Section 2: Single locus to multi-locus
‘Genes to Genomes’

Molecular Approaches to Clinical Microbiology in Africa 2024

Martin Maiden
Department of Biology

UNIVERSITY OF
OXFORD

Section 3, Translation and application: 'Germs, Genes, and Genomes', exemplified by the control of meningococcal disease in Africa

Molecular Approaches to Clinical Microbiology in Africa 2024

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UNIVERSITY OF OXFORD

Learning Outcomes

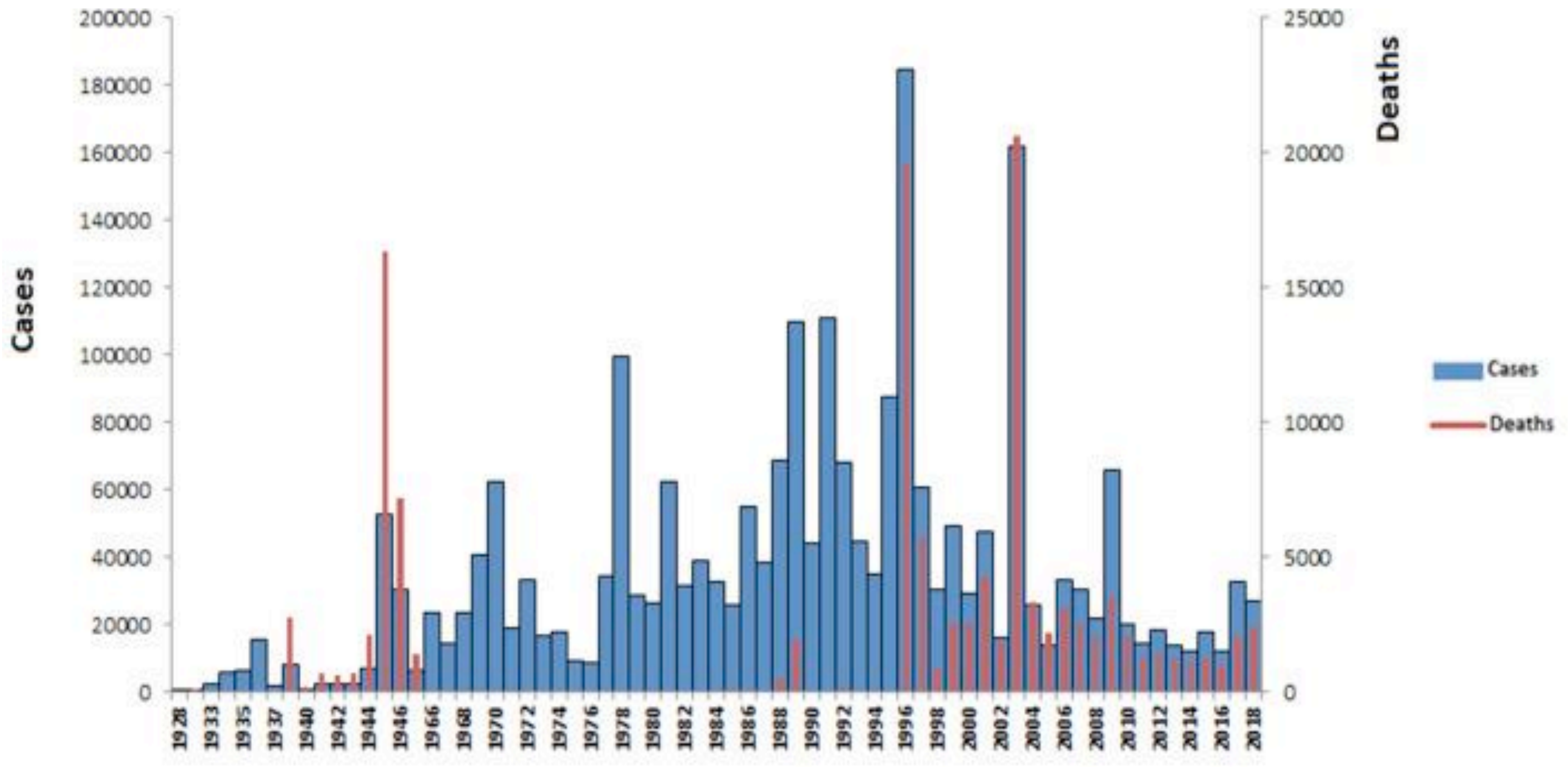
- The principles of the prevention of meningococcal disease and the advantages of conjugate polysaccharide vaccines.
- The role of genetic and genomic surveillance and studies.
- The importance of herd immunity.
- The meningitis vaccine project and vaccines for Africa.
- The on-going challenges in meningococcal disease prevention in Africa.
- Genomics practical using PubMLST

Meningococcal disease: still with us
Peltola, H. (1983). *Rev Infect Dis* **5**, 71-91.

Vieusseux, G. (1806). Mémoire sur la maladie qui a regné a Genêve au printemps de 1805. *J Med Chir Pharm* **11**, 163-182.

https://punchng.com/nigeria-records-961-meningitis-cases-56-deaths/
News Item 5th October 2022; accessed 27th January 2023.

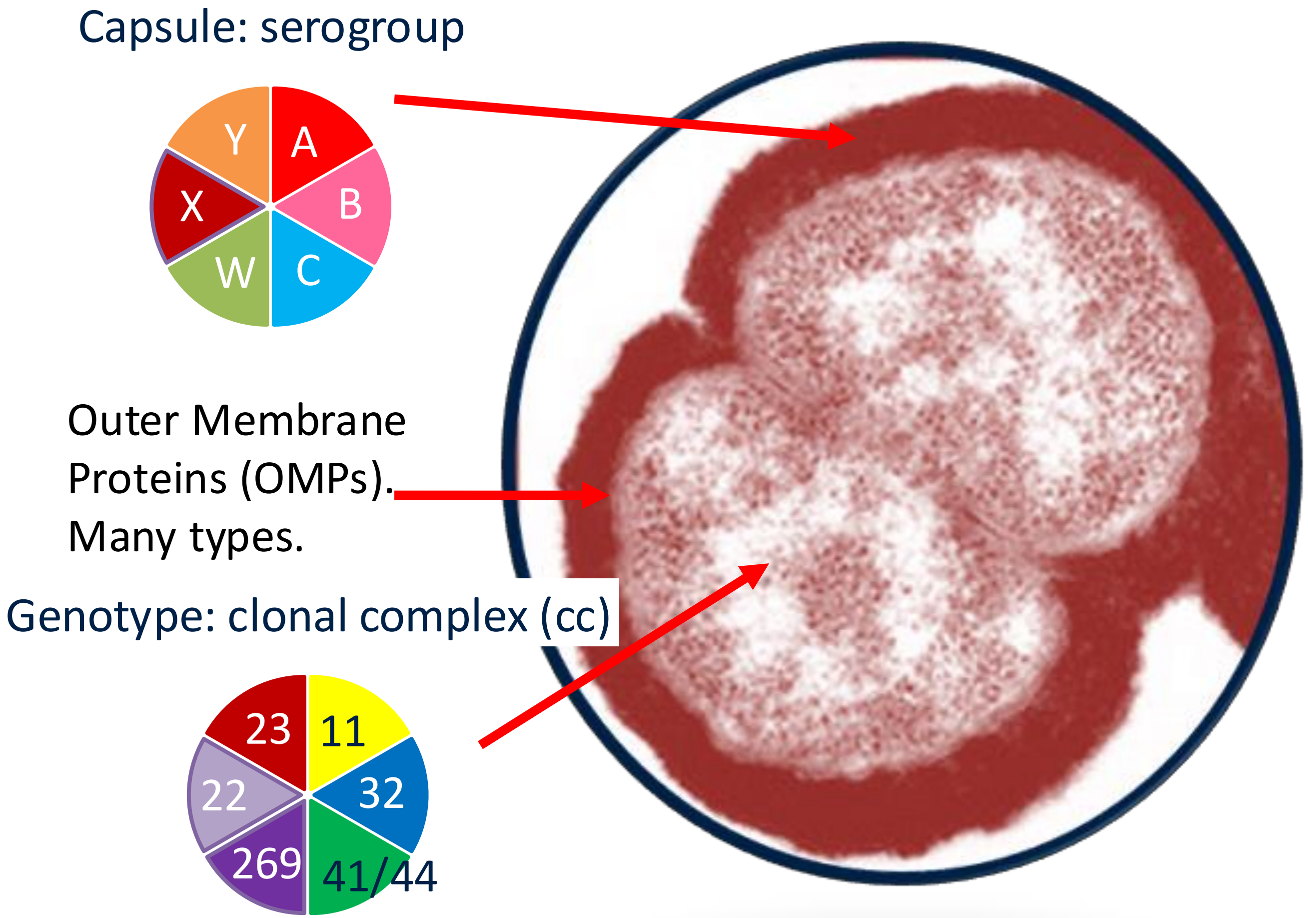
Meningococcal disease in Africa



Mazamay, S., Guegan, J. F., Diallo, N., Bompangue, D., Bokabo, E., Muyembe, J. J., Taty, N., Vita, T. P. & Broutin, H. (2021). An overview of bacterial meningitis epidemics in Africa from 1928 to 2018 with a focus on epidemics "outside-the-belt". *BMC Infect Dis.* **21**, 1027.

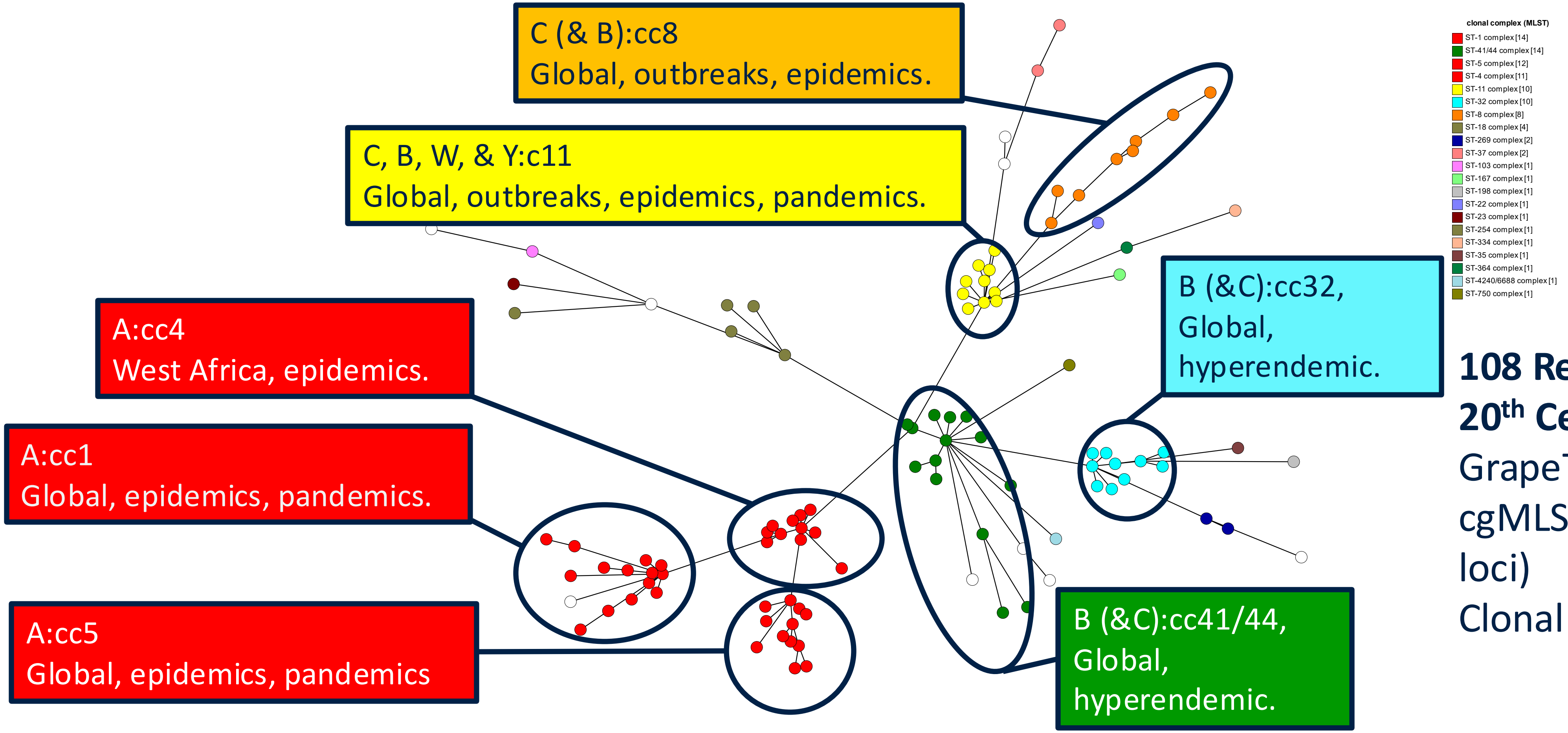
Within species diversity *Neisseria meningitidis*

- Meningococci are highly diverse antigenically and genetically,
  - this diversity is structured.
- 12 capsular serogroups,
  - 6 associated with invasive disease.
- Extensive evidence of HGT, but stable lineages are present,
  - these are associated with phenotypes, including invasive disease.



Ganesh, K., Allam, M., Wolter, N., Bratcher, H. B., Harrison, O. B., Lucidarme, J., Borrow, R., de Gouveia, L., Meiring, S., Birkhead, M., Maiden, M. C., von Gottberg, A. & du Plessis, M. (2017). Molecular characterization of invasive capsule null *Neisseria meningitidis* in South Africa. *BMC Microbiology* **17**, 40.

Age of Molecular Epidemiology: meningococcal disease in the 20th Century



108 Representative 20th Century Isolates

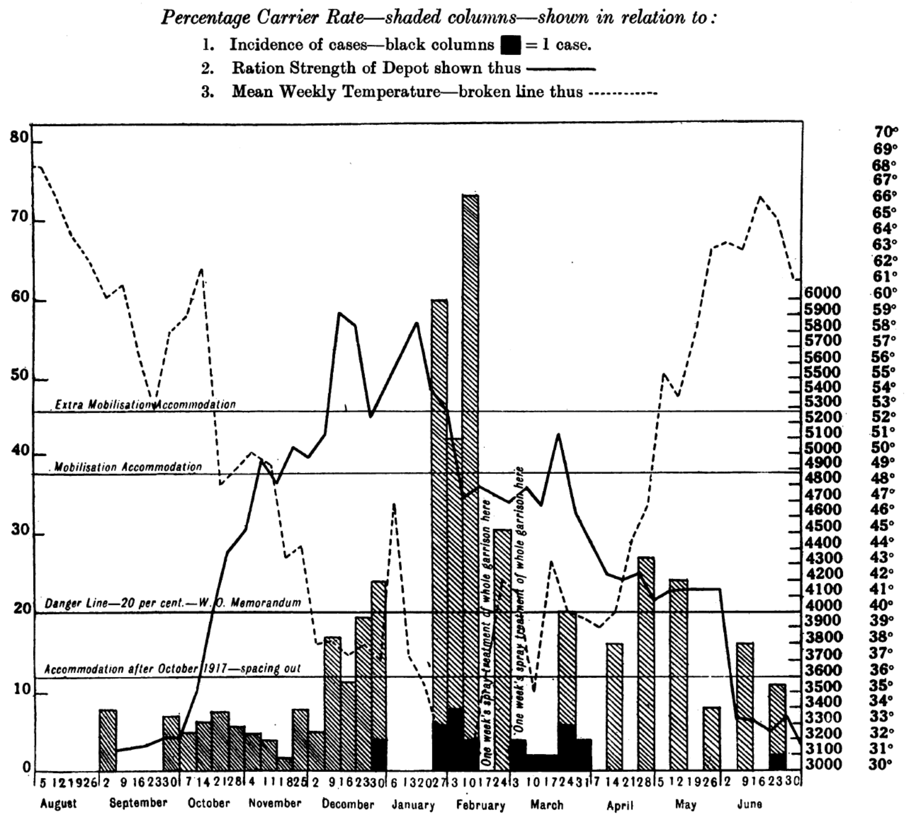
GrapeTree analysis

cgMLST v1.0 (1605 loci)

Clonal Complex

Bratcher, H. B., Corton, C., Jolley, K. A., Parkhill, J. & Maiden, M. C. (2014). A gene-by-gene population genomics platform: *de novo* assembly, annotation and genealogical analysis of 108 representative *Neisseria meningitidis* genomes. *BMC Genomics*. **15**, 1138.

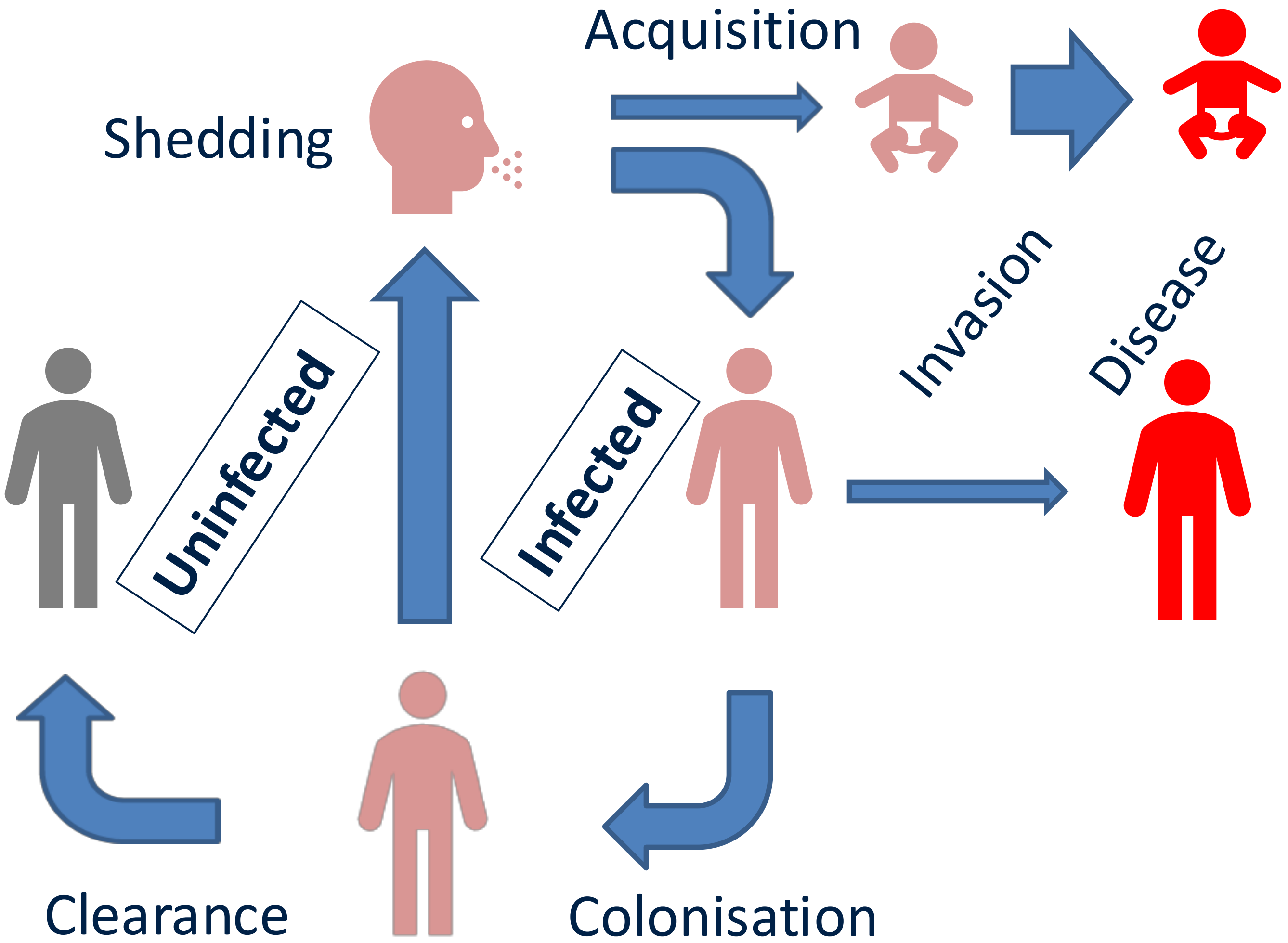
Meningococcal carriage 1917 & 2015



Glover, J. A. (1918). The Cerebro-Spinal Fever Epidemic of 1917 at X Depot. *J Hyg (Lond)* **17**, 350-365.

Bratcher, H. B., Rodrigues, C. M. C., Finn, A., Wootton, M., Cameron, J. C., Smith, A., Heath, P., Ladhani, S., Snape, M. D., Pollard, A. J., Cunningham, R., Borrow, R., Trotter, C., Gray, S. J., Maiden, M. C. J. & MacLennan, J. M. (2019). UKMenCar4: A cross-sectional survey of asymptomatic meningococcal carriage amongst UK adolescents at a period of low invasive meningococcal disease incidence. *Wellcome Open Res* **4**, 118.

Meningococcal Transmission, Infection, and Invasion

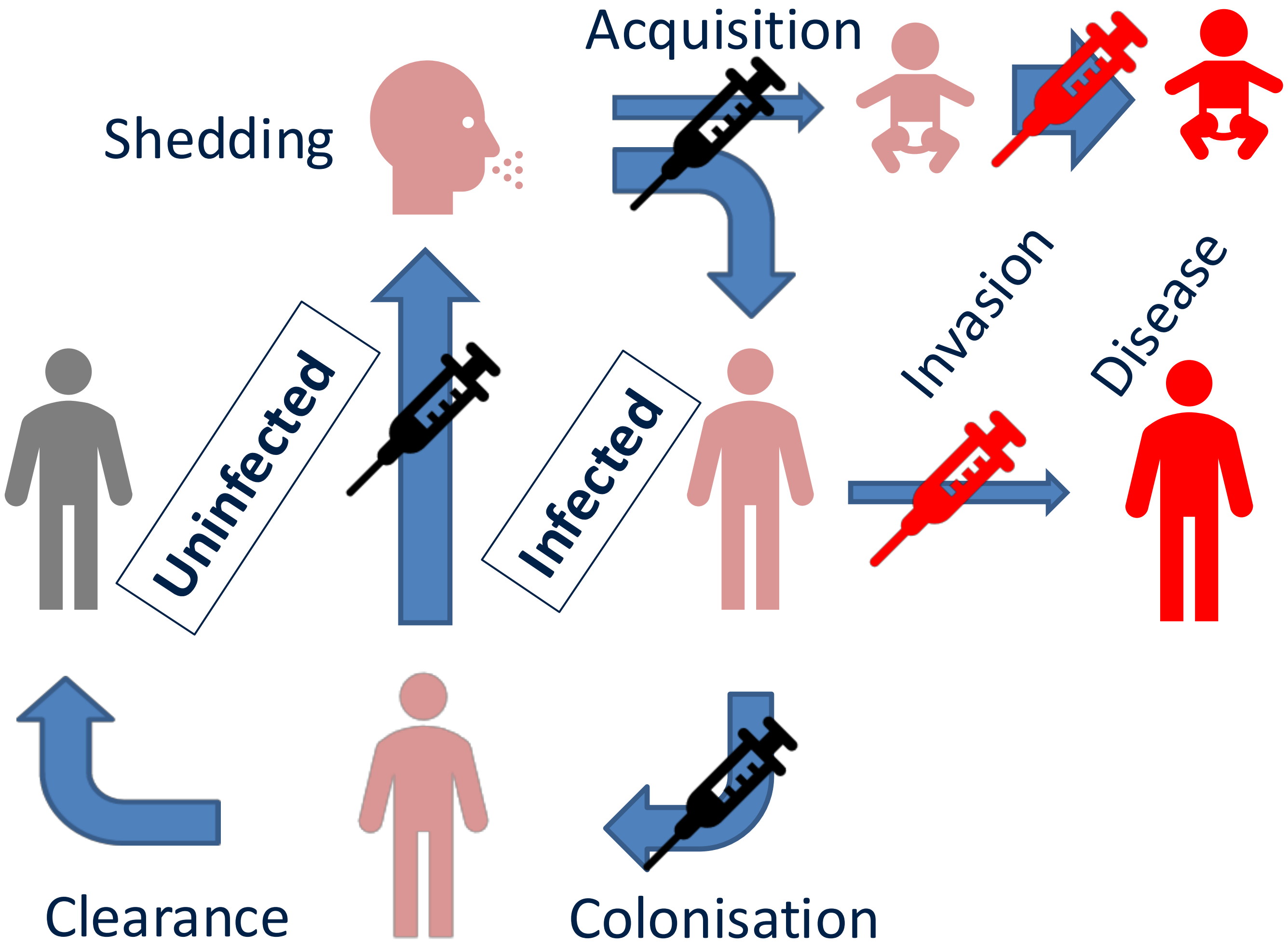


The meningococcus is ordinarily a commensal, causing disease rarely.

Invasion plays no role in transmission, so it can be thought of as an **accidental pathogen**.

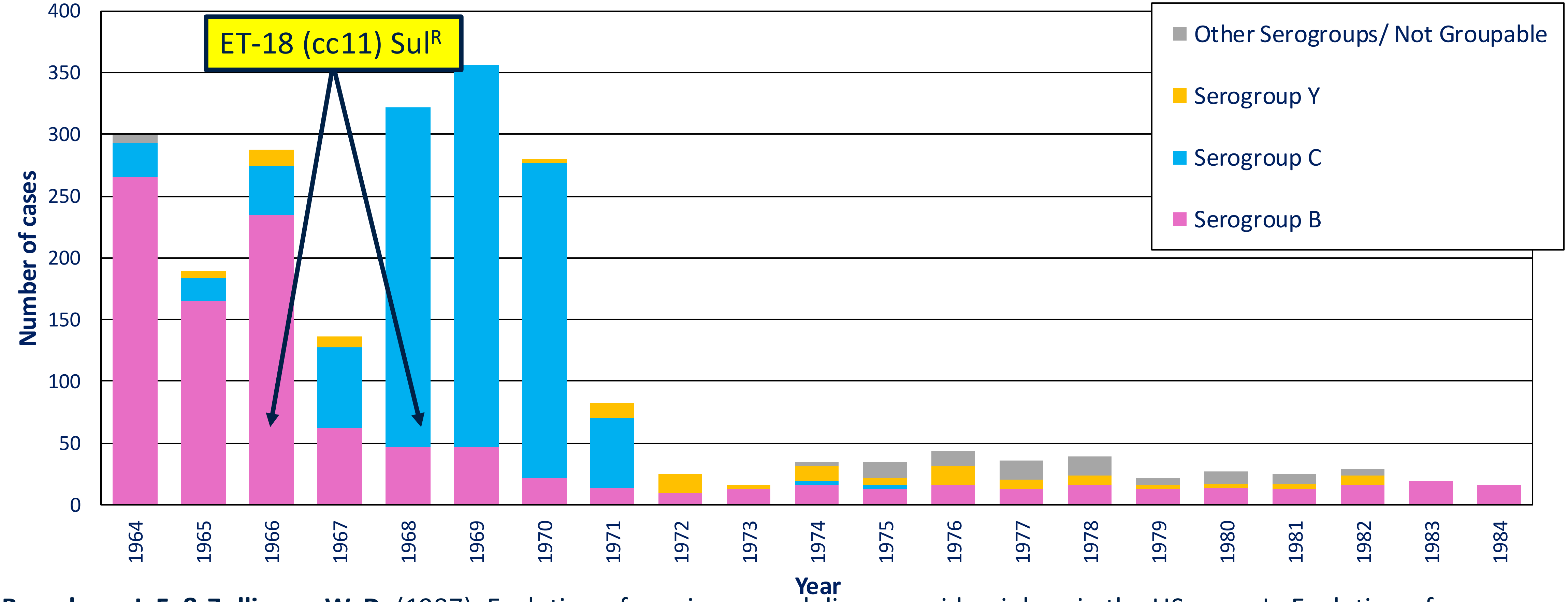
Trotter, C. L. & Maiden, M. C. (2009). Meningococcal vaccines and herd immunity: lessons learned from serogroup C conjugate vaccination programs. *Expert Rev Vaccines* **8**, 851-861.

The vaccine paradigm



Vaccine Interventions:

USA Army Outbreaks: AMR and the development of plain polysaccharide vaccines

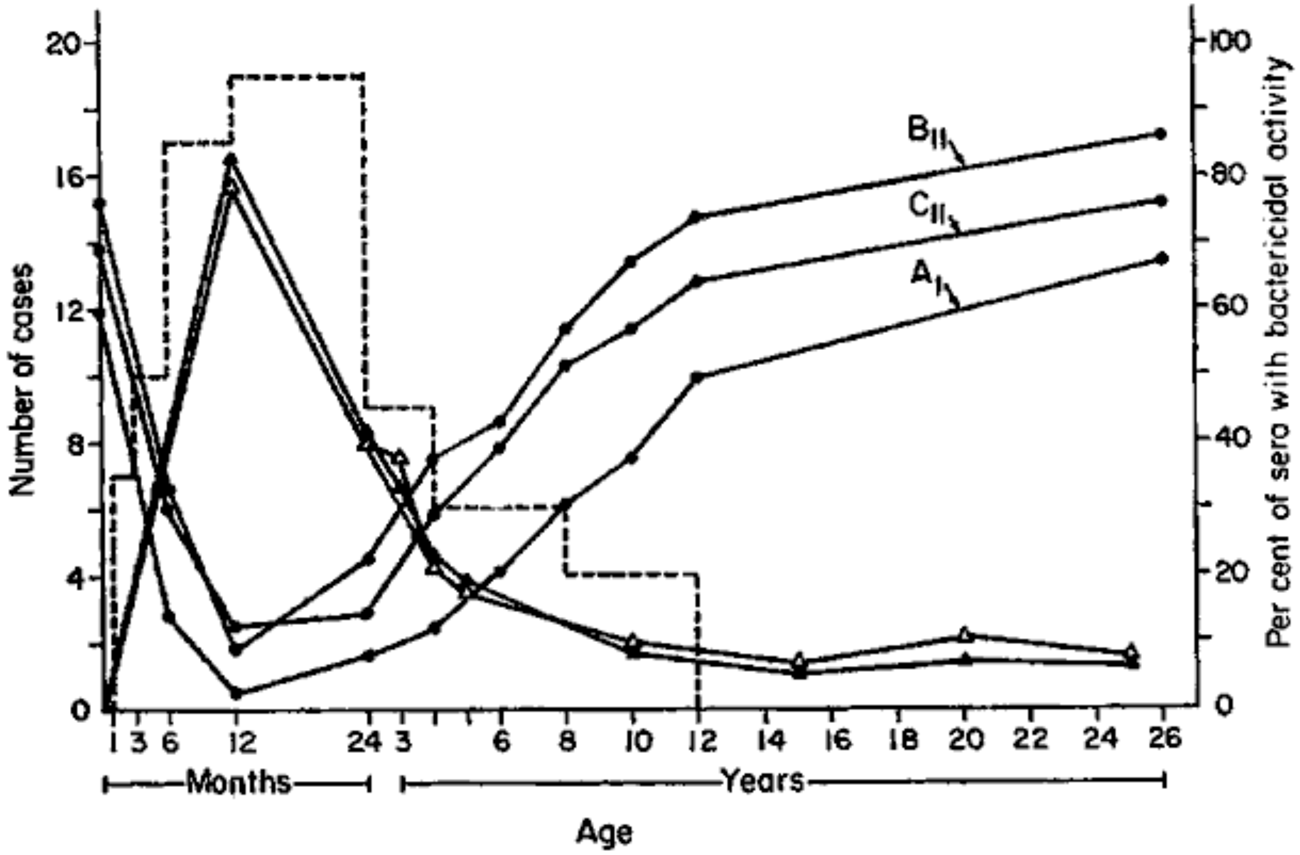


Brundage, J. F. & Zollinger, W. D. (1987). Evolution of meningococcal disease epidemiology in the US army. In Evolution of meningococcal disease, pp. 5-25. Edited by N. A. Vedros. Boca Raton, FL: CRC Press.

Wang, J. F., Caugant, D. A., Morelli, G., Koumaré, B. & Achtman, M. (1993). Antigenic and epidemiological properties of the ET-37 complex of *Neisseria meningitidis*. *J Infect Dis.* **167**, 1320-1329.

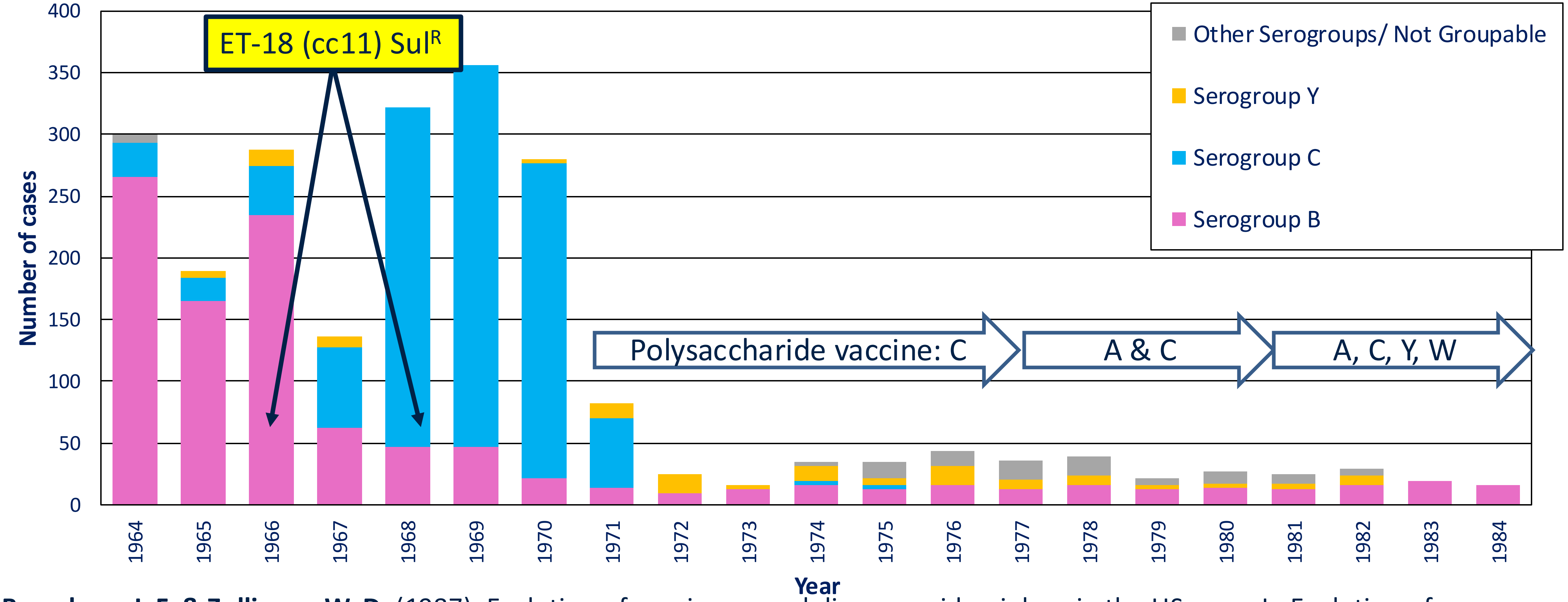
Meningococcal polysaccharide vaccines: establishing the paradigm

- Surveys of bactericidal activity of subjects' blood, compared with age-specific disease incidence.
- The inverse relationship, and loss of maternal immunity, suggests antibody-mediated immunity is important.
- This led to the development of the **plain polysaccharide** vaccines.



Goldschneider, I., Gotschlich, E. C. & Artenstein, M. S. (1969). Human Immunity to the Meningococcus. II. Development of Natural Immunity. *J Exp Med* **129**, 1327-1348.

USA Army Outbreaks: AMR and the development of plain polysaccharide vaccines



Brundage, J. F. & Zollinger, W. D. (1987). Evolution of meningococcal disease epidemiology in the US army. In Evolution of meningococcal disease, pp. 5-25. Edited by N. A. Vedros. Boca Raton, FL: CRC Press.

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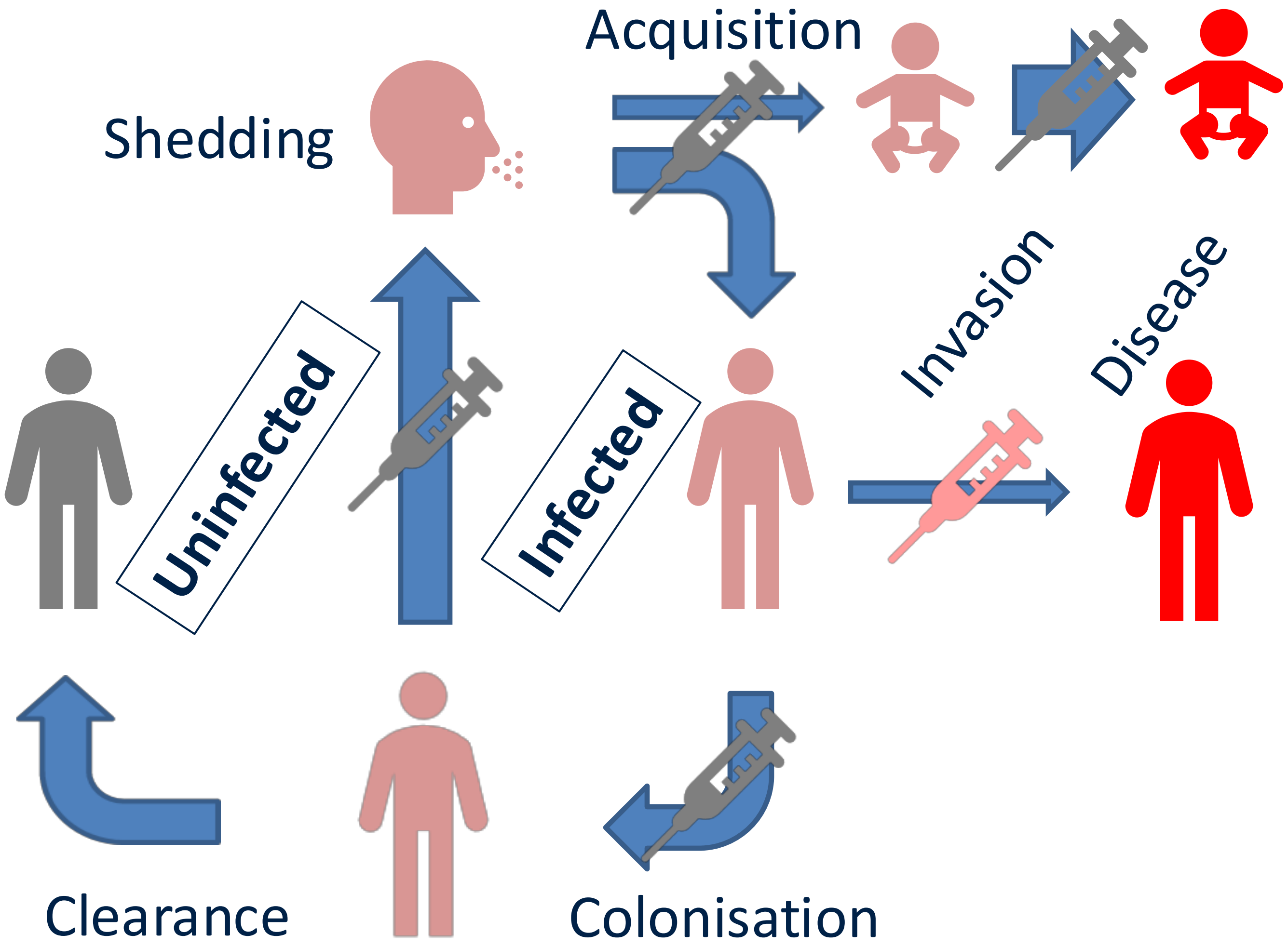
Plain polysaccharide vaccines (pre-1999)



Vaccine Interventions:

Direct Protection

Indirect protection
(Herd immunity)

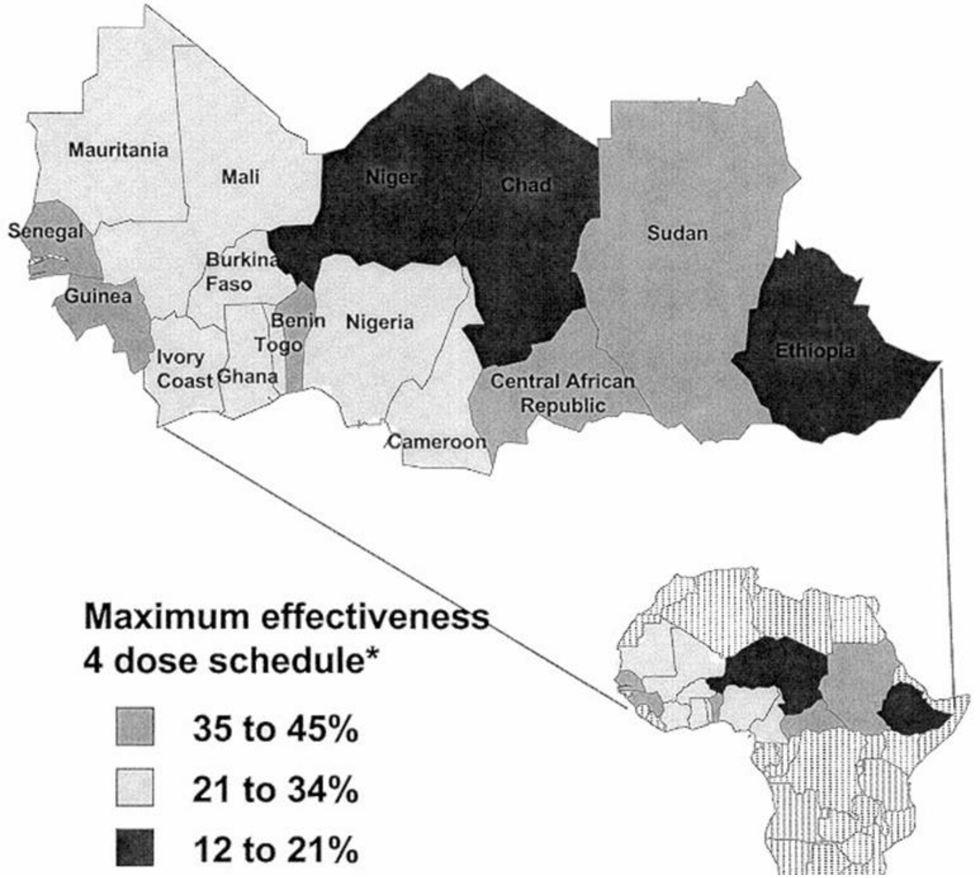
Provide time-limited direct protection to adults.
Do not protect infants.
Do not elicit herd immunity.

‘Plain’ polysaccharide vaccines in Africa

Table 2. Number of serogroup A meningococcal meningitis cases in the vaccine and vaccine control groups

Area	Vaccine employed			
	PAV		TTC	
	No. vaccinated	CSM cases	No. vaccinated	CSM cases
Khartoum South	7 966	0	7 950	6
Mahdia	2 925	0	2 799	1
Total	10 891	0	10 749	7

Erwa, H. H., Haseeb, M. A., Idris, A. A., Lapeyssonnie, L., Sanborn, W. R., and Sippel, J. E. (1973) A serogroup A meningococcal polysaccharide vaccine: studies in the Sudan to combat cerebrospinal meningitis caused by *Neisseria meningitidis* group A. *Bull World Health Organ* **49**, 301-305



Miller, M. A., Wenger, J., Rosenstein, N., and Perkins, B. (1999) Evaluation of meningococcal meningitis vaccination strategies for the meningitis belt in Africa. *Pediatr Infect Dis J* **18**, 1051-1059

Serogoup A plain polysaccharide vaccine performance

TABLE III—VACCINE EFFICACY THREE YEARS AFTER VACCINATION AS A FUNCTION OF AGE AT VACCINATION (UNIVARIATE ANALYSIS)

Age in 1981 (yr)	No of cases (1984)	Vaccine efficacy in 1984
1	9	24%
2	11	21%
3	11	24%
4–7	11	92%
8–16	65	75%

Reingold, A. L., Broome, C. V., Hightower, A. W., Ajello, G. W., Bolan, G. A., Adamsbaum, C., Jones, E. E., Phillips, C., Tiendrebeogo, H. & Yada, A. (1985). Age-specific differences in duration of clinical protection after vaccination with meningococcal polysaccharide A vaccine. *Lancet* **ii**, 114-118.

TABLE IV—RESULTS OF MULTIVARIATE ANALYSIS OF VACCINE EFFICACY MODEL, INCLUDING AGE IN 1981

Variable	Efficacy of vaccine (%)	Odds ratio	1-tailed p	90% confidence limits (%)
Year				
1982*	87†	. .	0·005	52 to 96
1983				
1–3 year olds	52†	. .	0·21	−107 to 89
4–16 year olds	74†	. .	0·003	42 to 88
1984				
1–3 year olds	8†	. .	0·43	−102 to 58
4–16 year olds	67†	. .	0·001	40 to 82
1984	96‡	. .	0·002	75 to 100
Ln of no of people sleeping/room	. .	1·96	0·0006	1·39–2·75
Arrival in Ouagadougou after 1981 vaccination campaign	. .	1·86	0·02	1·12–3·08
School attendance	. .	0·39	0·0002	0·25–0·61

*Insufficient nos to stratify by age for use in the multivariate model, but crude vaccine efficacies for 1–3 year olds and 4–16 year olds were 100% and 85%, respectively.

†Efficacy of vaccine given in 1981. ‡Efficacy of vaccine given in late 1983.

Limitations of the plain polysaccharide vaccines in Africa

- Ineffective in infants,
  - not suitable for infant immunisation.
- Short-term immunity in others,
  - re-immunisation required.
- Hyporesponsiveness,
  - repeated immunisation can give poorer responses.
- Not effective in stopping asymptomatic carriage,
  - No impact on transmission.
- Needed to be stockpiled and then used when required,
  - logistically very challenging.

Vaccination model	Cases prevented	Vaccine doses per case prevented	Deaths prevented	Vaccine doses per death prevented
Actual number of cases and deaths prevented	5438 (23%)	401	304 (18%)	7180
Vaccine coverage achieved before start of epidemic				
85%	17 442 (72%)	160	1199 (72%)	2341
72%	14 774 (61%)	160	1016 (61%)	2341
Vaccine coverage achieved within 1 week with knowledge of epidemics in adjacent countries				
85%	16 296 (68%)	172	995 (60%)	2821
72%	13 804 (60%)	172	843 (51%)	2821
Vaccine coverage achieved within 1 week without knowledge of ongoing epidemics				
85%	15 443 (64%)	182	884 (53%)	3175
72%	13 063 (54%)	182	749 (45%)	3175
Vaccine coverage achieved within 1 week in individuals aged ≤30 years				
85%	13 498 (56%)	153	820 (49%)	2533

Effect of the meningococcal vaccination campaign in Ghana

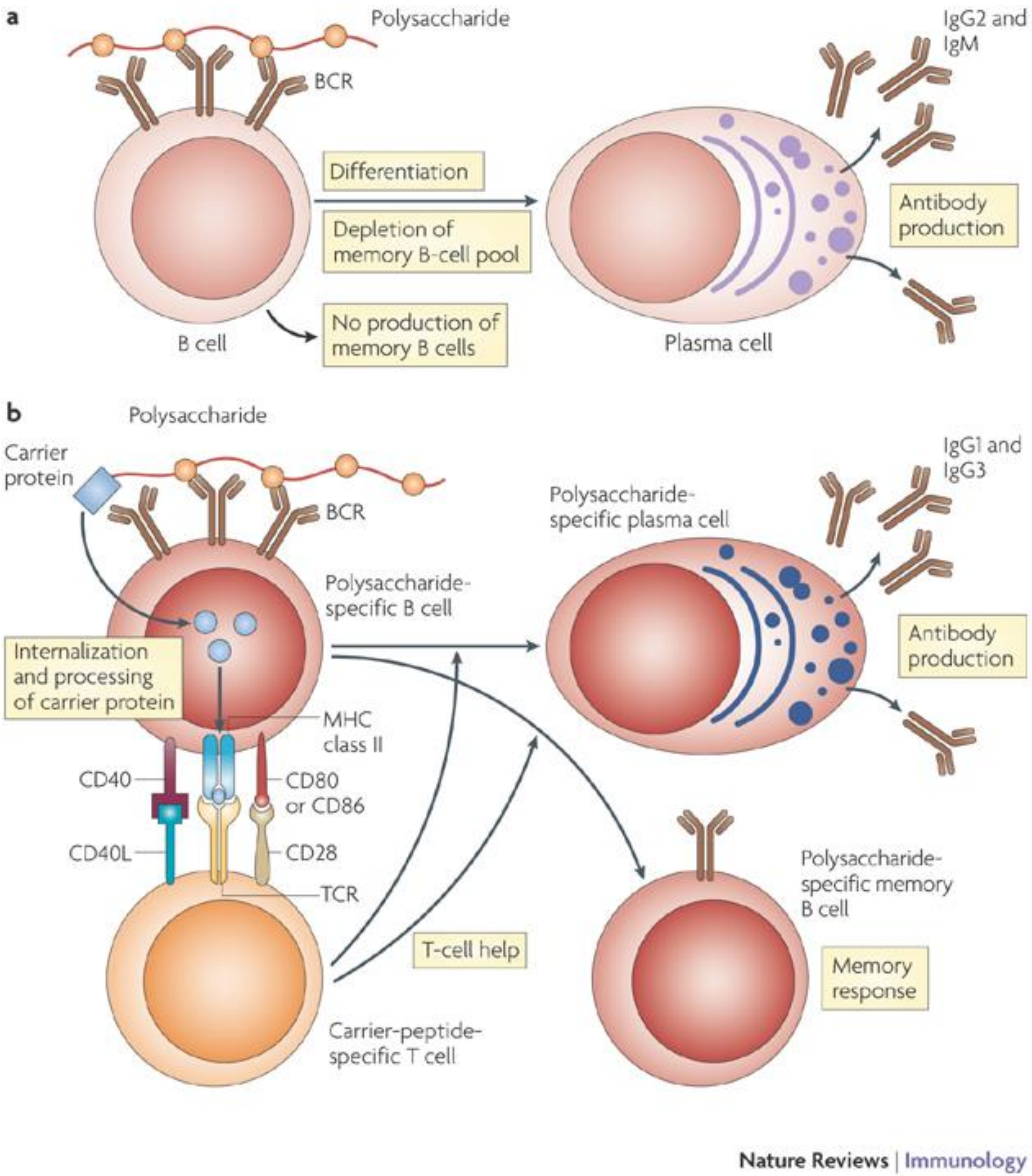
Woods, C. W., Armstrong, G., Sackey, S. O., Tetteh, C., Bugri, S., Perkins, B. A. & Rosenstein, N. E. (2000). Emergency vaccination against epidemic meningitis in Ghana: implications for the control of meningococcal disease in West Africa. *Lancet* 355, 30-33.

Protein-polysaccharide conjugate vaccines

- Chemical attachment (conjugation) of polysaccharides (conjugation) to T-cell antigens elicits T-cell help.

- This dramatically improves the immunogenicity of the vaccine antigen:
  - Improved immune responses;
  - Better in infants;
  - Elicit memory responses;
  - Effective against carriage.

Pollard, A. J., Perrett, K. P. & Beverley, P. C. (2009). Maintaining protection against invasive bacteria with protein-polysaccharide conjugate vaccines. *Nature Reviews Immunolog* **9**, *212-220.*



Conjugate vaccines: a new era for meningococcal disease prevention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Tuesday, 9 March, 1999, 18:01 GMT

Meningitis: The 1999 panic

William Hague's old school saw the first outbreak of the year

The government's vaccination programme was prompted by a series of serious meningitis outbreaks.

Throughout January 1999, a severe outbreak of meningitis in south Wales took a prominent position in the headlines.

As a public health emergency was declared, mass vaccinations were performed at schools in Pontypridd.

Doctors did their best to calm public fears about the likelihood of infection, but parents were alarmed and marched to demand blanket vaccinations - regardless of whether their children attended the affected schools.

See also:
- 09 Mar 99 | Medical notes
  Meningitis: The argument for mass vaccinations
- 09 Mar 99 | Medical notes
  Preventing meningitis
- 05 Jan 99 | Health
  Killer disease claims more victims
- 18 Jan 99 | Health
  Meningitis trauma service launched
- 05 Jan 99 | Health
  Meningitis research targets teenagers
- 11 Feb 99 | Health
  Meningitis study group set up

Internet links:
- PHLS facts and figures on meningococcal disease
- Meningitis Research Foundation
- National Meningitis Trust

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- IVF mix-up heads for court
- Transplant first for cancer patient
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HEALTH LATEST

Monday, November 1, 1999 Published at 06:33 GMT

Health

Mass meningitis vaccination programme begins

The vaccine could prevent many deaths from the brain disease

The government has officially launched its meningitis vaccination programme, first targeting 15 to 17-year-olds and then babies.

Children around the UK are to become the first in the world to take part in routine vaccinations against the C strain of meningitis.

SPECIAL REPORT
THE MENINGITIS FILE

The vaccine has already been tested on more than 4,000 British children and 21,000 children outside the UK.

The mass immunisation programme has also been piloted in Ironville, South Derbyshire, which has been particularly affected by the brain disease.

Health Contents
- Background Briefings
- Medical notes

Relevant Stories

01 Nov 99 | Northern Ireland
Doctors frustrated over vaccine scarcity

20 Jul 99 | Health
Mass vaccine targets meningitis

12 Feb 99 | Medical notes
The argument for mass meningitis vaccinations

10 Feb 99 | Medical notes
Meningitis: Preventive measures

Internet Links

National Meningitis Trust

Meningitis Research Foundation

Department of Health

The BBC is not responsible for the content of external internet sites.

In this section

Disability in depth

Spotlight: Bristol inquiry

Antibiotics: A fading wonder

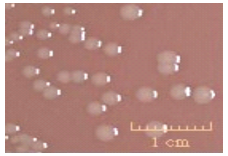
Miller, E., Salisbury, D. & Ramsay, M. (2001). Planning, registration, and implementation of an immunisation campaign against meningococcal serogroup C disease in the UK: a success story. *Vaccine* **20**, S58-67.

UK Meningococcal carriage study: Meningococcal C Conjugate (MCC) vaccine impact , 1999-2001

UKMenCar1-3

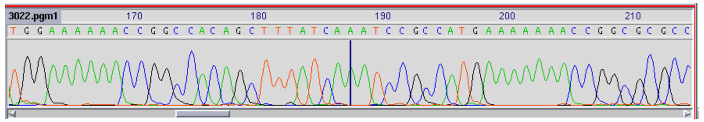
16,700 X 3

Questionnaire
Risk factors for carriage



2,500 X 3

MRU/SMPRL
Phenotype



Genotype

Capsule

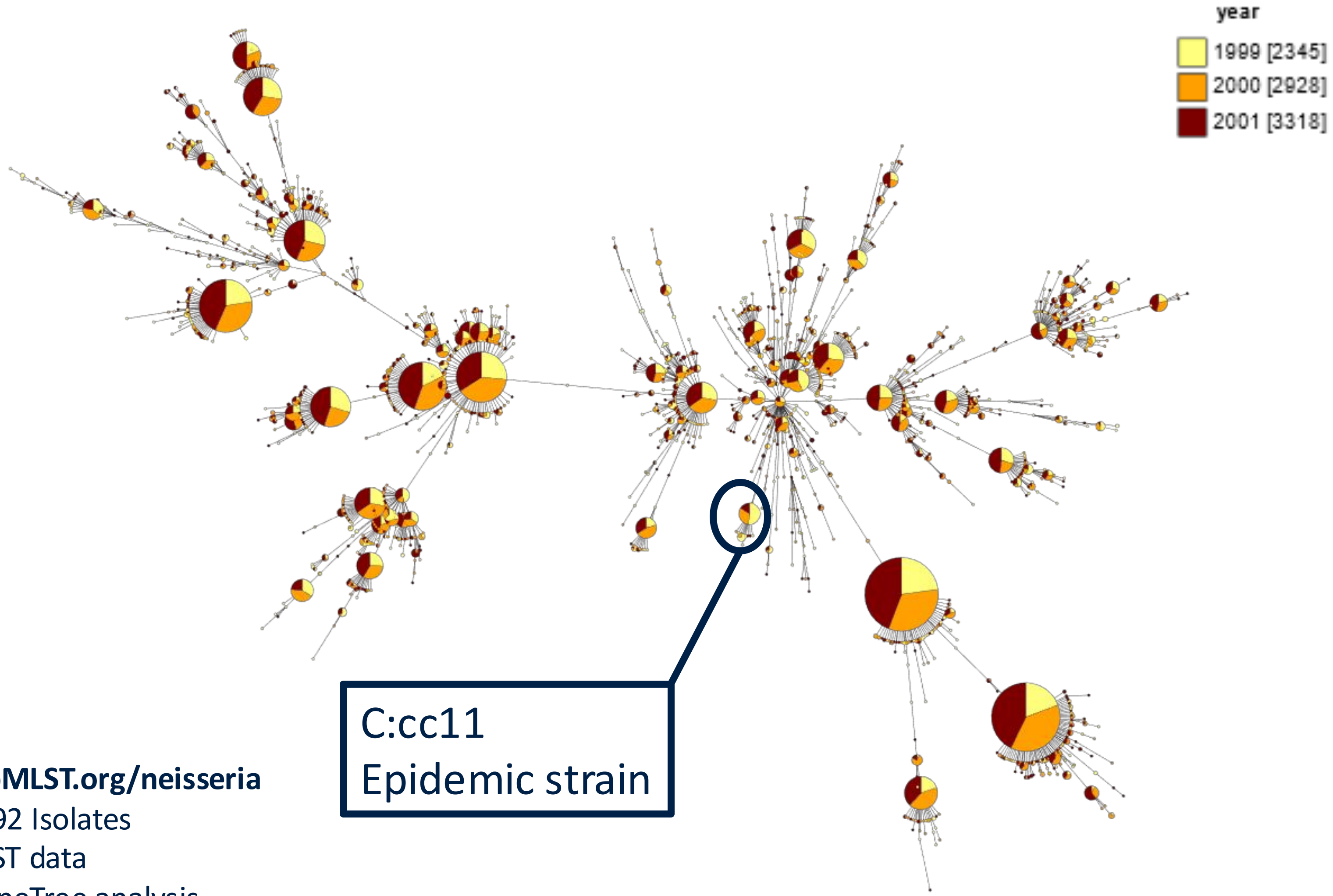
Maiden, M. C. J., and Spratt, B. G. (1999) Meningococcal conjugate vaccines: new opportunities and new challenges. *Lancet* **354**, 615-616

Maiden, M. C., Stuart, J. M. & United Kingdom Meningococcal Carriage Group, (2002). Carriage of serogroup C meningococci 1 year after meningococcal C conjugate polysaccharide vaccination. *Lancet* **359**, 1829-1831.

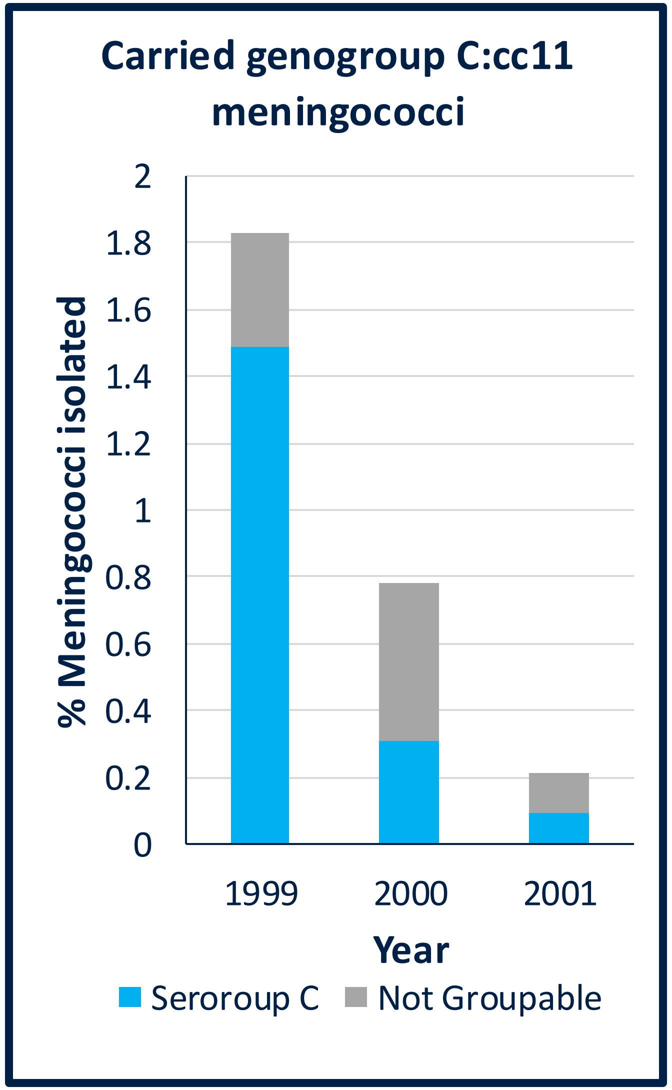
Maiden, M. C., *et al.* (2008). Impact of Meningococcal Serogroup C Conjugate Vaccines on Carriage and Herd Immunity. *J Infect Dis* **197**, 737-743.

Ibarz-Pavon, A. B., *et al.* (2011). Changes in serogroup and genotype prevalence among carried meningococci in the United Kingdom during vaccine implementation. *J Infect Dis* **204**, 1046-1053.

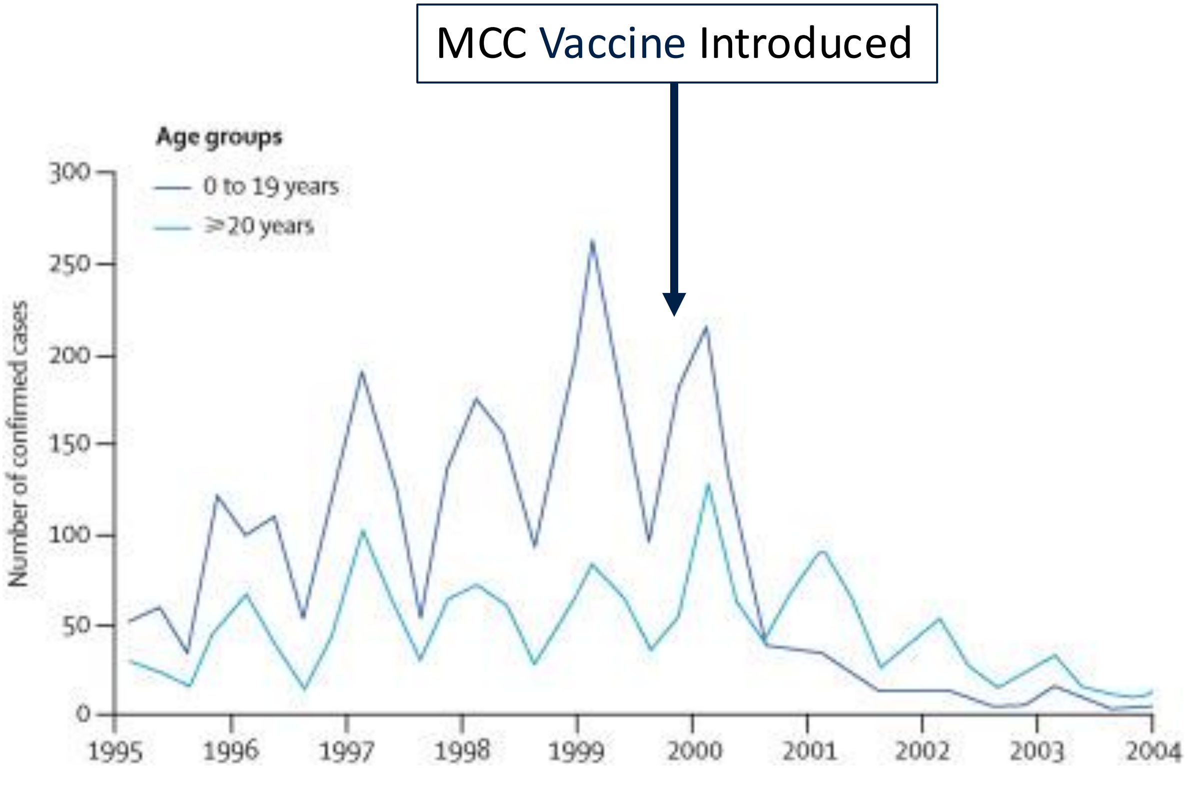
UK meningococcal carriage studies, 1999-2001

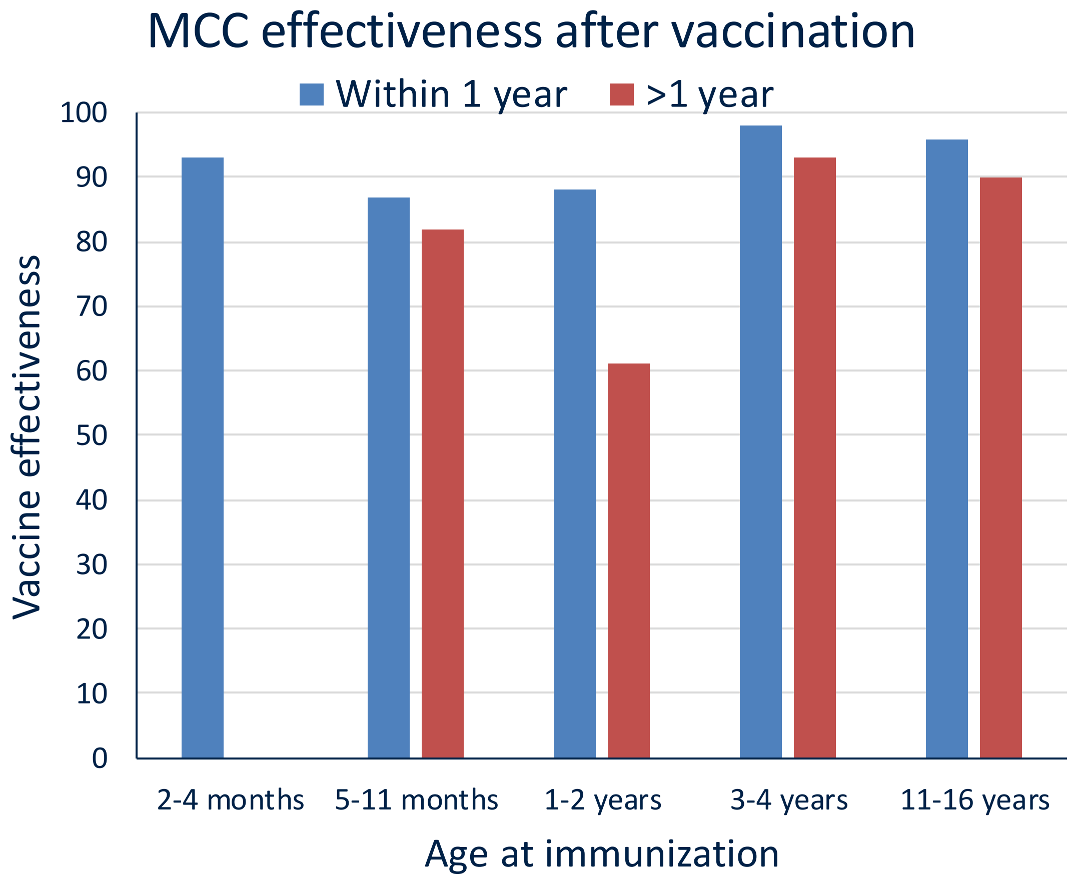


PubMLST.org/neisseria
8,592 Isolates
MLST data
GrapeTree analysis



Effect of MCC vaccination on serogroup C disease





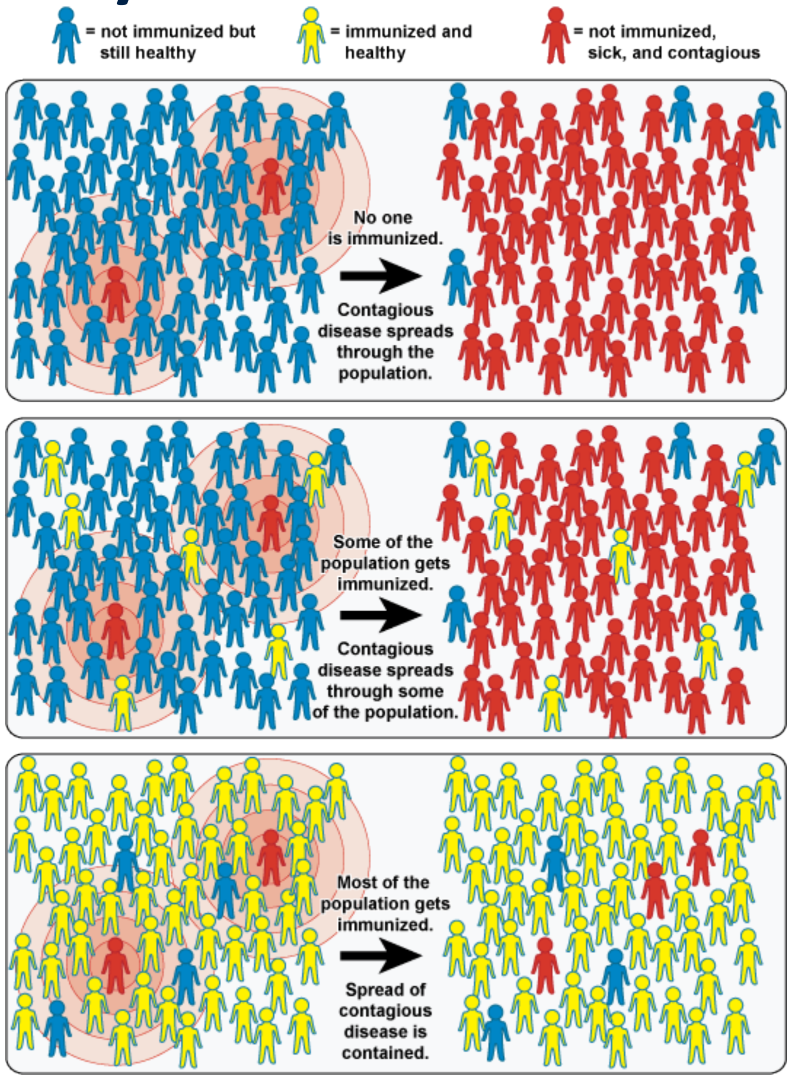
Trotter, C. L., N. J. Andrews, E. B. Kaczmarski, E. Miller, and M. E. Ramsay. (2004). Effectiveness of meningococcal serogroup C conjugate vaccine 4 years after introduction. *Lancet* **364**, 365-7.

Herd immunity

- The majority of vaccines were designed with protection of individuals in mind.
- However, the great majority are most effective through the action of herd immunity.
- Infectious agents, including those responsible for disease, depend upon transmission among susceptible hosts.
- If vaccination reduces the number of susceptible hosts, then transmission of the agent is reduced.
- If the proportion of susceptible hosts is reduced to:

$$<V_C=1-(1/R_0)$$

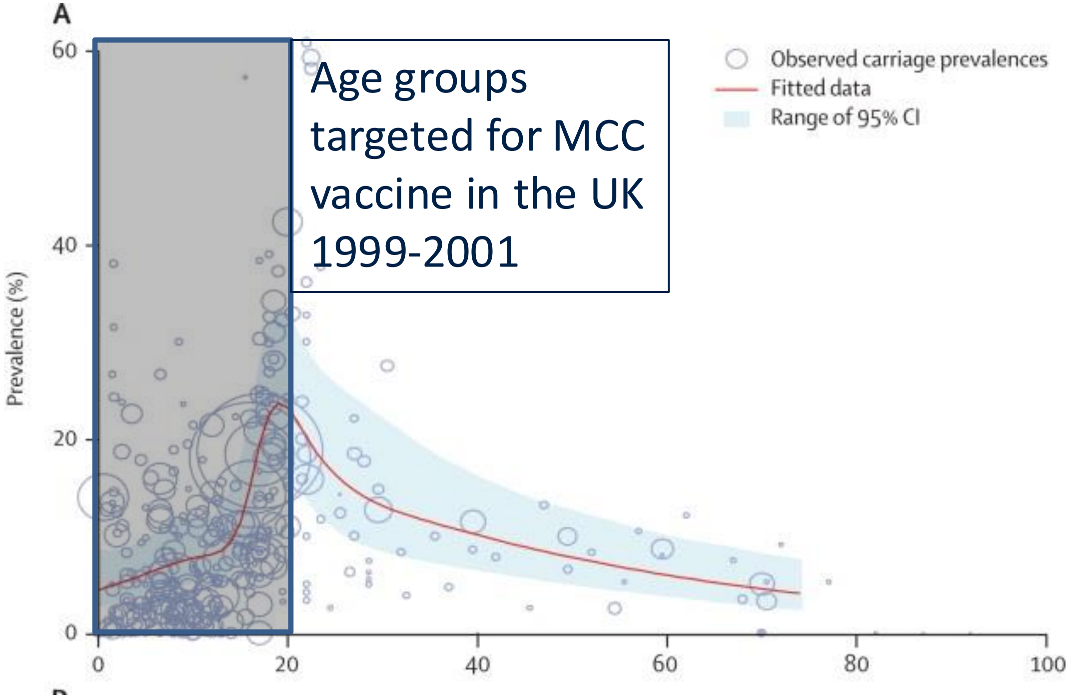
then the agent will be eradicated from the population and will not be able to re-invade for as long as population immunity persists.



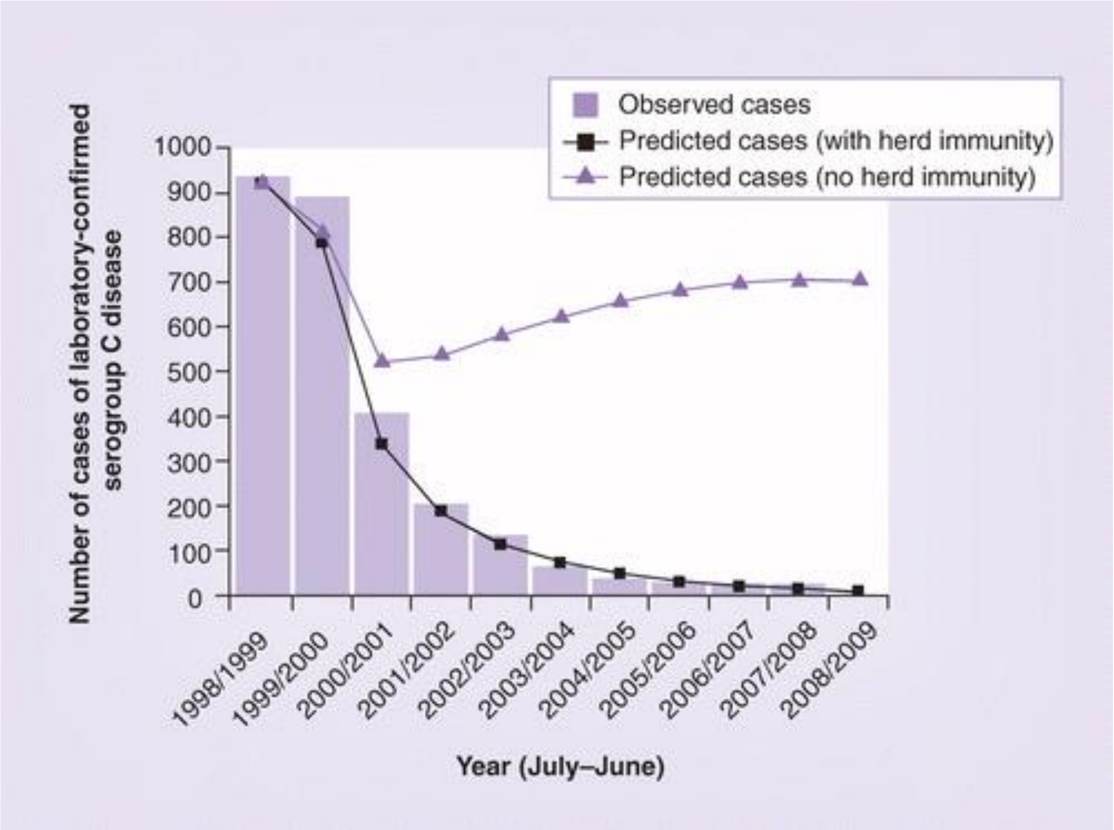
http://www.niaid.nih.gov/topics/pages/communityimmunity.aspx

MCC vaccine and herd immunity

Meningococcal carriage

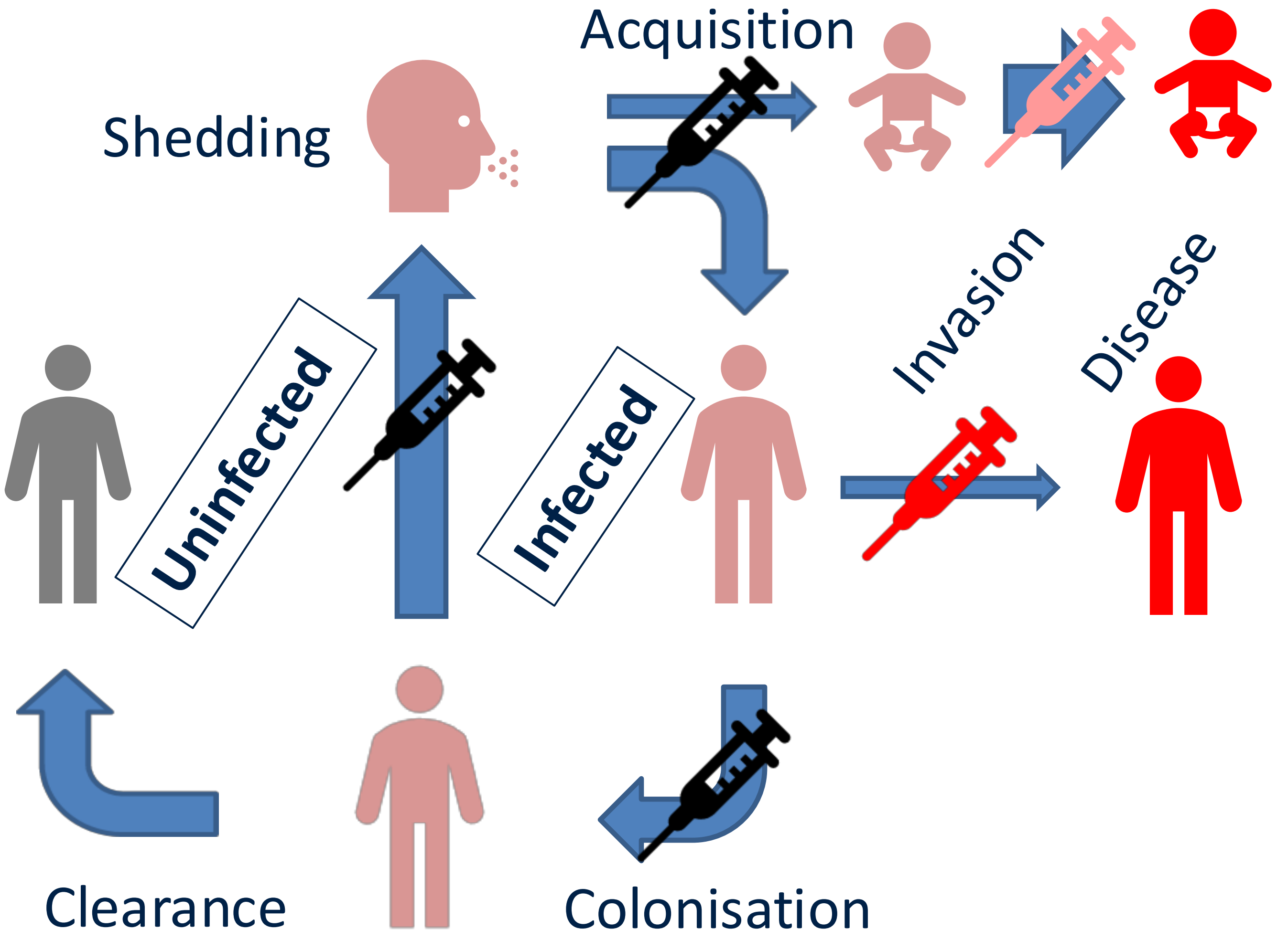


Observed and predicted herd immunity



Christensen, H., May, M., Bowen, L., Hickman, M. & Trotter, C. L. (2010). Meningococcal carriage by age: a systematic review and meta-analysis. *The Lancet Infectious Diseases* **10**, 853-861.
Trotter, C. L. & Maiden, M. C. (2009). Meningococcal vaccines and herd immunity: lessons learned from serogroup C conjugate vaccination programs. *Expert Review Vaccines* **8**, 851-861.

Protein conjugate polysaccharide vaccines



Vaccine Interventions:

Direct Protection

Indirect protection (Herd immunity)

Provide excellent direct protection to adults.
Provide time-limited direct protection to infants.
Elicit strong herd immunity.

Meningitis Vaccine Project

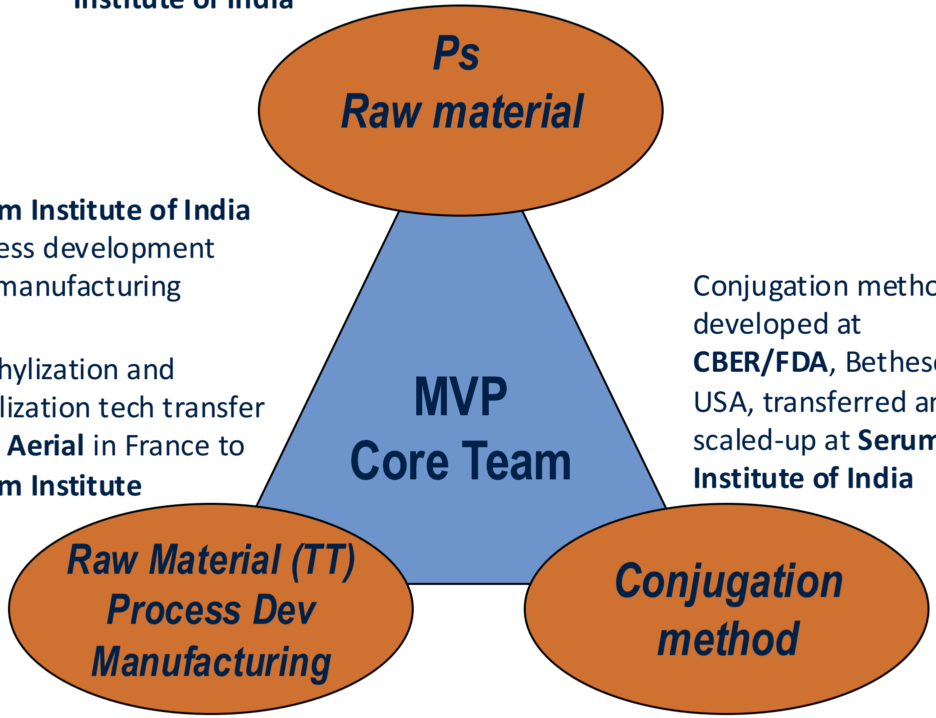
- Bill and Melinda Gates Foundation funded, coordinated by PATH and WHO.
- MVP produced a serogroup A conjugate vaccine at less than one US dollar a dose.
- Transfer of conjugation technology from FDA to Serum Institute of India for production.

Serogroup A polysaccharide produced by **SynCo BioPartners**, Amsterdam for initiaL development then transferred to **Serum Institute of India**

Serum Institute of India process development and manufacturing

Lyophylization and stabilization tech transfer from **Aerial** in France to **Serum Institute**

Conjugation method developed at **CBER/FDA**, Bethesda, USA, transferred and scaled-up at **Serum Institute of India**



Target price US$ <0.50/dose

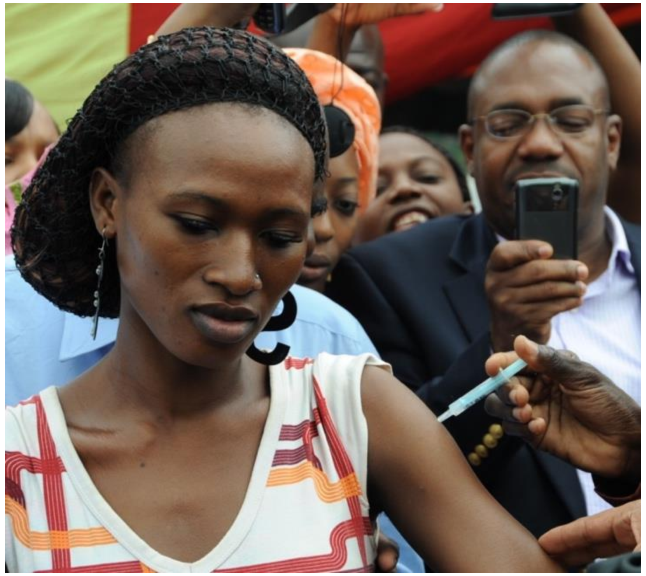
LaForce, F. M., Konde, K., Viviani, S. & Preziosi, M. P. (2007). The Meningitis Vaccine Project. *Vaccine* 25, A97-A100.
http://www.meningvax.org

MenAfriVac®: a solution to epidemic meningococcal disease in Africa

Meningitis Vaccine Project (MVP):

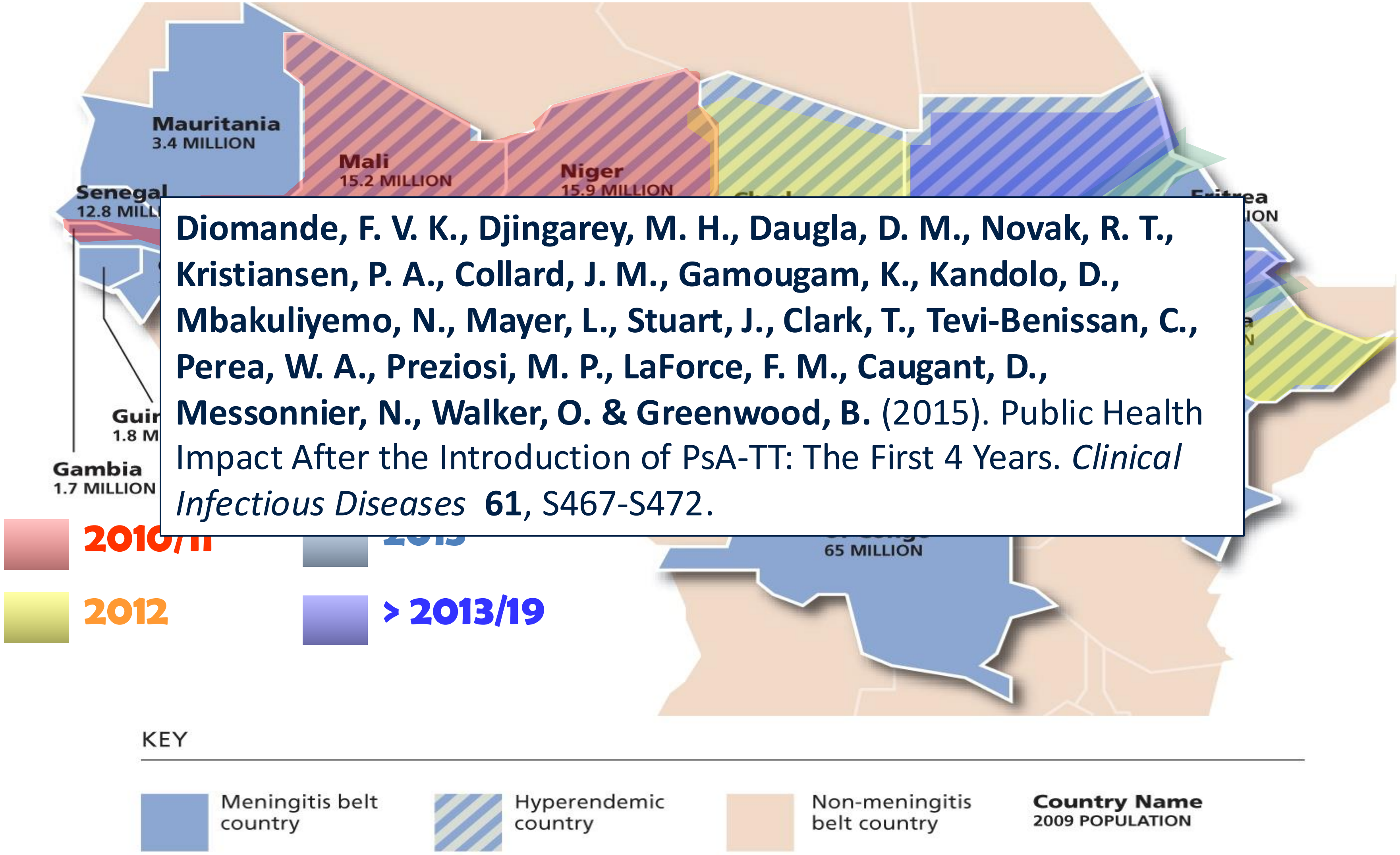
- Gates funded, partnership with WHO and PATH;
- Innovative development – Northern technology, southern manufacturer;
- Low cost (less than $1 per dose, for sustainable use;
- MenAfriVac, a polysaccharide-protein conjugate vaccine, introduced 2010 in Burkina Faso;
- Everyone aged 1-29 years immunised;
- Immediate reduction in disease levels.

Diomande, F. V. K., Djingarey, M. H., Daugla, D. M., Novak, R. T., Kristiansen, P. A., Collard, J. M., Gamougam, K., Kandolo, D., Mbakuliyemo, N., Mayer, L., Stuart, J., Clark, T., Tevi-Benissan, C., Perea, W. A., Preziosi, M. P., LaForce, F. M., Caugant, D., Messonnier, N., Walker, O. & Greenwood, B. (2015). Public Health Impact After the Introduction of PsA-TT: The First 4 Years. *Clinical Infectious Diseases* 61, S467-S472.



Marc La Force

Roll-out of MenAfriVac



Diomande, F. V. K., Djingarey, M. H., Daugla, D. M., Novak, R. T., Kristiansen, P. A., Collard, J. M., Gamougam, K., Kandolo, D., Mbakuliyemo, N., Mayer, L., Stuart, J., Clark, T., Tevi-Benissan, C., Perea, W. A., Preziosi, M. P., LaForce, F. M., Caugant, D., Messonnier, N., Walker, O. & Greenwood, B. (2015). Public Health Impact After the Introduction of PsA-TT: The First 4 Years. *Clinical Infectious Diseases* **61**, S467-S472.

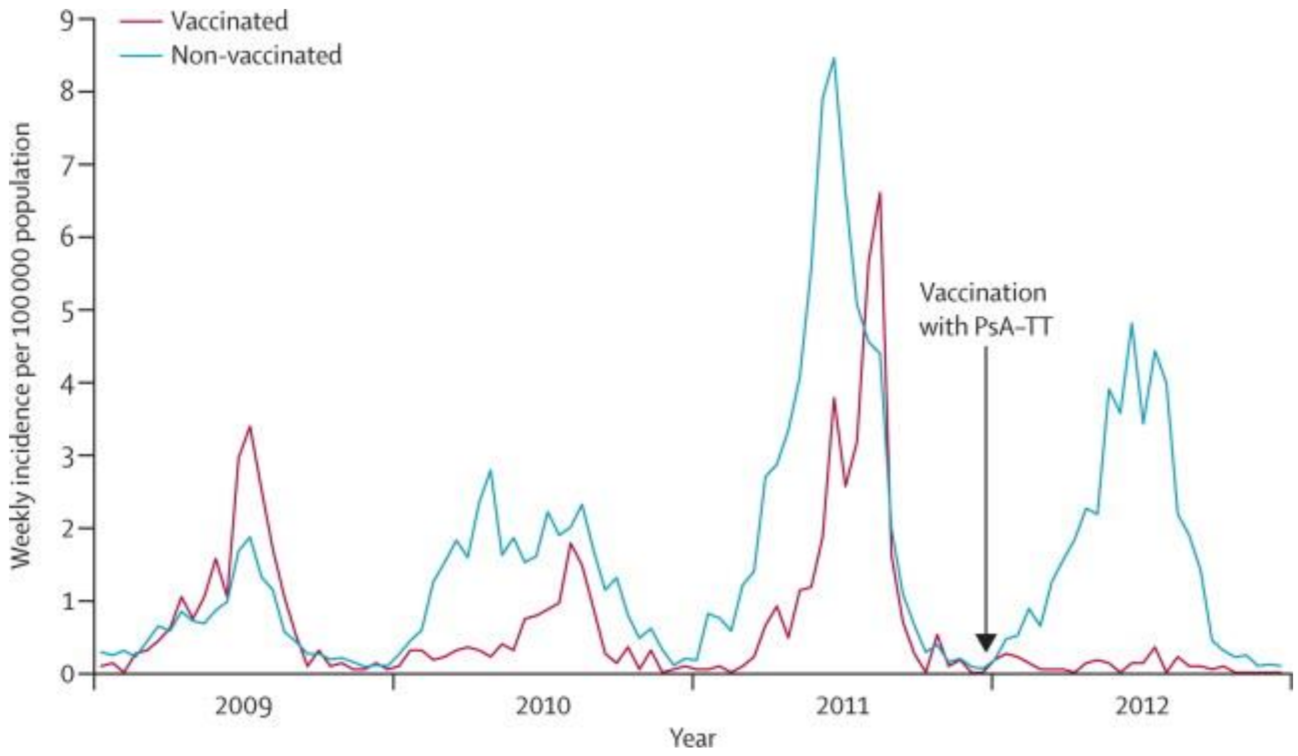
Meningitis Vaccine Project

Chad outbreak, 2011-2012

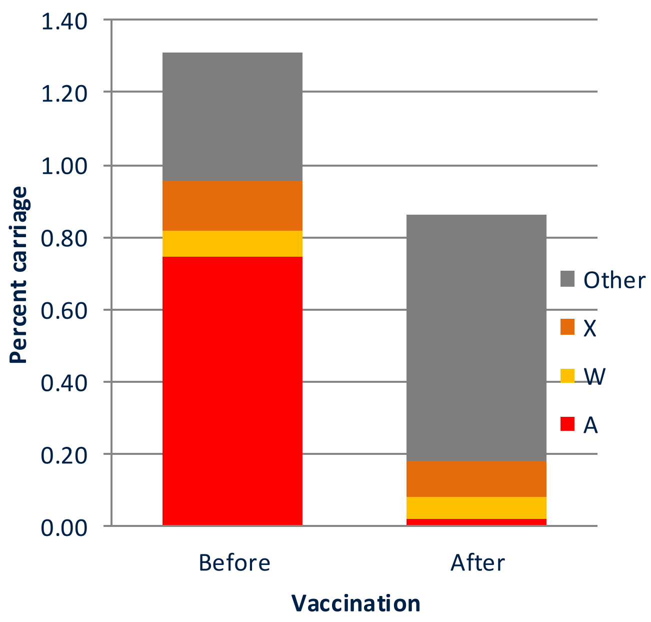
MenAfriVac™ vaccine in the village of Sari, Chad, December 2011

MenAfriVac® in Chad

a) Disease in Chad



b) Carriage in Chad, vaccinated districts



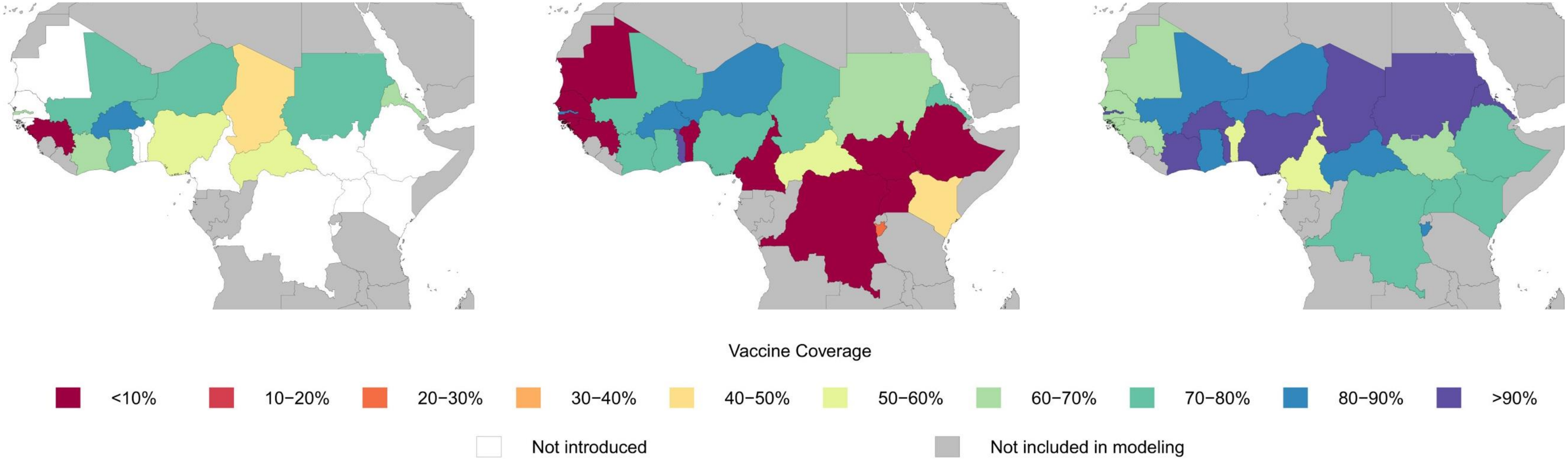
Daugla, D. M., Gami, J. P., Gamougam, K., Naibei, N., Mbainadji, L., Narbe, M., Toralta, J., Kodbesse, B., Ngadoua, C., Coldiron, M. E., Fermon, F., Page, A. L., Djingarey, M. H., Hugonnet, S., Harrison, O. B., Rebbetts, L. S., Tekletsion, Y., Watkins, E. R., Hill, D., Caugant, D. A., Chandramohan, D., Hassan-King, M., Manigart, O., Nascimento, M., Woukeu, A., Trotter, C., Stuart, J. M., Maiden, M. C. & Greenwood, B. M. (2014). Effect of a serogroup A meningococcal conjugate vaccine (PsA-TT) on serogroup A meningococcal meningitis and carriage in Chad: a community study. *Lancet* **383**, 40-47.

MenAfriVac® coverage estimates, year-end 2021

Routine infant immunization for target age, varying by country 9 to 18 months.

Combined coverage estimates ages 1–4 years.

Combined coverage estimates for ages 1–29.



Bender, R.G. et al. (2023) Meningococcal A conjugate vaccine coverage in the meningitis belt of Africa from 2010 to 2021: A modelling study. *eClincal Medicine* 101797. DOI: 10.1016/j.eclinm.2022.101797

Exercise

- What happened to invasive meningococcal disease after the introduction of PsA-TT (MenAfriVac®) vaccine?
  - Was this uniform across the meningitis belt?

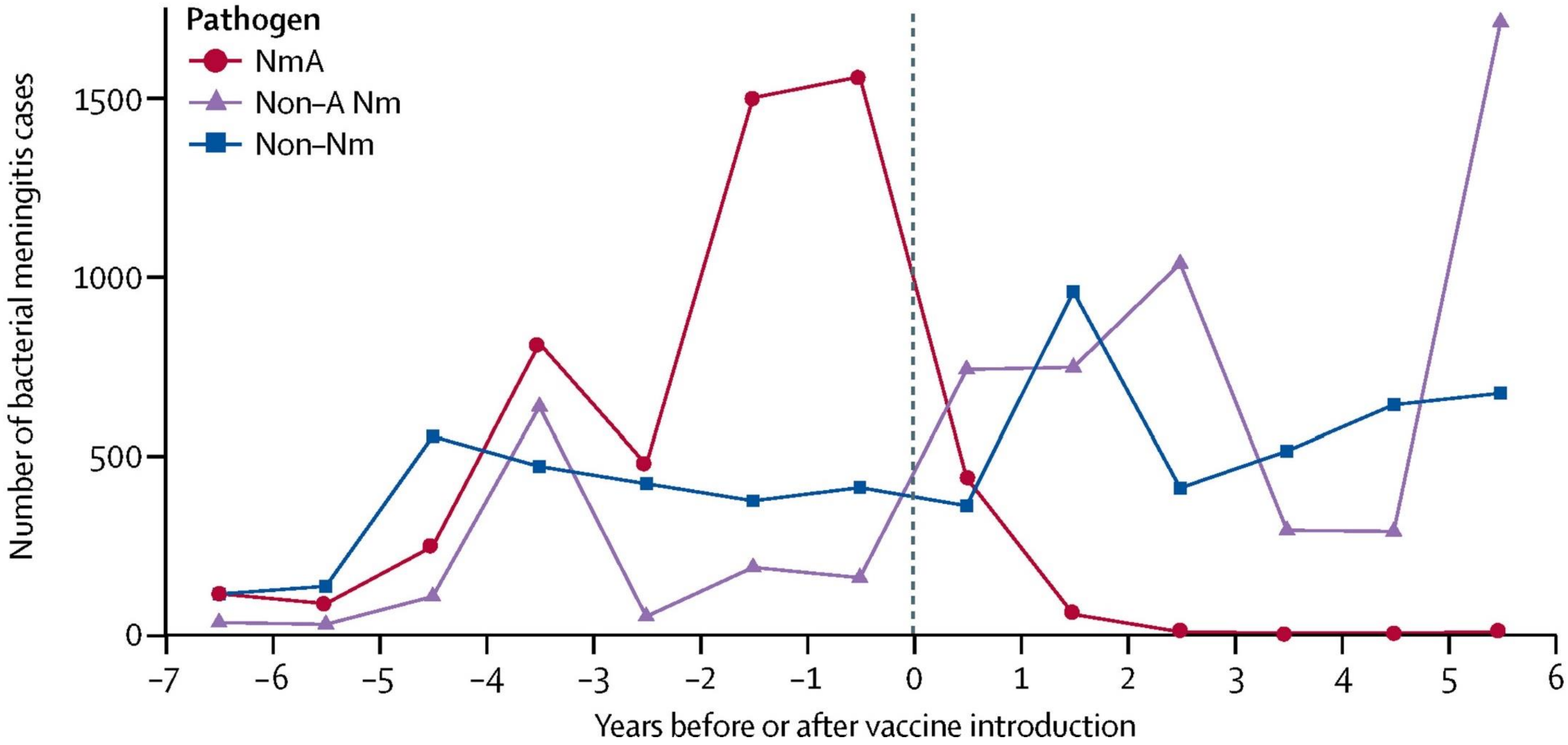
- What would be your advice to policy makers?
  - Should vaccination programmes be continued, ended, or changed?

- How would you support this advice with genomic data?
  - How can this information be presented to different audiences?

Insert:

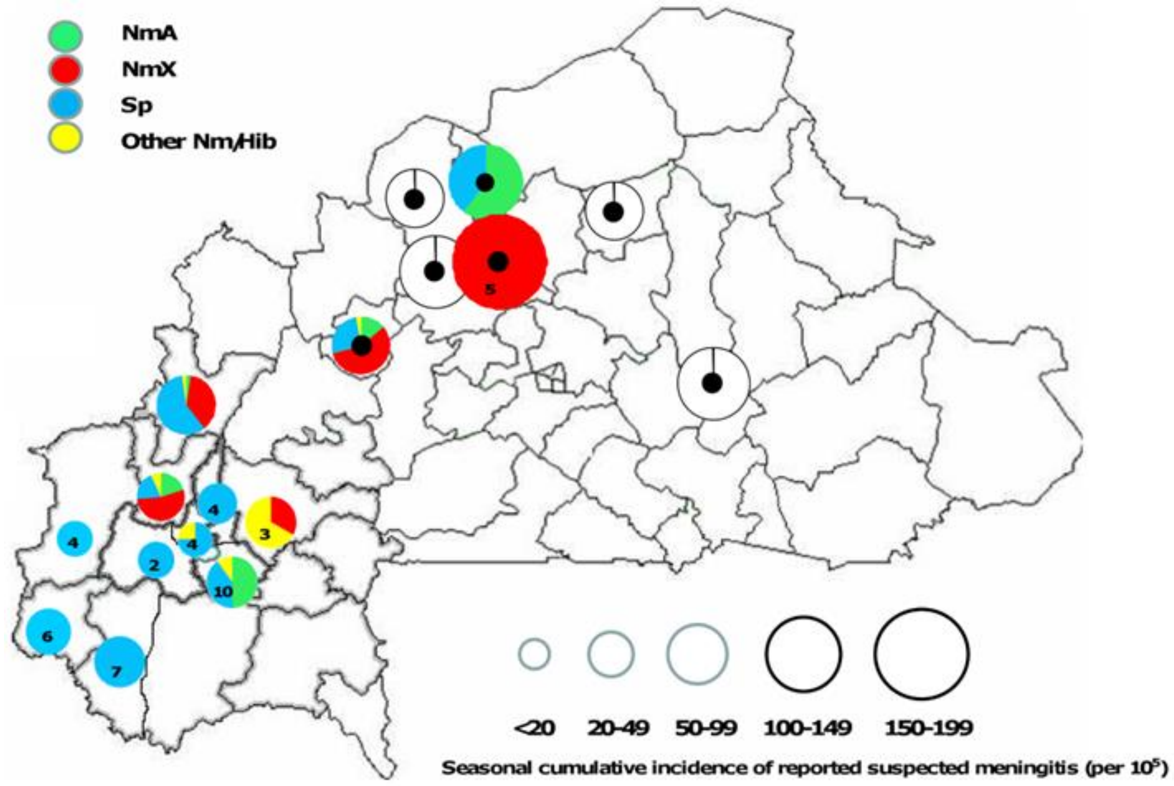
Keith: 4. Topaz Data Practical

MenAfriVac®: impact on confirmed meningitis cases



Trotter, C. L., Lingani, C., Fernandez, K., Cooper, L. V., Bita, A., Tevi-Benissan, C., Ronveaux, O., Preziosi, M. P. & Stuart, J. M. (2017). Impact of MenAfriVac in nine countries of the African meningitis belt, 2010-15: an analysis of surveillance data. *Lancet Infectious Diseases* **17**, 867-872.

Serogroup C, W, and X meningococcal disease in Africa



Wang, J. F., Caugant, D. A., Morelli, G., Koumaré, B. & Achtman, M. (1993). Antigenic and epidemiological properties of the ET-37 complex of *Neisseria meningitidis. Journal of Infectious Diseases* 167, 1320-1329.

Kwara, A., Adegbola, R. A., Corrah, P. T., Weber, M., Achtman, M., Morelli, G., Caugant, D. A. & Greenwood, B. M. (1998). Meningitis caused by a serogroup W135 clone of the ET-37 complex of *Neisseria meningitidis in West Africa. Trop Med Int Health* 3, 742-746.

Delrieu, I., Yaro, S., Tamekloe, T. A., Njanpop-Lafourcade, B. M., Tall, H., Jaillard, P., Ouedraogo, M. S., Badziklou, K., Sanou, O., Drabo, A., Gessner, B. D., Kambou, J. L. & Mueller, J. E. (2011). Emergence of epidemic *Neisseria meningitidis* serogroup X meningitis in Togo and Burkina Faso. *PLoS One* 6, e19513.

IMD Outbreaks in Africa 2010-17

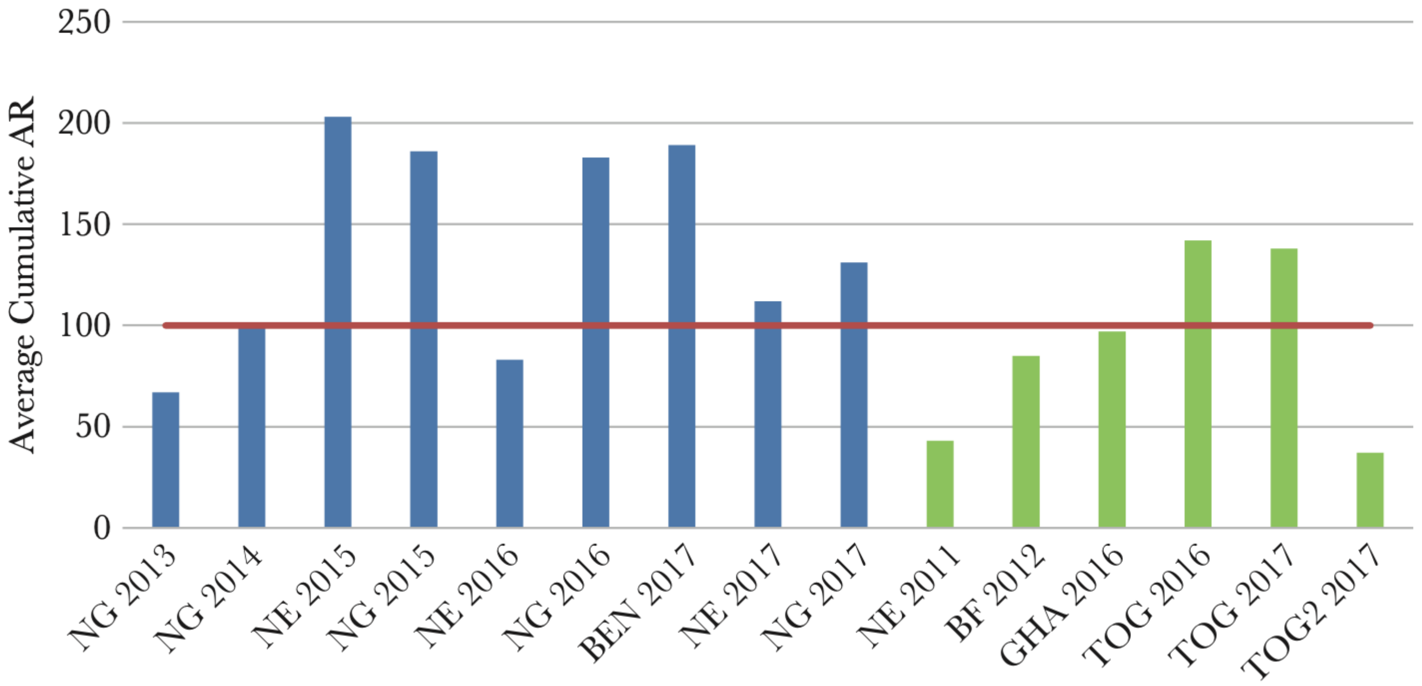
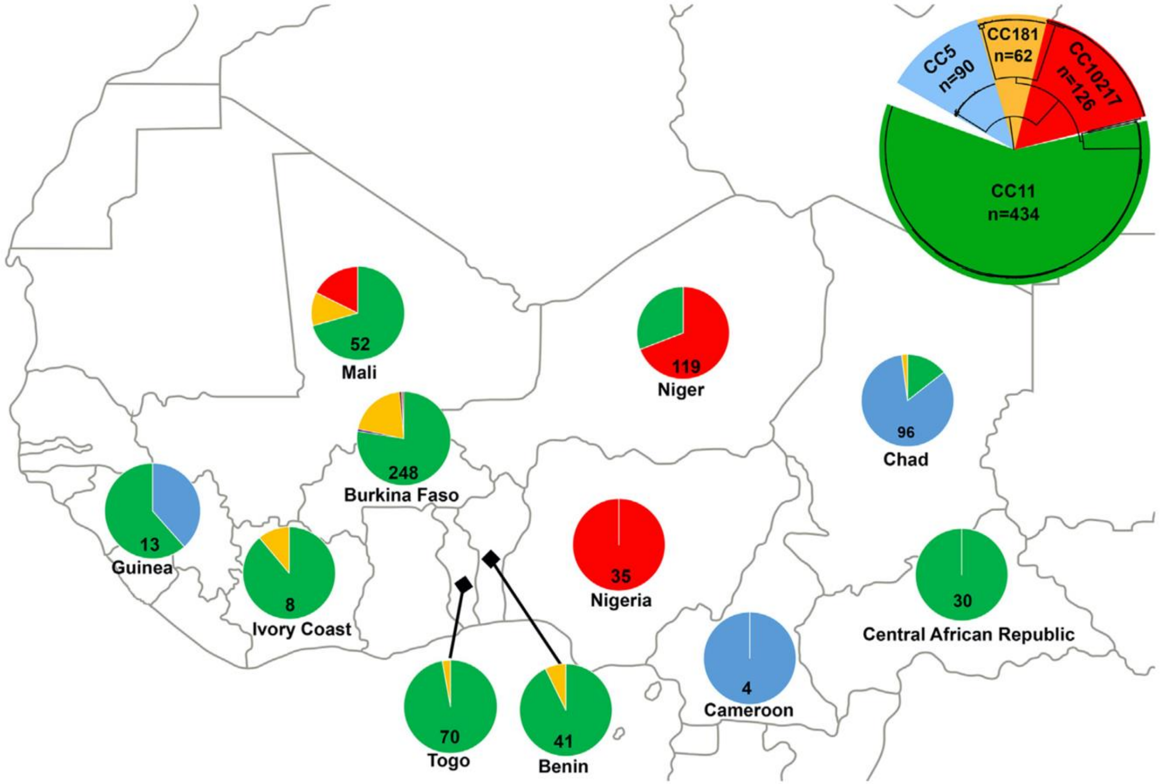


Figure 1. Cumulative attack rates per outbreak (district average), stratified by serogroup, excluding special situations outbreaks in Cameroon and Ethiopia. *Neisseria meningitidis* serogroup C outbreaks are shown in blue and *N. meningitidis* W outbreaks in green. Red line indicates epidemic criterion. Abbreviations: AR, attack rate; BEN, Benin; BF, Burkina Faso; GHA, Ghana; NE, Niger; NG, Nigeria; TOG, Togo.

Fernandez, K., Lingani, C., Aderinola, O. M., Goumbi, K., Bicaba, B., Edea, Z. A., Glele, C., Sarkodie, B., Tamekloe, A., Ngomba, A., Djingarey, M., Bwaka, A., Perea, W. & Ronveaux, O. (2019). Meningococcal Meningitis Outbreaks in the African Meningitis Belt After Meningococcal Serogroup A Conjugate Vaccine Introduction, 2011-2017. *J Infect Dis* **220**, S225-S232.

IMD Isolates 2011-2016

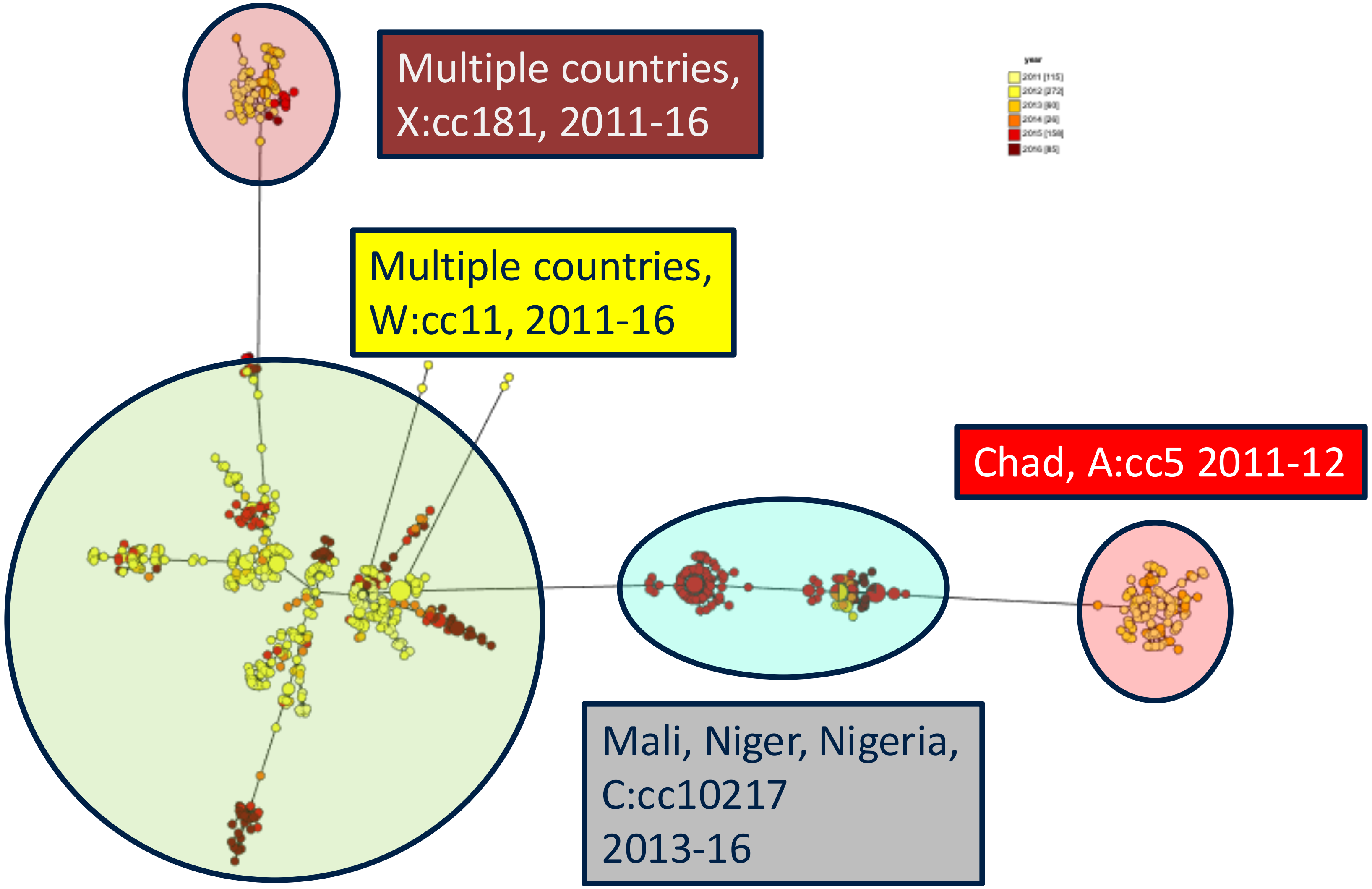


Geographic clonal complex distribution of study isolates

The clonal complex distribution for all 716 meningococcal isolates collected between 2011 and 2016 are shown. The top right includes a circular phylogeny of these isolates and presents the colour key for each clonal complex, which is as follows: CC11 (green), CC10217 (red), CC181 (dark yellow), CC5 (light blue). Two additional clonal complexes were identified (CC175 and CC23) from Burkina Faso, which are not represented with a colour in the figure. Within each country, a pie chart rep- resents the proportions of each clonal complex identified, as well as the total number of isolates included from that country.

Topaz, N., Caugant, D. A., Taha, M. K., Brynildsrud, O. B., Debech, N., Hong, E., Deghmane, A. E., Ouedraogo, R., Ousmane, S., Gamougame, K., Njanpop-Lafourcade, B. M., Diarra, S., Fox, L. M. & Wang, X. (2019). Phylogenetic relationships and regional spread of meningococcal strains in the meningitis belt, 2011-2016. *EBioMedicine* **41**, 488-496.

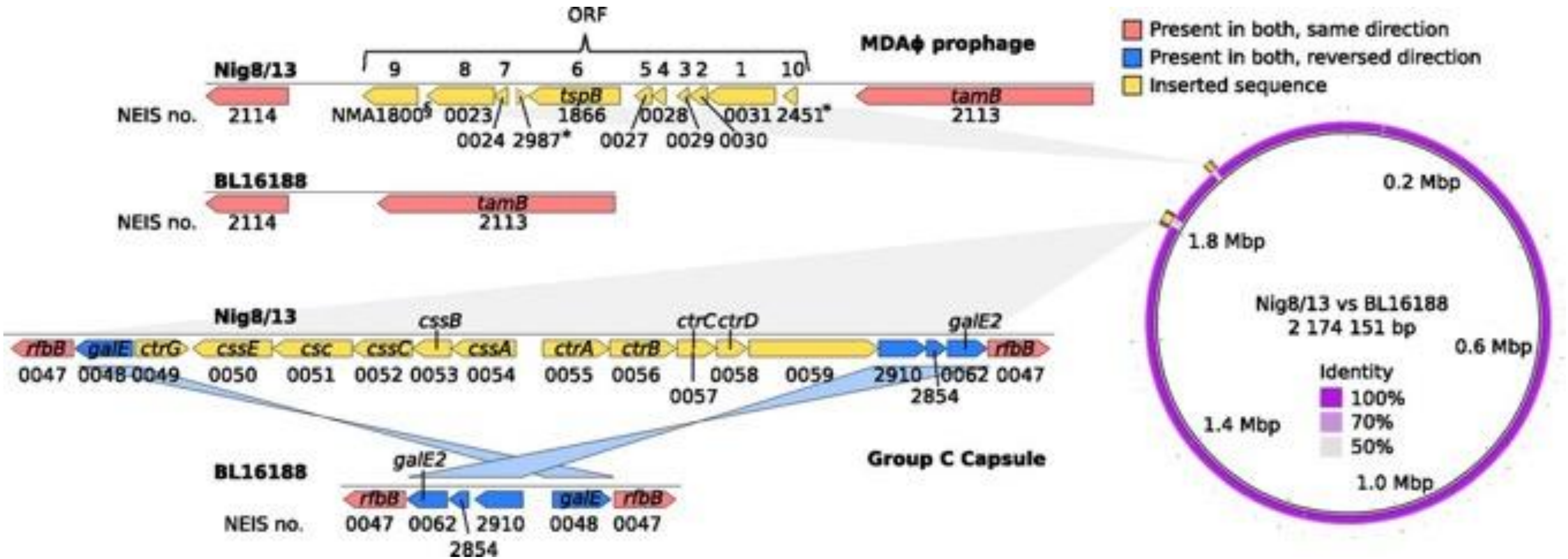
Genomes: African IMD Isolates 2011-2016



Data from:
Topaz, N., Caugant, D. A., Taha, M. K., Brynildsrud, O. B., Debech, N., Hong, E., Deghmane, A. E., Ouedraogo, R., Ousmane, S., Gamougame, K., Njanpop-Lafourcade, B. M., Diarra, S., Fox, L. M. & Wang, X. (2019). Phylogenetic relationships and regional spread of meningococcal strains in the meningitis belt, 2011-2016. *EBioMedicine* **41**, 488-496.

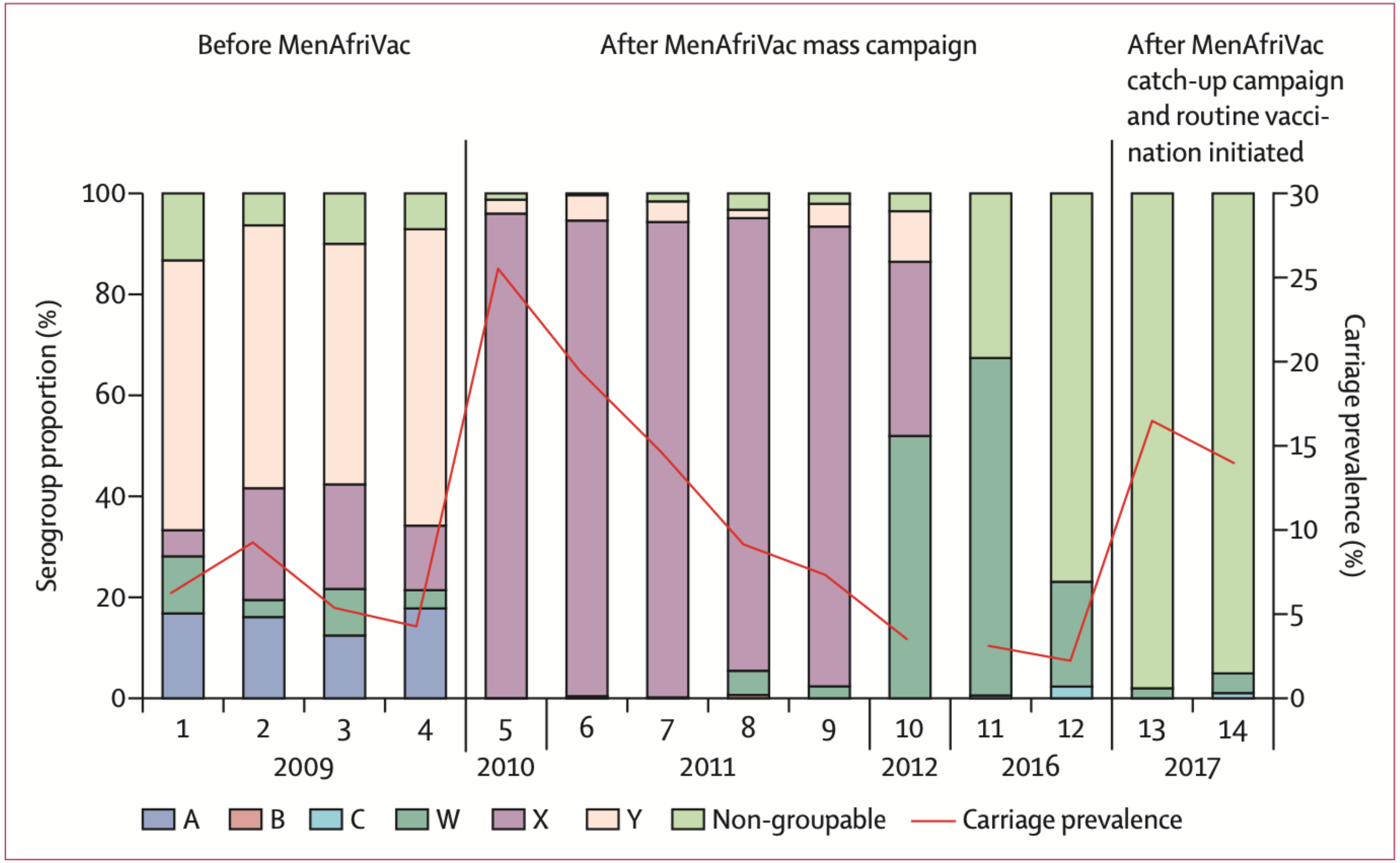
Analysis:
PubMLST, GrapeTree, cgMLST 1.0

Capsule acquisition and virulence



Brynildsrud, O. B., Eldholm, V., Bohlin, J., Uadiale, K., Obaro, S. & Caugant, D. A. (2018). Acquisition of virulence genes by a carrier strain gave rise to the ongoing epidemics of meningococcal disease in West Africa. *Proc Natl Acad Sci U S A*. **115**, 5510-5515.

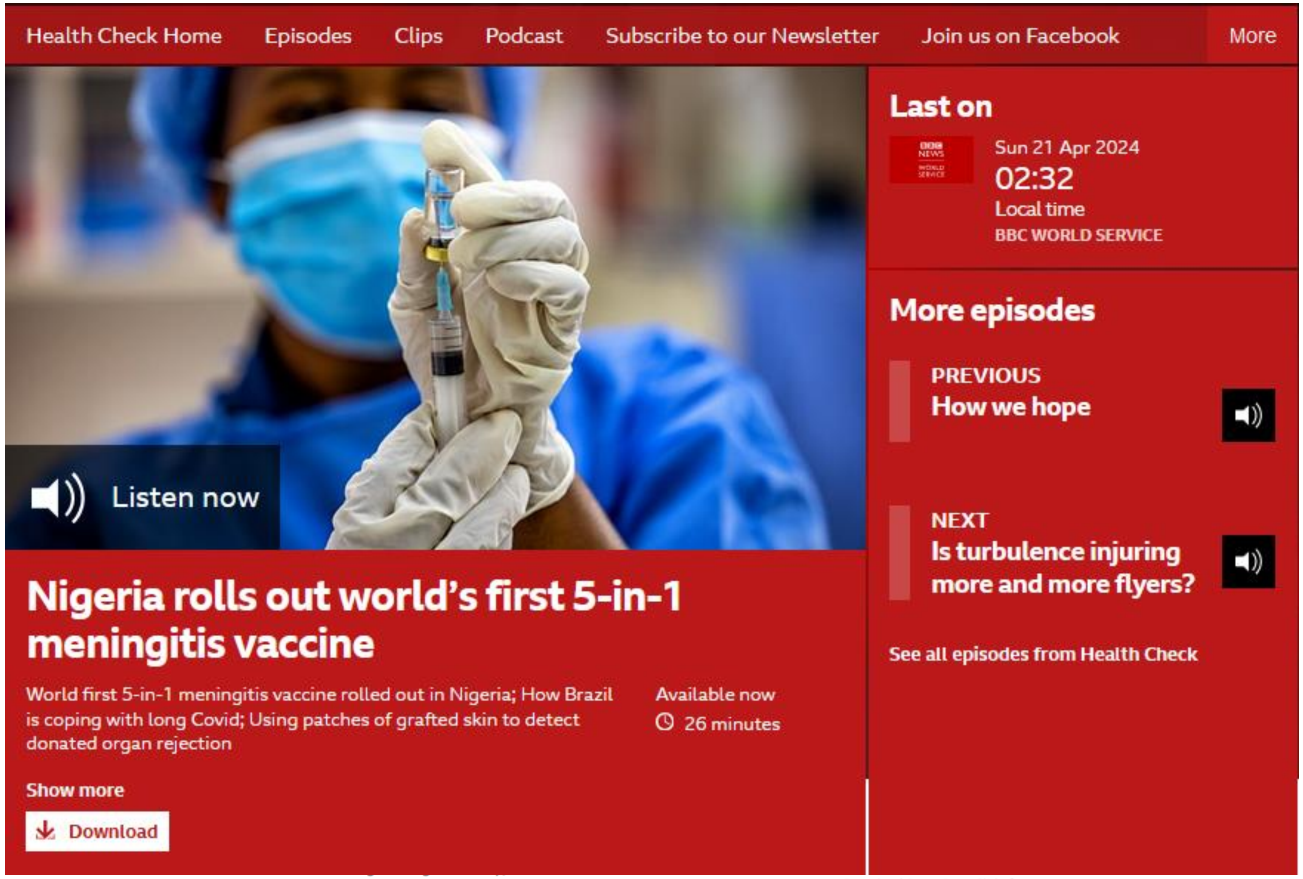
Meningococcal carriage in Burkina Faso



Mbaeyi, S., Sampo, E., Dinanibe, K., Yameogo, I., Congo-Ouedraogo, M., Tamboura, M., Sawadogo, G., Ouattara, K., Sanou, M., Kiemtore, T., Dioma, G., Sanon, B., Somlare, H., Kyetega, A., Ba, A. K., Ake, F., Tarbangdo, F., Aboua, F. A., Donnou, Y., Kamate, I., Patel, J. C., Schmink, S., Spiller, M. W., Topaz, N., Novak, R., Wang, X., Bicaba, B., Sangare, L., Ouedraogo-Traore, R. & Kristiansen, P. A. (2020). Meningococcal carriage 7 years after introduction of a serogroup A meningococcal conjugate vaccine in Burkina Faso: results from four cross-sectional carriage surveys. *Lancet Infect Dis* 20, 1418-1425.

The future of meningococcal disease and vaccination in Africa

- The MenAfriVac created a serogroup A epidemic-free Africa.
  - Immunisation must, however, be sustained to maintain herd immunity.
- An affordable pentavalent (A, C, Y, W, X) vaccine, Men 5CV, has been developed at the Serum Institute of India.
  - Implemented in Nigeria April 2025.
- Questions remain over serogroup B meningococci.
  - B polysaccharide vaccines, including conjugates, have not been made because of poor responses and safety concerns.
  - There are coverage issues with protein-based 'serogroup B substitute' vaccines
- On-going surveillance essential to maintain protection.
  - WHO global road map.



Pollard, A. J., and Maiden, M. C. (2003) Epidemic meningococcal disease in sub-Saharan Africa – towards a sustainable solution? *Lancet Infectious Diseases* **3**, 68-70.
Obaro, S. (2020). Has meningococcal serogroup A disease been eradicated? *Lancet Infect Dis* **20**, 1354-1355.