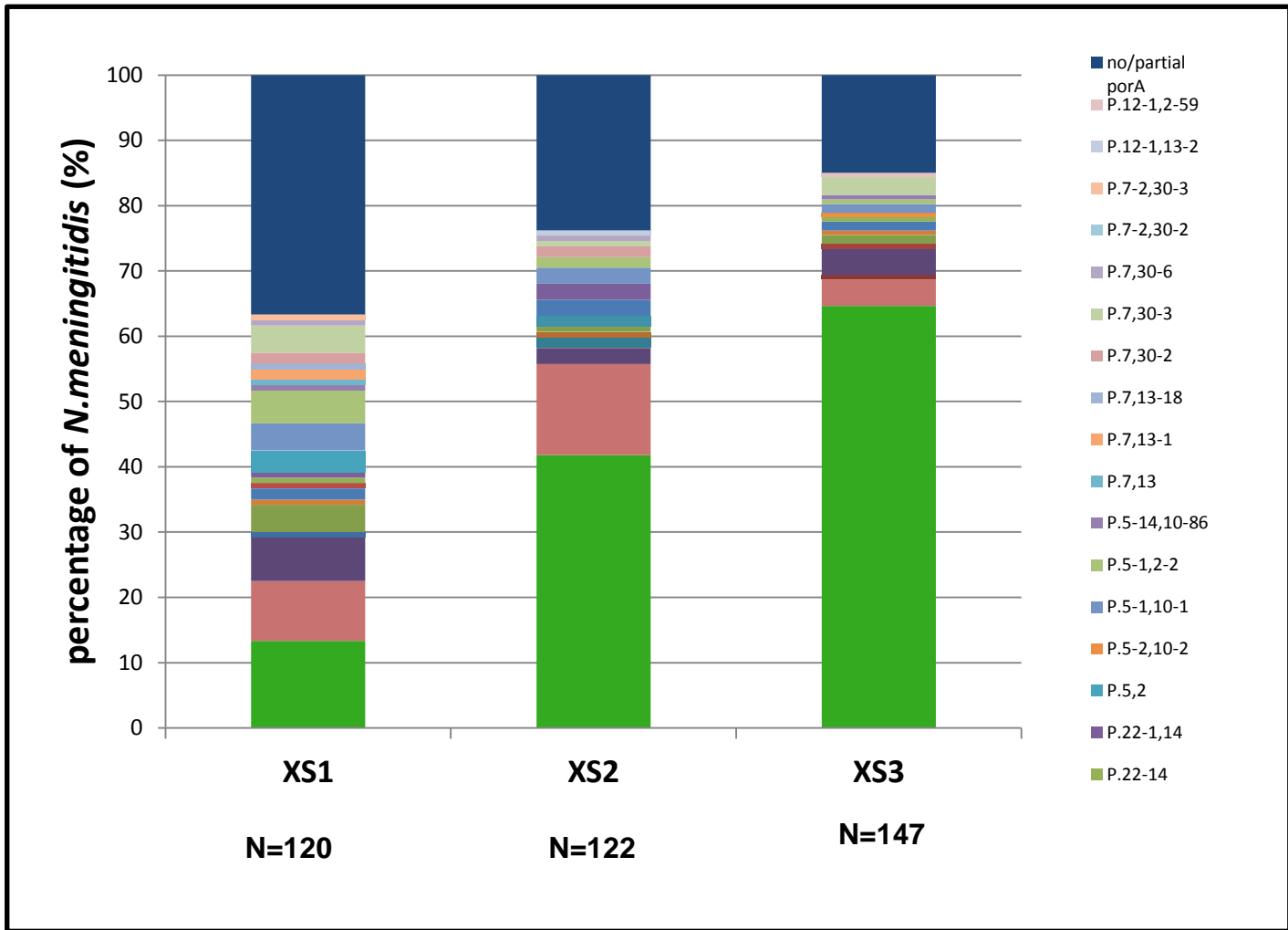


# CHANGES IN CARRIAGE STRAINS FOLLOWING VACCINATION CHAD



K. Diallo

# CHANGE IN CARRIAGE STRAINS IN ETHIOPIA



**NO VACCINATION!**

K Diallo

.....and they all lived happily ever after!

THE END

Not quite !

# REMAINING ISSUES

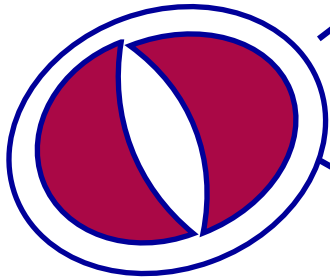
## SEROGROUP A

- How long will the protection provided by MenAfrivac last?
- How can immunity at the population level be sustained?

## OTHER SEROGRAMS

- Will there be serogroup replacement?
- How should non-serogroup A outbreaks be managed?
- What should be done about serogroup X?

# OUTBREAKS OF MENINGOCOCCAL DISEASE DUE TO NON-SEROGROUP A MENINGOCOCCI



*Neisseria meningitidis*

## Serogroup C

Epidemics in the 1970s.  
Occasional cases subsequently.

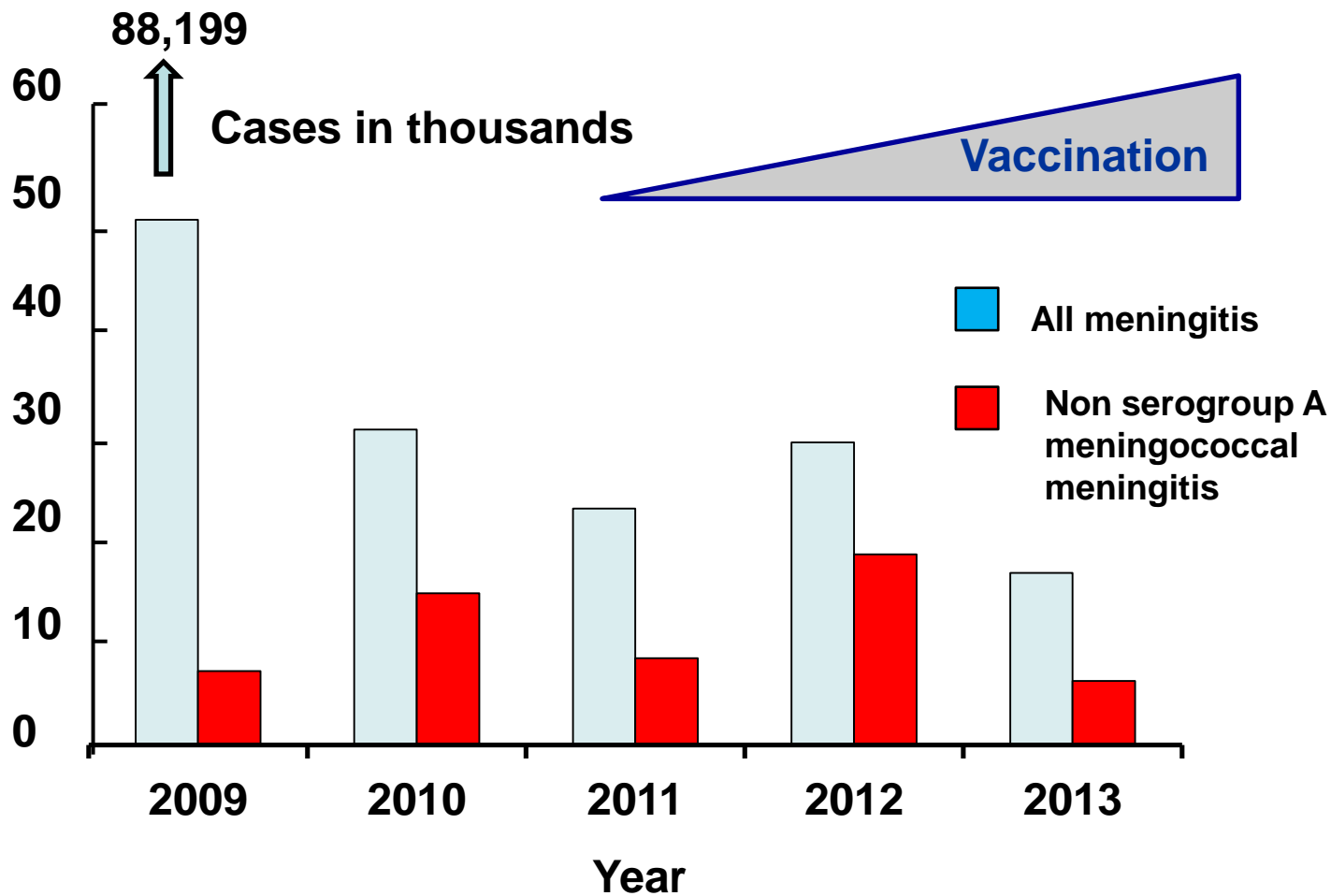
## Serogroup W135

Major epidemic in Burkina Faso in 2002  
(12,000 cases, 1,400 deaths)  
Persistent outbreaks subsequently.

## Serogroup X

Major outbreak in Niger in 2005/6.  
(approx 2,000 cases)  
Occasional outbreaks subsequently.

# INCIDENCE OF NON-SEROGROUP A MENINGOCOCCAL DISEASES 2009-2013



# NEXT STEPS

## MANAGING NON-SEROGROUP A OUTBREAKS

- **Maintaining surveillance (MenAfriNet).**
- **Reactive vaccination with A+C or A+C+W polysaccharide vaccines.**
- **Adjustment of the epidemic threshold?**
- **Managing a serogroup X epidemic?**

## PREVENTION OF NON-SEROGROUP EPIDEMICS

- **Development and deployment of a pentavalent (A+C+W+X+Y) conjugate vaccine.**
- **Development of a common protein vaccine.**

## CONCLUSIONS

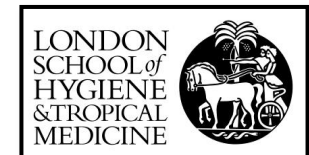
- **The development and deployment of MenAfriVac within a 10 year period has been a major public health success.**
- **There are still questions to be addressed about the duration of protection that it can provide and on how this can be sustained.**
- **Final control of meningococcal epidemics in Africa would almost certainly require the use of a polyvalent conjugate vaccine, including a serogroup X conjugate, but this would be expensive and might not be cost effective.**



# ACKNOWLEDGMENTS



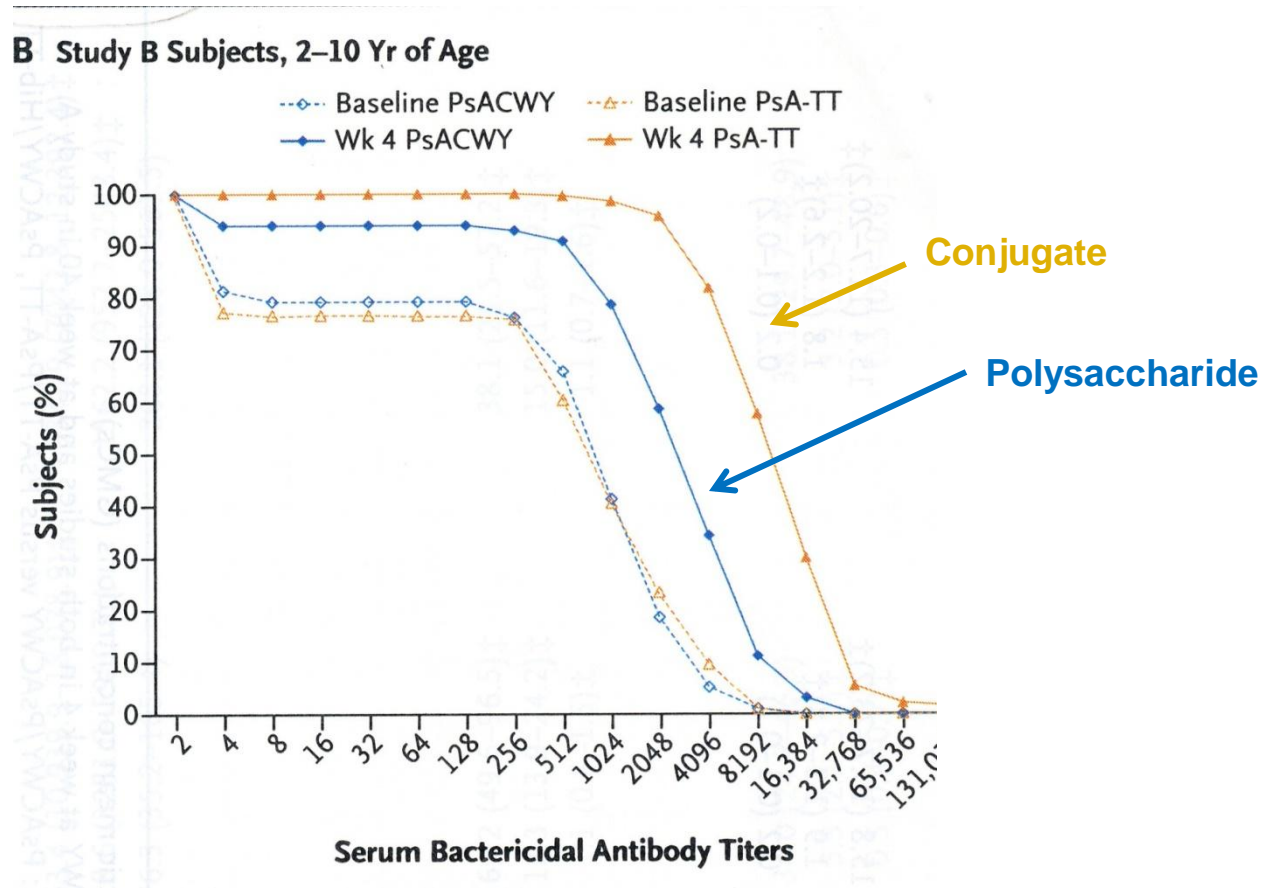
## The MenAfriCar consortium





# PHASE 2 STUDIES

## Immunogenicity in older children



(Sow et al. NEJM 2011; 364:2293-304)