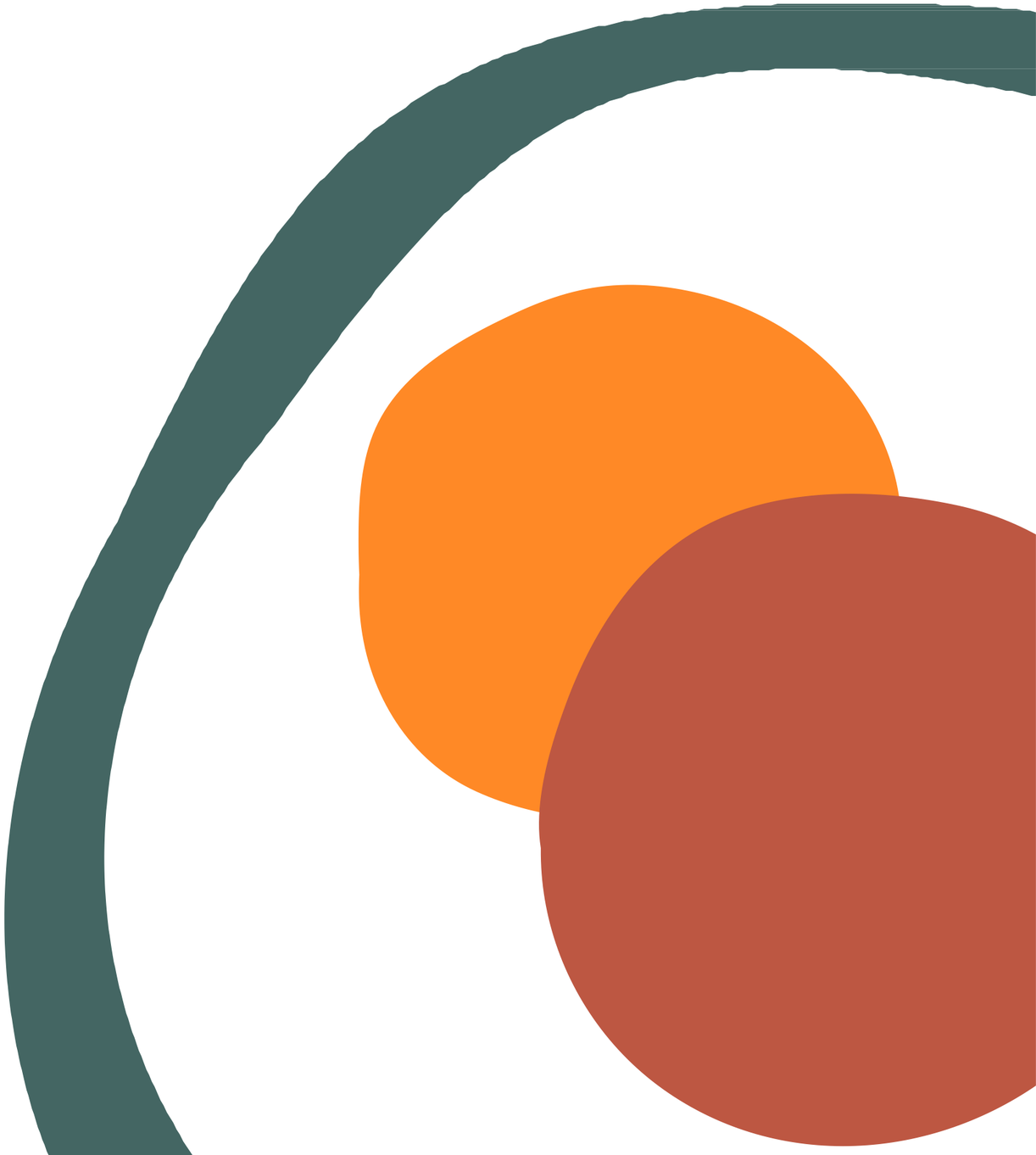
Case study

Development and introduction of vaccines to prevent invasive meningococcal disease



neis CRE Centre for Research Excellence in Neisseria disease control

Adelaide University

Disclosure

Principal investigator for the

- National Health and Medical Research Centre funded Centre of Research Excellence in Neisseria disease control (NEIS CRE)

HM Investigator on clinical vaccine trials and investigator led research sponsored by Industry (ILiAD, Pfizer, Sanofi, GSK, WHO co-ordinating centre/Seqirus). All funding is to the institution.

Scientific advisory board GSK related to the NHMRC CRE in Neisseria disease control.

HM does not receive personal payments from Industry

Presentation

1. Meningococcal disease and disease burden

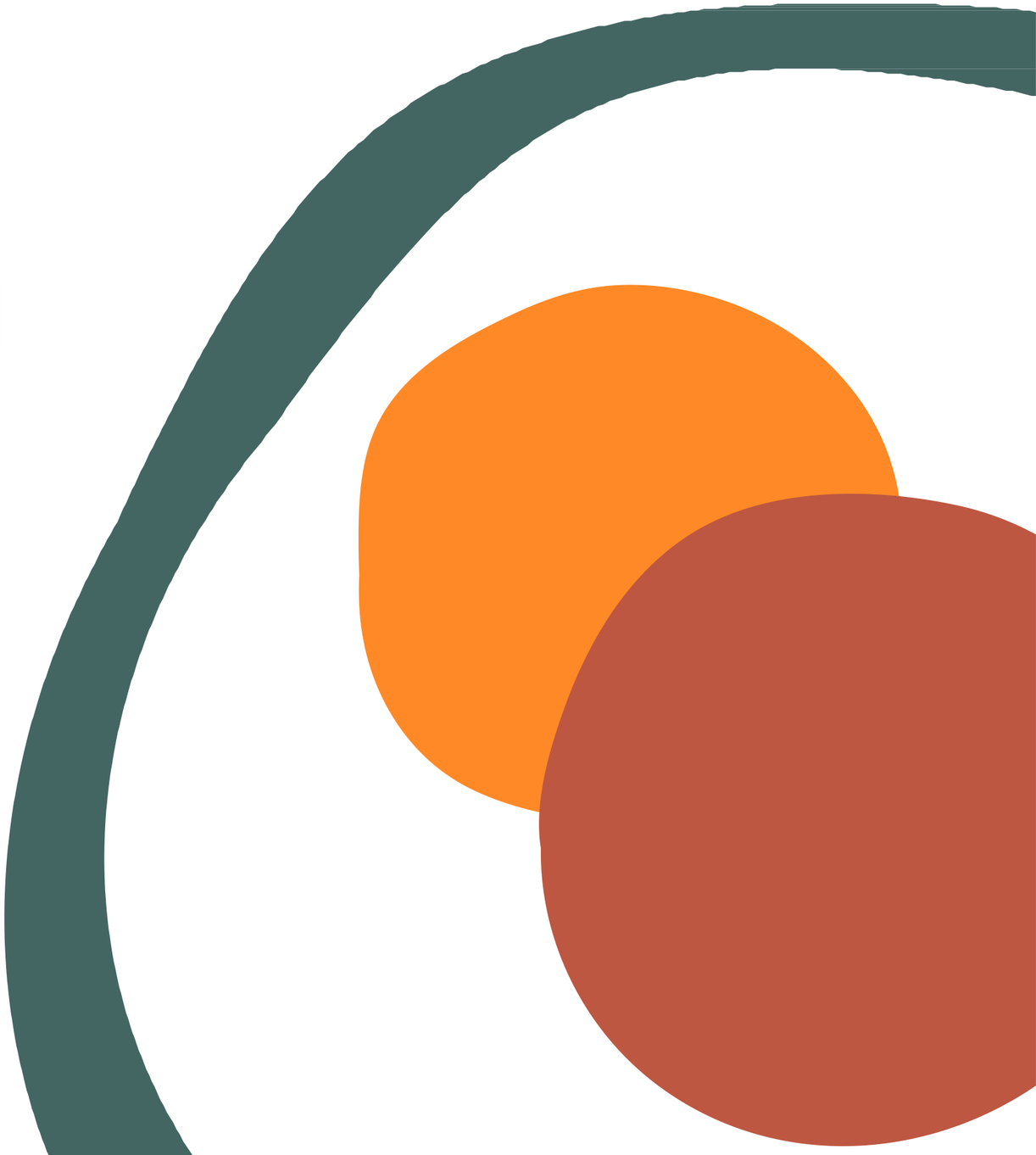
2. Development of conjugate meningococcal vaccines including a vaccine for epidemics in the African meningitis belt

3. Challenges in development of meningococcal B protein-based vaccines

It’s my birthday



Burden of meningococcal disease



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Invasive meningococcal disease (IMD)

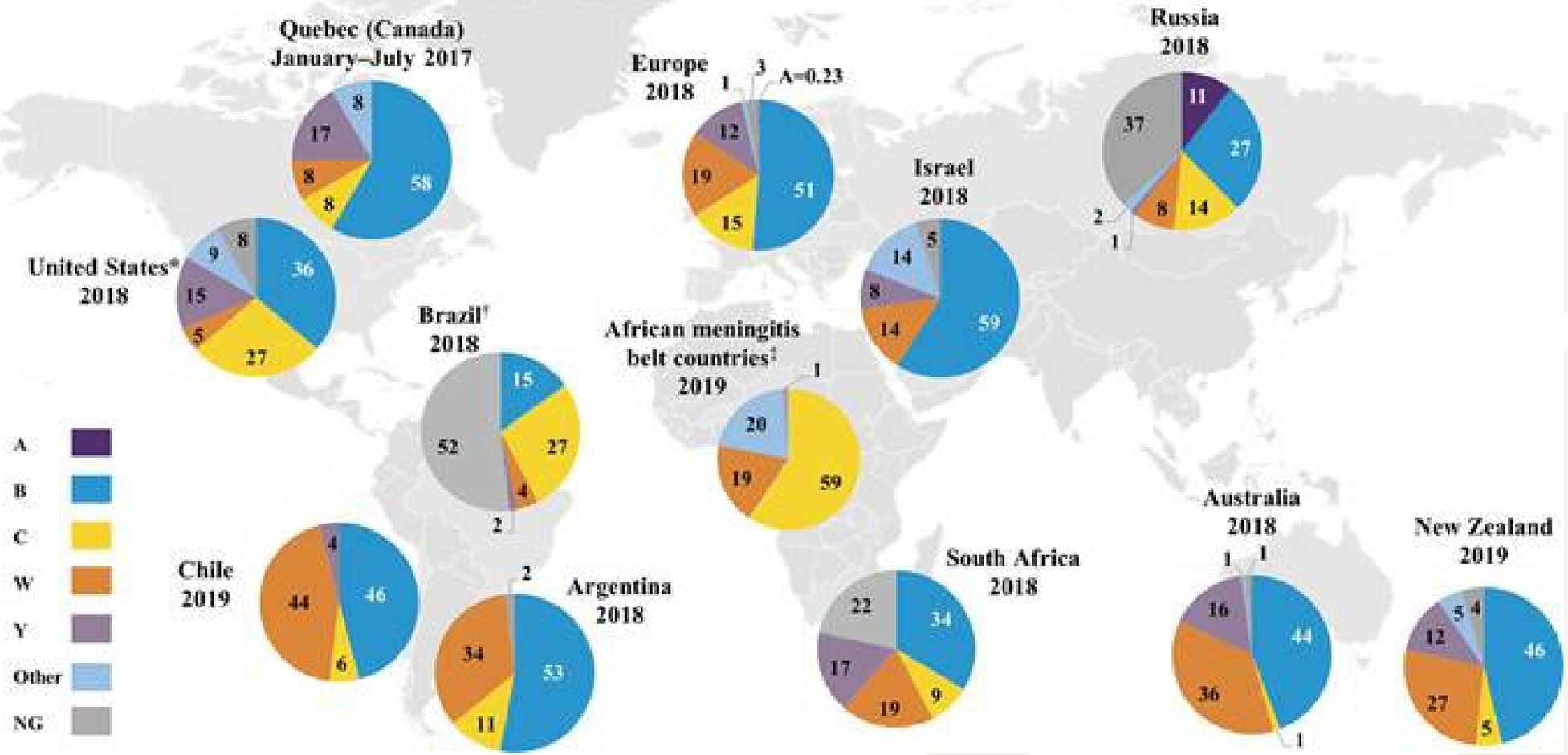
- *Neisseria meningitidis* causes sepsis and/or meningitis with highest rates in infants and adolescents
- Uncommon (1-2/100,000 population)
- 5-10% case fatality rate
- ~40% of children have life-long disability – blindness, deafness, neurological, mobility from limb amputation
- 5 of 13 known serogroups cause most disease (A,B,C,W,Y), majority of cases (85%) in Australia are due to group B
- Accidental pathogen: 5-10% of adolescents carry the meningococcus in their oropharynx and transmit it through coughing, kissing
- Seasonal variation in incidence, with higher rates in winter/spring
- Recent outbreaks of serogroup B in young people in the UK





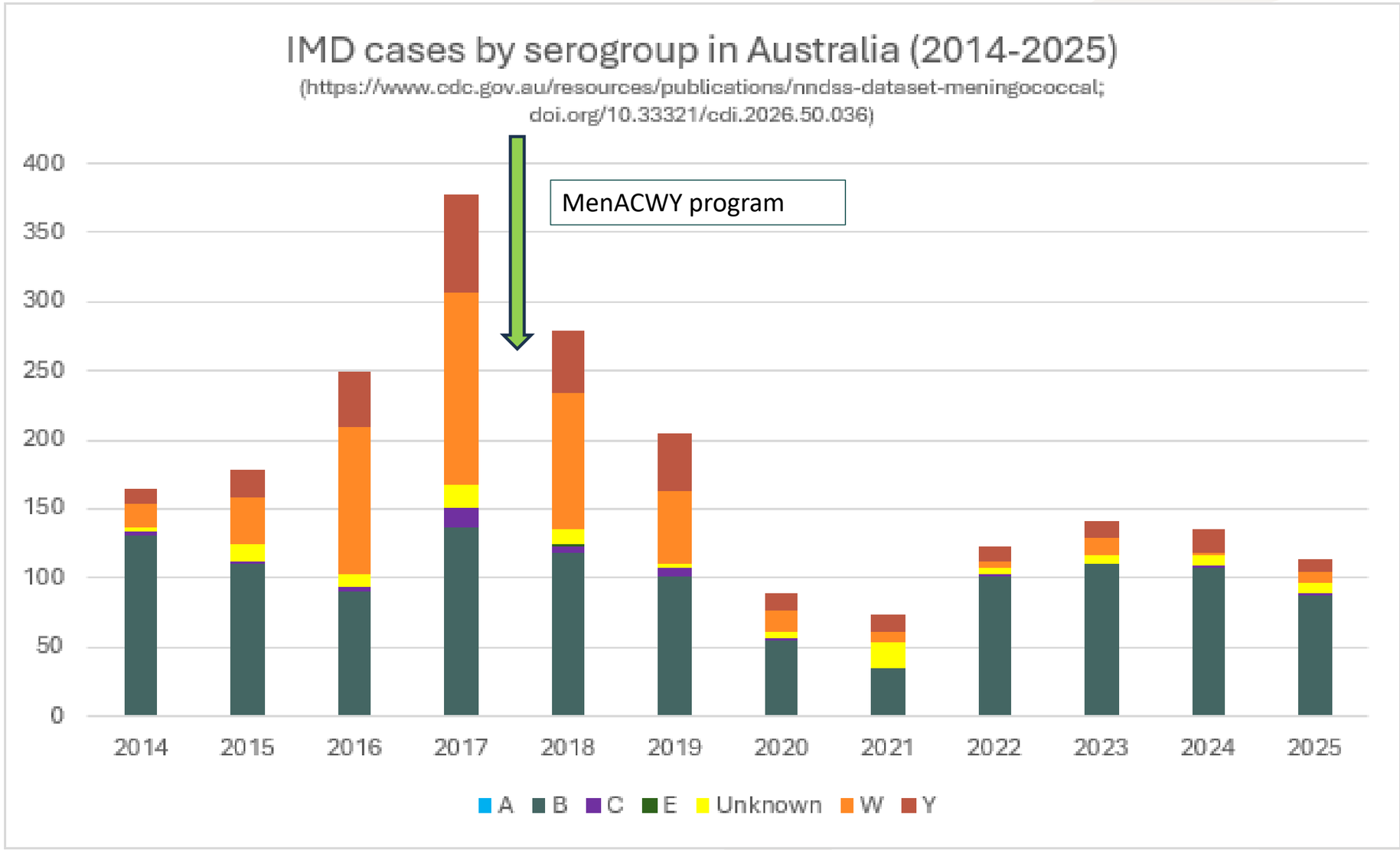
1. Marshall et al. Int J Evidence-Based Healthcare 2016:14:3-14. Marshall et al. NEJM 2020;382(4):318-327.

Global epidemiology of meningococcal disease by serogroup



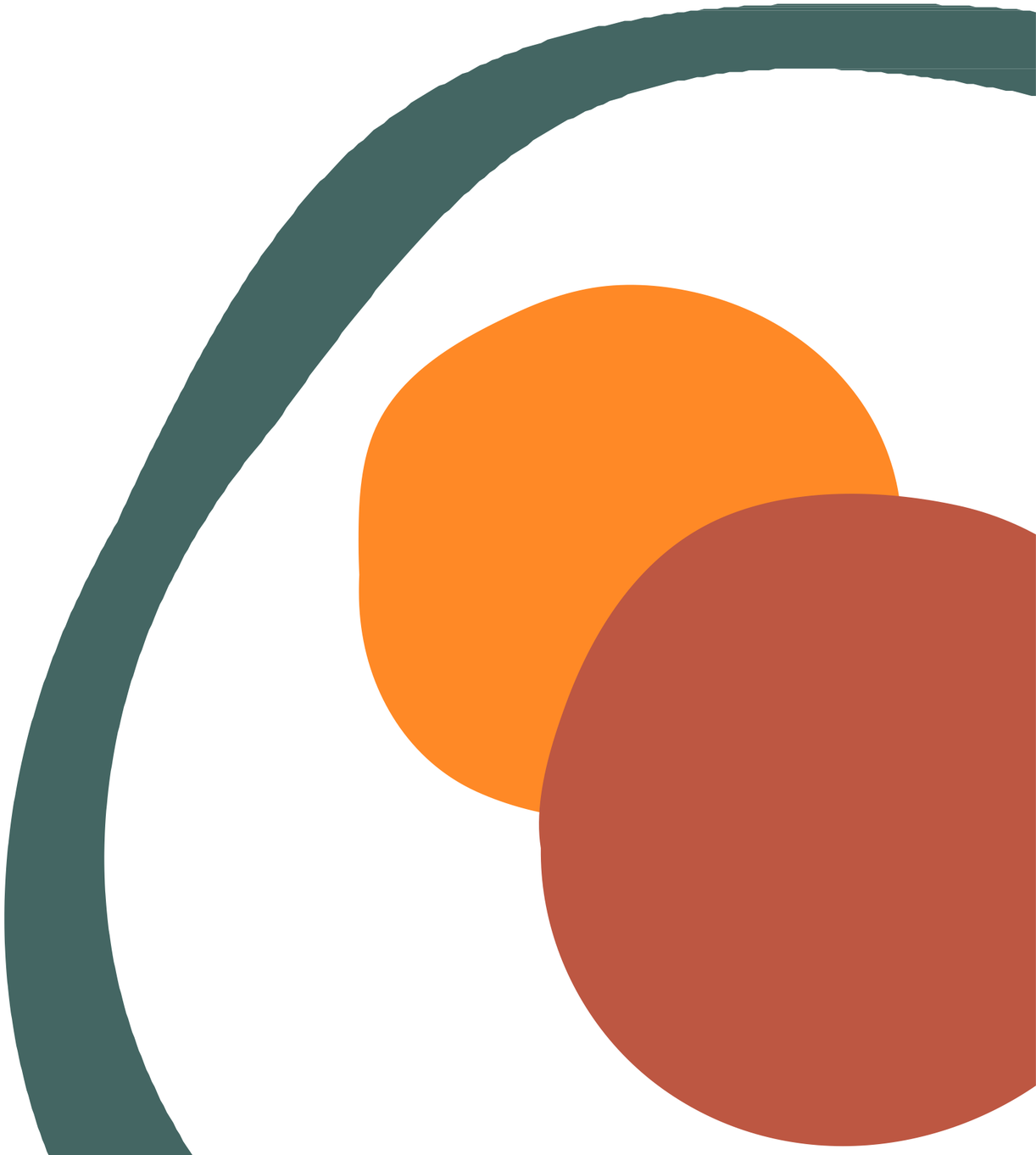
de Santayana P et al. Epidemiology and Infection 2023;151, e57, 1–9.

Epidemiology of Invasive Meningococcal Disease (IMD) in Australia



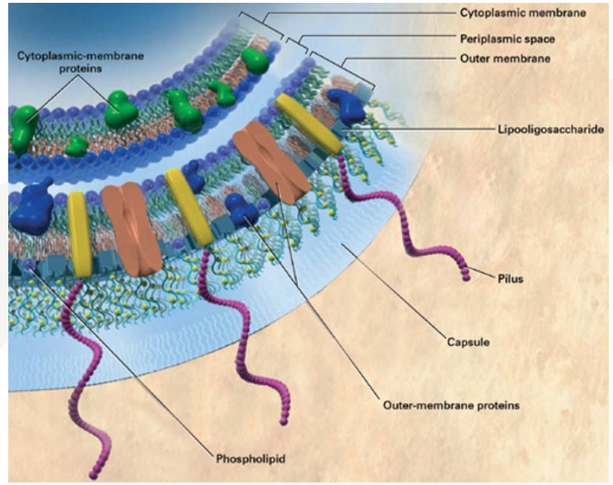
www.cdc.gov.au/resources/publiocations/nndss-dataset-meningococcal

Development of meningococcal vaccines



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The first meningococcal vaccines – overcoming immunity challenges

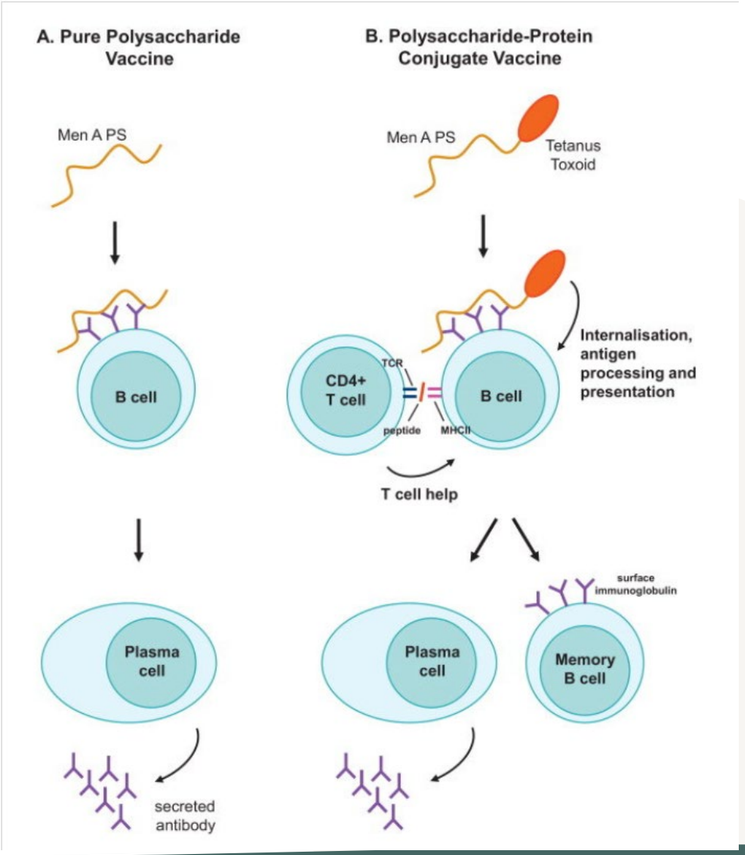


Polysaccharide meningococcal vaccines were derived from capsular polysaccharide (MenAC, MenACW, Men ACWY) in 1970s

- Inability to induce immune memory, short duration of protection
- Ineffective in young children < 2 years
- Lack of efficacy against nasopharyngeal carriage

Conjugate meningococcal vaccine development (late 1990s/2000)

- Capsular polysaccharide is conjugated to a carrier protein (TT, DT, CRM) (MenA, MenC, MenACWY etc.)
- Induce a T-cell-dependent response, immune memory
- Vaccines immunogenic from early infancy.



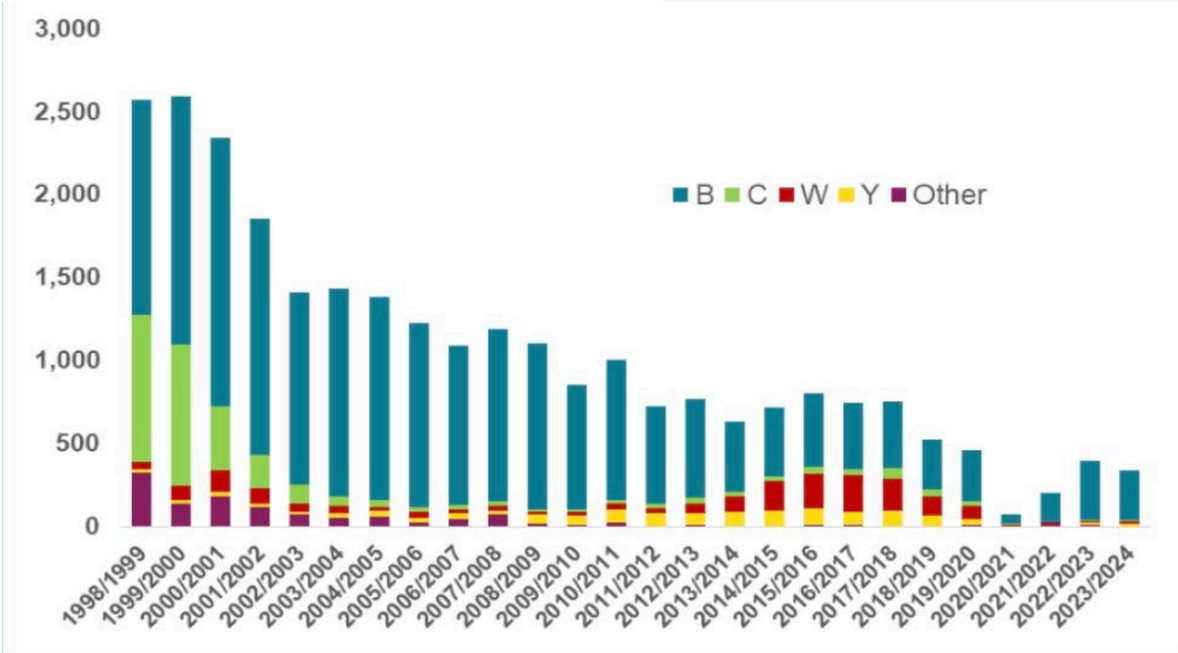
1.Marshall et al. *Int J of Evidence Based Healthcare,* 2016;14(1):3-14 2. Crum-Cianfone et al. Infect Dis Ther 2016;5(2):89-112.

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MenC was the first conjugate vaccine developed and introduced and was highly effective in reducing IMD

Meningococcal C vaccines

- Introduced in the UK in response to increase in MenC ST-11 IMD cases.
- Licensed using immunological correlates of protection (functional antibodies =Serum Bactericidal Antibodies (SBA titres)) rather than clinical efficacy trials
- Following introduction MenC vaccine was 87% effective against MenC disease [1]



Meningococcal ACWY vaccines

- Introduced in many countries following increase in ST-11 globally
- 69% effective against group ACWY IMD [2]





1. Villena R et al. Hum Vaccin Immunother. 2023;19(2):2251825. 2. McMillan et al. Clinical Infectious Diseases 2021;73(3):e609–19 3. UKHSA invasive meningococcal disease in England annual report 2023/2024.

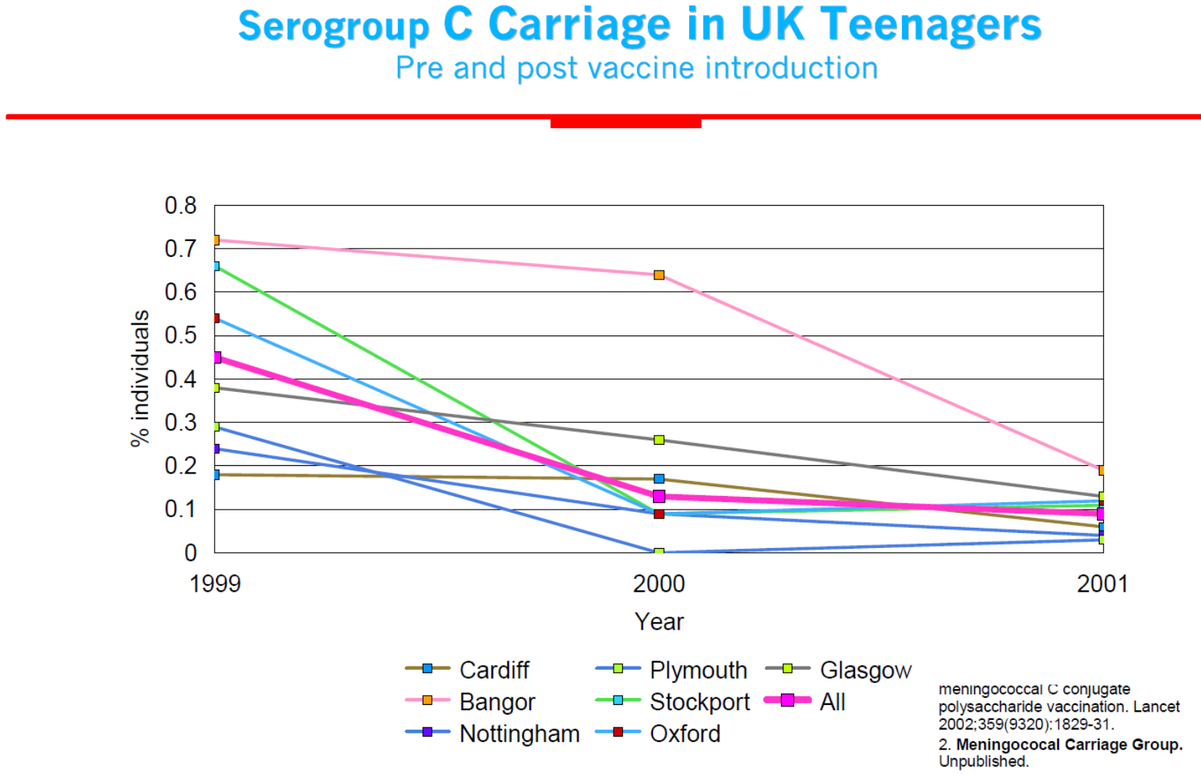
Impact of meningococcal conjugate vaccines on acquisition of carriage and herd immunity



Martin Maiden

Can MenC vaccine reduce carriage and transmission of *N. meningitidis* serogroup C ?

- 3 consecutive carriage studies in 15-19 yr olds, 1999-2001 following MenC vaccine introduction 1999
- Reduction in serogroup C carriage; rate ratio 0.19 for at least 2 years
- Disproportionate vaccine impact on carriage of serogroup C ST-11; rate ratio 0.06 (high rates of expression)
- No evidence of serogroup replacement
- Vaccine effectiveness=75% against carriage



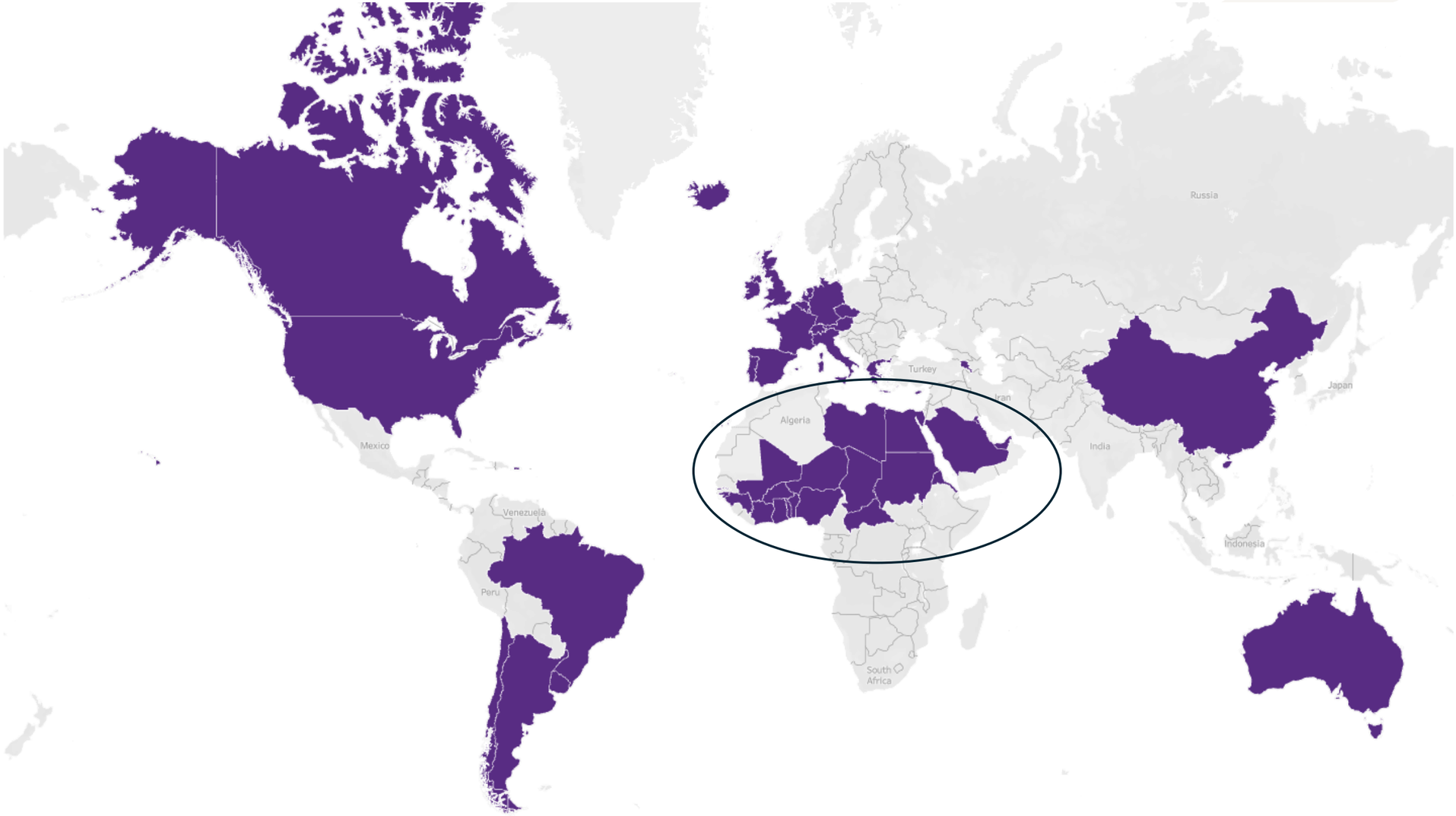
Vaccine introduction

Year 1

Year 2

1. Maiden M et al. Lancet 2002;359:1829-31. 2. Maiden M et al. JID 2008:197: 737-43.

Use of conjugate meningococcal vaccines globally



Meningitis Research Foundation https://tracker.meningitis.org/vaccines/

Meningococcal A epidemics in sub-Saharan Africa's "meningitis belt"

Sub-Saharan Africa, outbreaks annually and large epidemics every 8-12 years (attack rates up to 1%)

Reactive MenA PS vaccine campaigns ineffective and inefficient

Catastrophic outbreak of meningitis 1996-1997 that infected 250,000 people with 25,000 deaths

WHO recommended development of a conjugate MenA vaccine

"***Please don't give us a vaccine that we can't afford," "That's worse than no vaccine." African public health official***

Meningitis Project est. in 2001

- A historic public private partnership between the WHO, PATH, GAVI, GATES Foundation and Serum Institute of India
- Seed funding from GATES foundation $70 million to WHO & PATH
- Acquired raw materials from Synco BioPartners in Amsterdam, the Netherlands, conjugation technology from the US FDA and manufacture through Serum Institute of India
- Vaccine cost maximum US 50 cents



Meningitis belt – population 350 million



Meningococcal A incidence prior to MenA vaccine

1. Trotter CL et al. Lancet ID 2017;17:867-72. 2. Daugla DM et al. Lancet 2014; 383: 40–47. 3. Frasch C et al. Human Vaccines & Immunotherapeutics, 2012;8:6, 715-724. 4. Jaca A et al. Pan Afr Med 2021;39(57).

Clinical trial development of MenAfriVac® for the meningitis belt

Followed the successful clinical trial development of MenC conjugate vaccine in the UK including use of SBA titres as correlate of protection

Preclinical trials of PsA-TT vaccine in mice and rabbits was more immunogenic than MenA/C PS vaccine (2004)

Phase 1 study RCT of safety and immunogenicity in healthy adults 18-35 yrs in India (2005)

- Local & systemic symptoms mild & transient
- 83% PsA-TT compared to 72% in PsA/C SP had ≥ 4-fold increase in SBA titres

5 Phase 2/3 RCTs in African meningitis belt countries comparing PsA-TT to PSACWY (2006-2009)

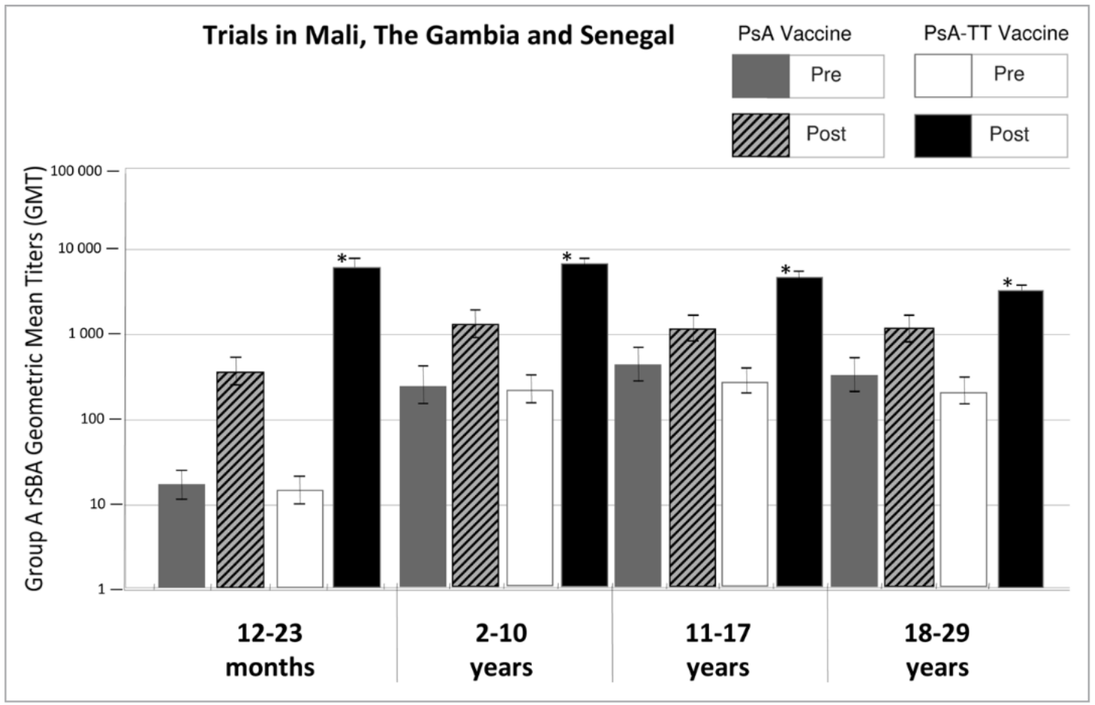


Figure 4. Geometric Mean rSBA Titers prior to and 28 d after a dose of either PsA-TT or PsA vaccine in African toddlers, adolescents and young adults.

- 1-29 year olds were completed in 2009 **showing acceptable safety compared to polysaccharide vaccine**
- Monovalent MenA vaccine **shown to be more immunogenic than licensed meningococcal polysaccharide vaccines**
- **Antibody persistence -** At 40 weeks 82% in PsA-TT compared to 38% in PsACWY still showed ≥ 4-fold increase in rSBA

Frasch C et al. Human Vaccines & Immunotherapeutics, 2012;8:6, 715-724.

MenAfriVac® licensing and implementation

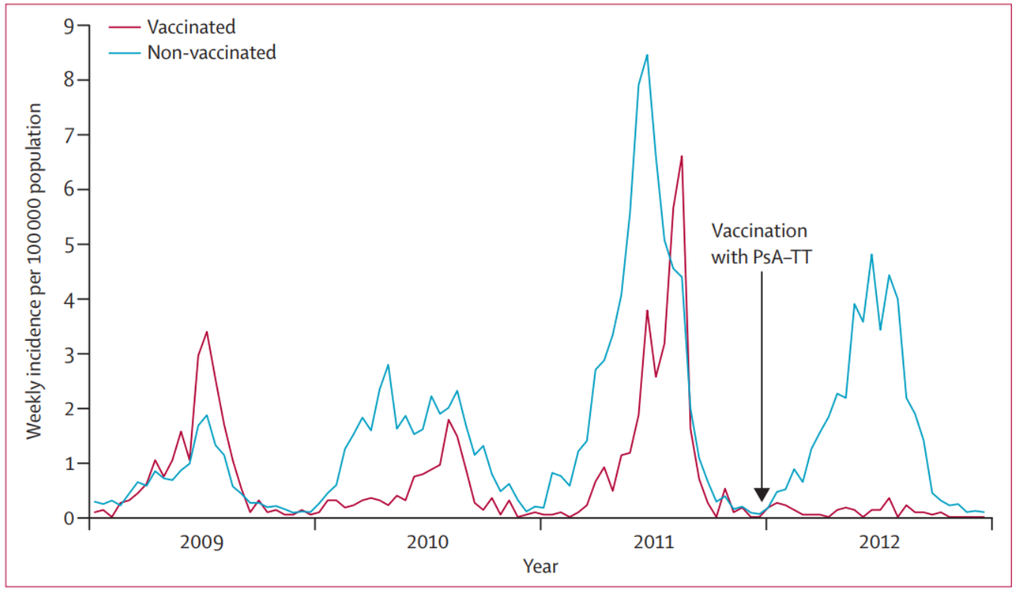
- Licensed by the Indian Drugs Controller General of India (Dec 2009) and WHO prequalification (June 2010)
- Followed by licensing in African countries
- Population program commenced in Dec 2010, initially in Burkina Faso, Mali and Niger
- Single MenA-TT 10 ug dose in individuals 1-29 years of age
- 2011 epidemic season ended with NO REPORTED CASES of Group A meningitis in vaccinated individuals





MenAfriVac® defeated MenA epidemics

- By 2017, vaccinated > 300 million people
- Group A epidemics eliminated
- Prevented > 140,000 deaths, > 1 million cases averted
- 99% reduction in the incidence of confirmed group A disease in fully vaccinated populations
- 98% reduction in the carriage of the epidemic strain
- Introduced into the Expanded Program on Immunisation schedule in 9-18 month infants
- Epidemics caused by other groups remain a threat (MenW and MenC) – natural ecological changes and enhanced surveillance
- Led the way for multivalent conjugate meningococcal vaccines such as MenACWXY



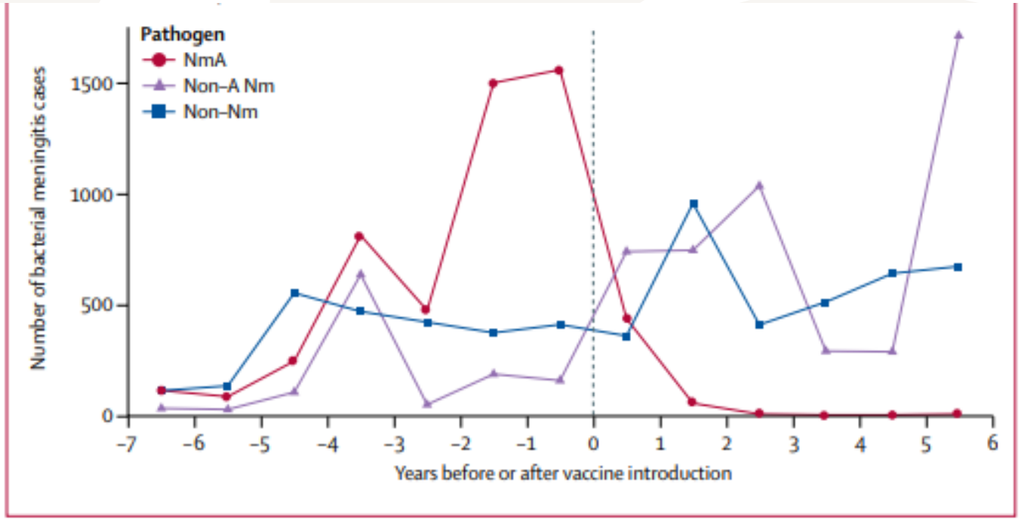
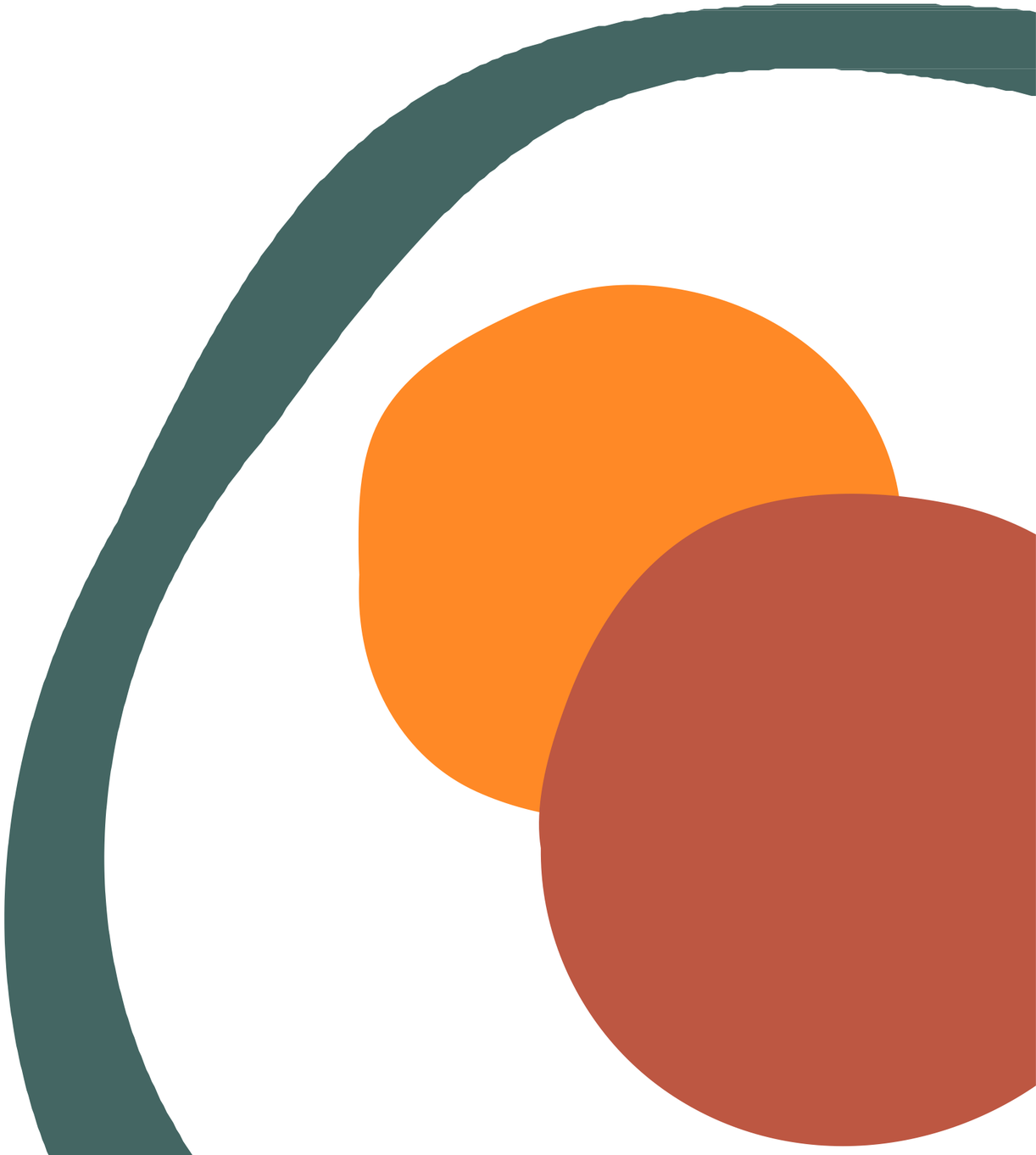


Figure: **Total annual suspected and confirmed cases of bacterial meningitis across all nine countries in relation to MenAfriVac introduction (dotted line)**
Nm=*N meningitidis*. Non-A Nm=other meningococcal serogroups. Non-Nm=Pathogens other than *N meningitides*.

Trotter CL et al. Lancet ID 2017;17:867-72. Daugla DM et al. Lancet 2014; 383: 40–47

Meningococcal B vaccine development

neis CRE
Centre for Research Excellence in Neisseria disease control



Development of meningococcal B (MenB) vaccines

Capsular polysaccharide Men B vaccines

- poorly immunogenic [1]
  - mimics neural cell adhesion molecule (PSA-NCAM) expressed on surface of human foetal neural tissue
- potential to induce auto-antibodies
- Phase 1 Men B vaccine study in adults, antibodies were non-functional

Vaccines to protect against **epidemic disease**

- Epidemic outbreaks in Cuba[2], Norway[3], Chile[4] and New Zealand[5]
- Outer membrane vesicles (immunodominant outer membrane protein, porin A (PorA))
- Strain specific response, unable to generate antibodies against heterologous strains
  - OMV VA-MENGOC-BC (Cuba)
  - OMV MeNZB (New Zealand)

THE JOURNAL OF INFECTIOUS DISEASES • VOL. 126, NO. 5 • NOVEMBER 1972
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Immunologic Response of Man to Group B Meningococcal Polysaccharide Vaccines

F. A. Wyle,* M. S. Artenstein, B. L. Brandt, E. C. Tramont, D. L. Kasper, P. L. Altieri, S. L. Berman, and J. P. Lowenthal

From the Department of Bacterial Diseases and the Department of Biologics Research, Walter Reed Army Institute of Research, Washington, D.C.

Table 2. Antibody responses to graded doses of polysaccharide vaccine (lot B-1) from *Neisseria meningitidis*.

Dose (μg)	Indirect fluorescence: No. positive*/ no. tested	Latex agglutination: No. positive/ no. tested
10	2/ 8 (4, 7)†	0/4
50	4/9 (4, 4, 7, 7)	0/6
100	1/18 (2)	0/16
250	1/16 (2)	1/23
None	0/8	. . .

* Fourfold or greater increase in titer.

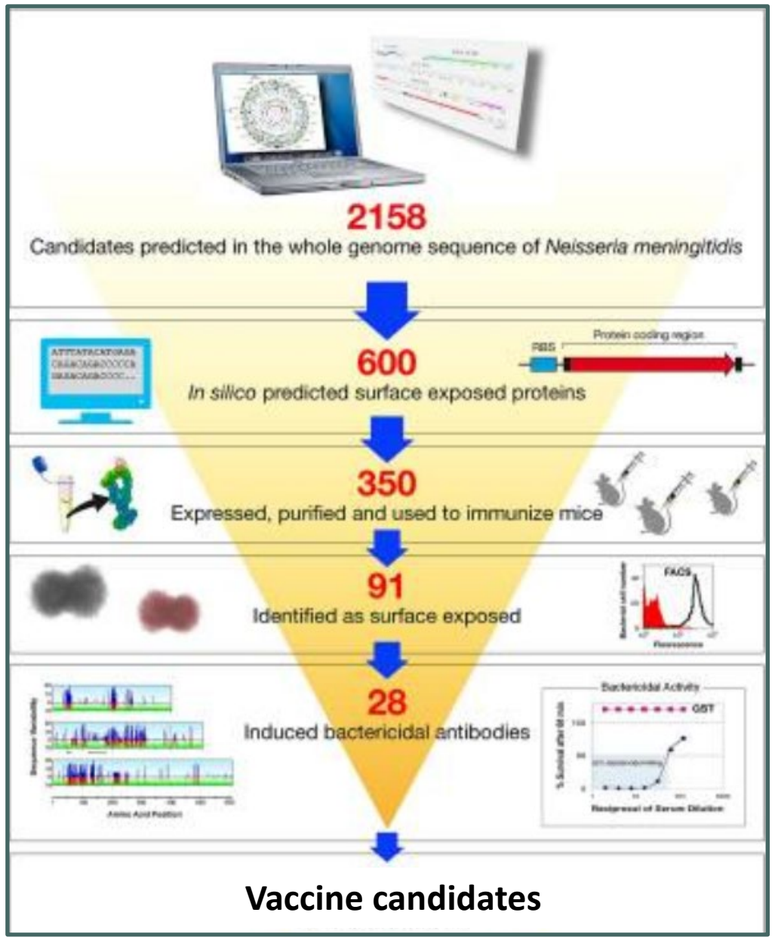
† Numbers in parentheses represent week after vaccination in which rise in titer was observed.

1. Wyle FA et al. I Infect Dis 1972;126:514-21. 2. Sierra G et al. NIPH Ann. 1991;14:195-207. 3. Bjune G et al. Lancet 1991;338:1093-6. 4. Boslego J et al. Vaccine 1995;13:821-9. 5. Kelly C et al. Am J Epidemiol. 2007;166:817-23

Development of broadly protective MenB vaccines required a new approach – Meningococcus Vaccine Targets identified through **reverse vaccinology**



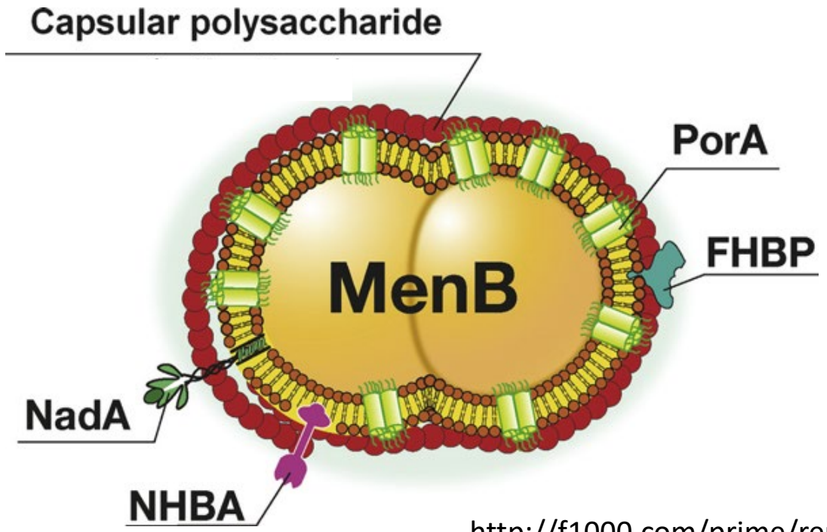
Rino Rappuoli



Vaccines to protect against **endemic disease**

Subcapsular antigens for protection against endemic disease

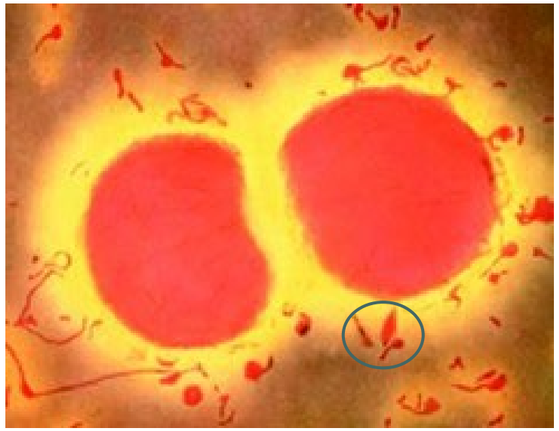
Identification of outer membrane proteins that are **immunogenic, conserved and surface exposed - Reverse vaccinology**

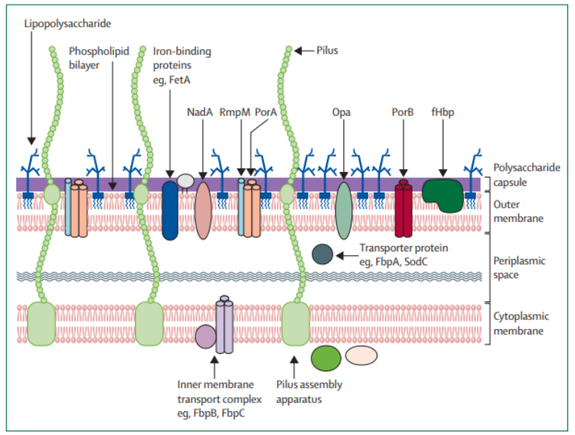


http://f1000.com/prime/reports/m/3/16/fig-002

1. Sadarangani M et al. Lancet Inf Dis 2010; 10:112-24. 2. Caron F et al. Lancet Infect Dis. 2011;11:455-463. 3. Serruto D et a. Vaccine 2012;30(2):B87-B9. 4. Masignani et al. Front in Immunology 2019; 10:751

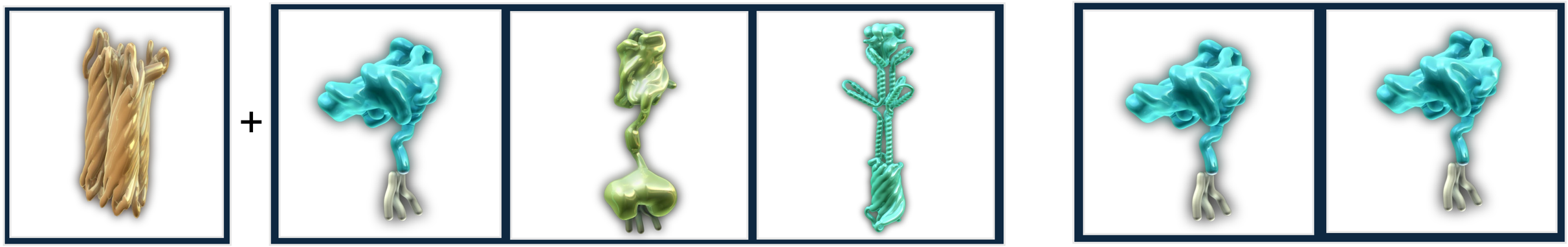
Meningococcal B protein-based vaccines





4CMenB

MenBfHbp



PorA (P1.4) + fHbp + NadA + NHBA

fHbp (subfamily A) fHbp (subfamily B)

OMVs from the New Zealand strain (NZ 98/254)

Three recombinant proteins discovered by reverse vaccinology

Recombinant lipidated factor H binding protein meningococcal serogroup B vaccine

Antigens selected for maximum coverage of extensive antigenic variability of MenB strains

Donnelly J, et al. *Proc Natl Acad Sci U S A*. 2010;107:19490-19495. Sadarangani M et al. Lancet Inf Dis 2010; 10:112-24. Caron F et al. Lancet ID. 2011;11:455-463.

Meningococcal B Vaccines

4CMenB

Licensed in the EU, Australia, Canada, USA

- Use from 6 weeks of age
- OMV + fHBP + NadA + NHBA
- clinical trials in adults, adolescents, toddlers and infants
- Immunogenic with acceptable safety profile in clinical trials

1. Snape M et al. PIDJ 2010;29:e71-9
2. Findlow J. CID 2010;51:1127-37
3. Santolaya ME et al. Lancet 2012;379(9816):617–624
4. Vesikari T et al. Lancet 2013;381(9869):825-35.
5. Gossger N et al. JAMA 2012;307(6):573-82.

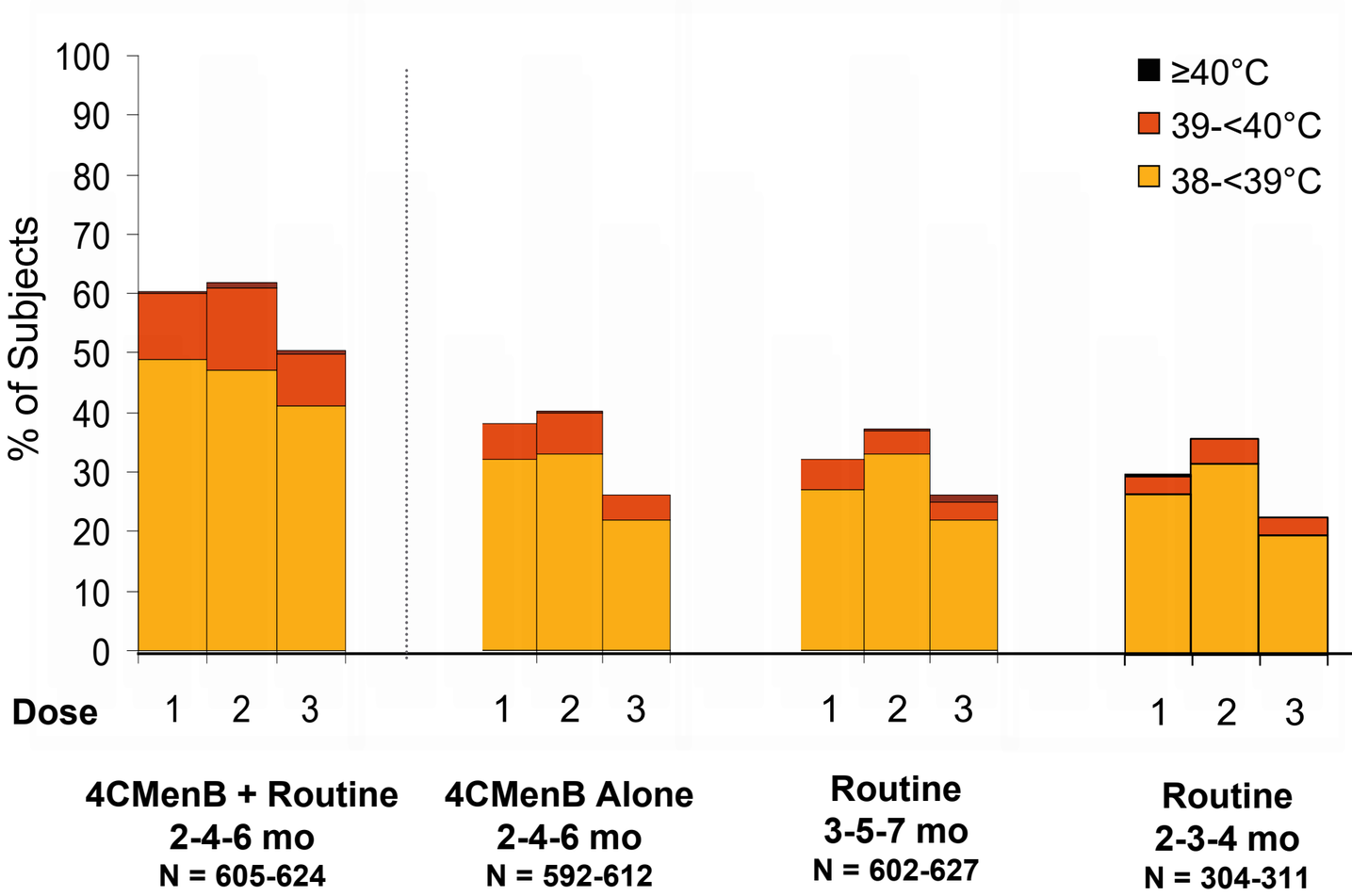
MenB:fHbp

- Licensed in Australia, USA, EU, Canada for ≥ 10 years of age
- fHBP, subfamily A & subfamily B
- Clinical trials in adults, adolescents and toddlers (infant study discontinued)
- Immunogenic with acceptable safety profile in clinical trials

1. Marshall et al. Lancet Infect Dis. 2017
2. Richmond P et al. Lancet Inf Dis 2012;12(8):597–607.
3. Marshall H et al. PIDJ 2012;31(10):1061-68.
4. Marshall H et al. Vaccine 2013;31(12):1569-75.
5. Nissen et al. PIDJ 2013; 32 (4):364-371
6. Martinon-Torres F et al. Vaccine 2014;32:5206-5211

Safety of 4CMenB vaccine in infants

Increased risk of fever with co-administration of routine vaccinations



Safety of multicomponent meningococcal group B vaccine (4CMenB) in routine infant immunisation in the UK: a prospective surveillance study

Philip Bryan, Suzie Seabroke, Jenny Wong, Katherine Donegan, Elizabeth Webb, Charlotte Goldsmith, Caroline Vipond, Ian Feavers

Summary

Background Safety data for the multicomponent meningococcal group B vaccine (4CMenB) has so far been limited to experience from clinical trials and isolated local outbreaks. Since the UK is the first country to implement a nationwide routine immunisation programme with 4CMenB (at age 8 weeks, 16 weeks, and then 1 year), we aimed to assess the safety of 4CMenB in this setting.

Methods In this prospective surveillance study, we assessed suspected adverse reactions of 4CMenB in children up to age 18 months reported in the UK Yellow Card Scheme and primary care records extracted from the Clinical Practice Research Datalink (CPRD). We proactively assessed reports of fever, local reactions, Kawasaki disease, seizures, and sudden death, and compared the number of spontaneous reports with the expected number of events based on background incidence and the number of children vaccinated. We also identified any unexpected adverse reactions and estimated compliance with subsequent doses of routine vaccinations.

Findings From Sept 1, 2015, to May 31, 2017, approximately 1·29 million children aged 2–18 months received about a combined 3 million doses of 4CMenB. 902 reports of suspected adverse reactions were received through the UK Yellow Card Scheme, of which 366 (41%) were related to local reactions and 364 (40%) related to fever. The only unexpected finding was that 160 reports of local reactions described a persistent nodule at the site of injection, usually without other local symptoms. There were 55 (6%) reports of seizures, with an age-adjusted observed-to-expected ratio of 0·13 (95% CI 0·10–0·17). Ecological analyses found similar rates of seizures within 7 days of

Lancet Child Adolesc Health 2018
Published Online
April 24, 2018
http://dx.doi.org/10.1016/S2352-4642(18)30103-2
See Online/Comment
http://dx.doi.org/10.1016/S2352-4642(18)30135-4

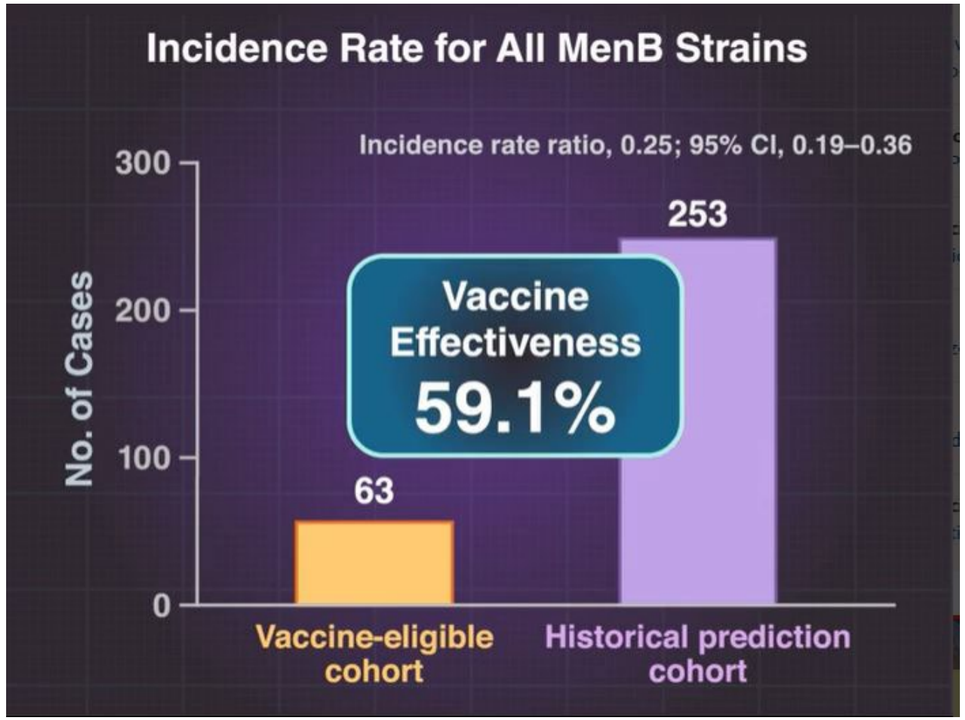
Vigilance and Risk Management of Medicines, Medicines and Healthcare Products Regulatory Agency, London, UK (P Bryan PhD, S Seabroke PhD, J Wong MSc, K Donegan PhD, E Webb BSc, C Goldsmith BSc); and Division of Bacteriology, National Institute for Biological Standards and Control, Hertfordshire, UK (C Vipond PhD, I Feavers PhD)

Prophylactic paracetamol prior to and following 4CMenB vaccination in infants < 2 years

Routine vaccines: Infanrix-hexa, Prevenar

Adapted from Gossger, Snape et al JAMA 2012;307(6):573–582.

Vaccine effectiveness (VE) against diverse MenB strains in a 4CMenB infant population program, UK, from 2015



VE = 59.1% (95%CI -31.1-87.2) 3 doses[1]
Vaccine Impact =75% (95%CI 0.19-0.36) reduction in serogroup B IMD


Irish Independent News Opinion Business Sport Life Style Enter

Life-saving vaccine for babies rolled out after GPs agree fee

Health Minister Simon Harris was 'pleased' to be able to roll out the meningitis B and rotavirus vaccines




Meningitis B vaccine offered to all babies from September

21 June 2015 · Comments





1. Ladhani s et al. NEJM 2020; 382(4): 309-317 2. Parikh SR et al. Lancet 2016;388:2775-82.

4CMenB vaccine coverage predicted by MATS is variable by region

Meningococcal Antigen Typing System (MATS) is a system for assessing panels of region specific meningococcal strains for presence of at least one expressed antigen sufficiently matched to allow killing by vaccine induced antibodies

Prediction based on a proprietary Meningococcal Antigen Typing System

Australia:~76% (95%CI 63–87%) preventable by 4CMenB

Varies by country

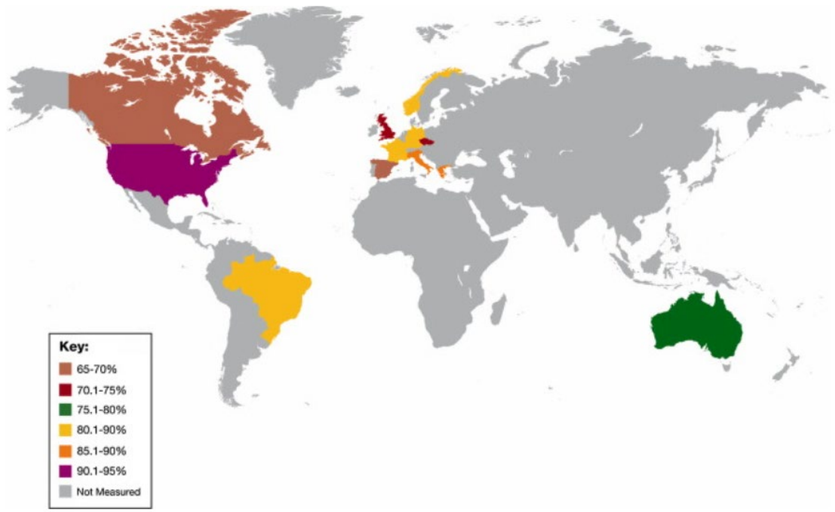


Fig. 4

Global MATS coverage estimates for 4CMenB.

Table 1. Strain coverage predicted by MATS and gMATS, overall and by year of sample collection, state/territory, and the patient's age group.

	N	MATS coverage, % (95% CI)	gMATS coverage, % (LL-UL)
Overall	**520**	**74.6 (61.1–85.6)**	**81.0 (75.0–86.9)**
By year			
2007	108	70.4 (57.4–83.3)	79.2 (74.1–84.3)
2008	119	81.5 (69.7–89.0)	82.8 (76.5–89.1)
2009	103	70.9 (58.2–81.5)	80.1 (75.7–84.5)
2010	93	77.4 (60.2–87.1)	87.6 (81.7–93.5)
2011	97	72.2 (58.8–86.6)	75.3 (67.0–83.5)
By state/territory			
New South Wales & ACT	156	71.8 (54.5–82.0)	78.5 (71.8–85.3)
Northern Territory	4	–*	62.5 (50.0–75.0)
Queensland	141	85.1 (73.0–94.3)	87.2 (84.4–90.1)
South Australia	40	90.0 (90.0–95.0)	93.8 (92.5–95.0)
Tasmania	9	–*	66.7 (66.7–66.7)
Victoria	118	73.7 (56.8–85.6)	80.9 (71.2–90.7)
Western Australia	52	51.9 (42.3–71.1)	65.4 (57.7–73.1)
By age group**			
<1 year	75	64.0 (53.3–74.7)	68.7 (58.7–78.7)
1–<2 years	28	71.4 (64.3–89.3)	76.8 (67.9–85.7)
2–<5 years	30	83.3 (66.7–90.0)	98.3 (96.7–100)
5–29 years	118	80.5 (66.1–91.5)	86.4 (82.2–90.7)
>29 years	68	75.0 (58.8–86.8)	77.9 (72.1–83.8)

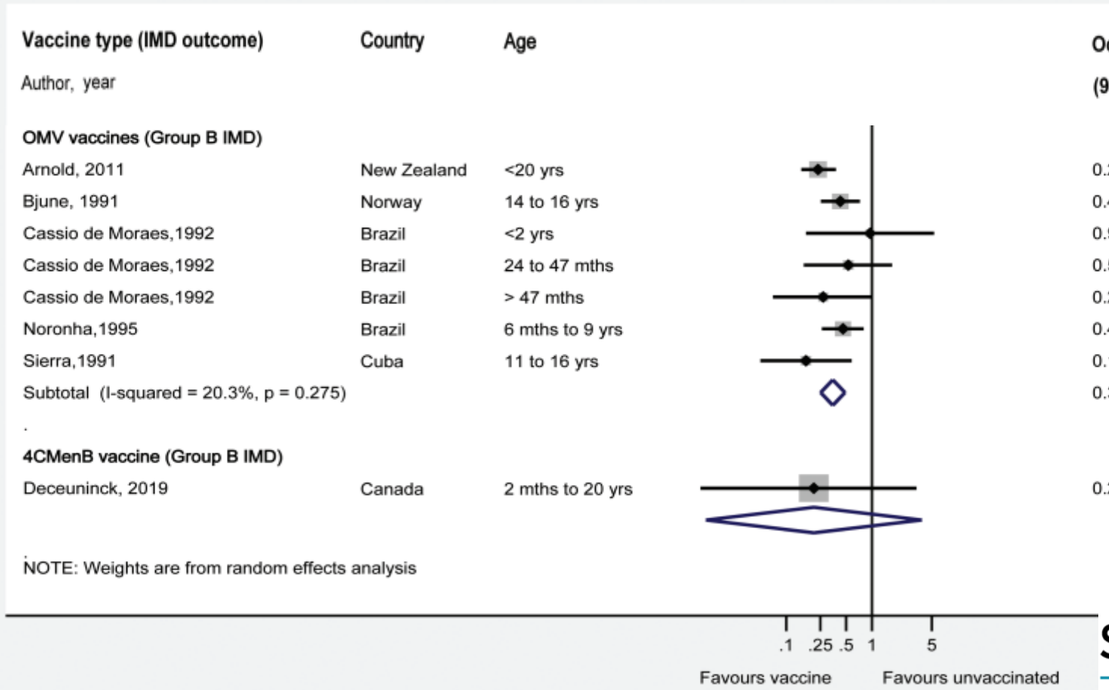
MATS, meningococcal antigen typing system; gMATS, genetic MATS; 4CMenB, 4-component meningococcal serogroup B vaccine; N, number of tested isolates; CI, coverage interval; LL, lower limit; UL, upper limit; ACT, Australian Capital Territory.

Notes: * Not calculated, due to the small number of strains isolated.

** The age of the patient from whom the sample was collected was only documented for 319 of the total 520 strains.

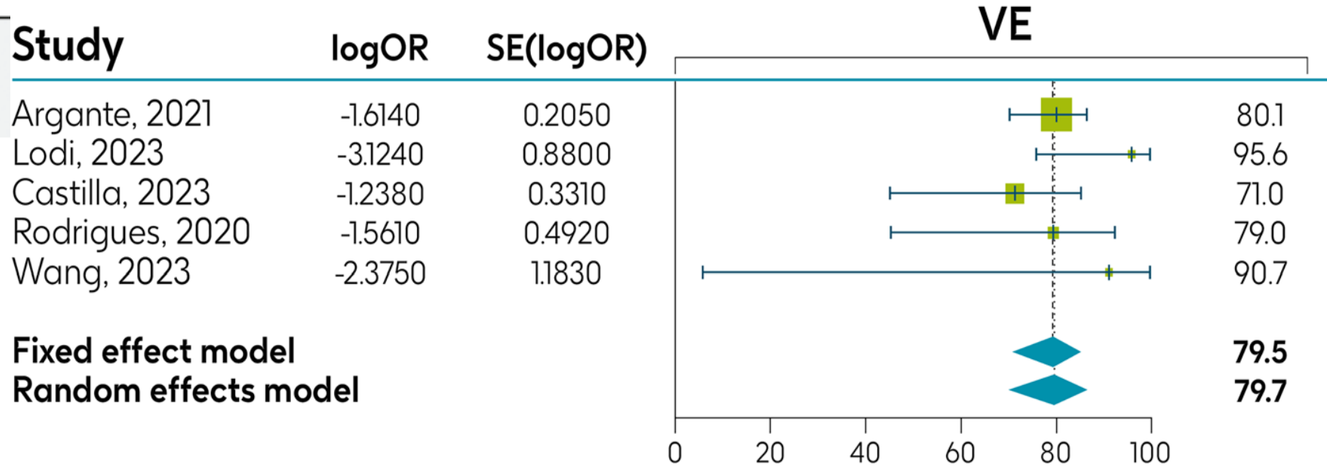
1. Medini et al. *Vaccine* 2015;33:2629-2636 2. Tozer S et al. Human vaccines and immunotherapeutics 2021;17(9):3230-3238

MenB OMV vaccines are highly effective in reducing IMD in population programs



OMV vaccines against MenB disease
VE=65% OR=0.35 (95%CI 0.20-0.49)[1]

4CMenB against MenB disease[2]
VE=79.7% (95%CI 70.4-86.1)



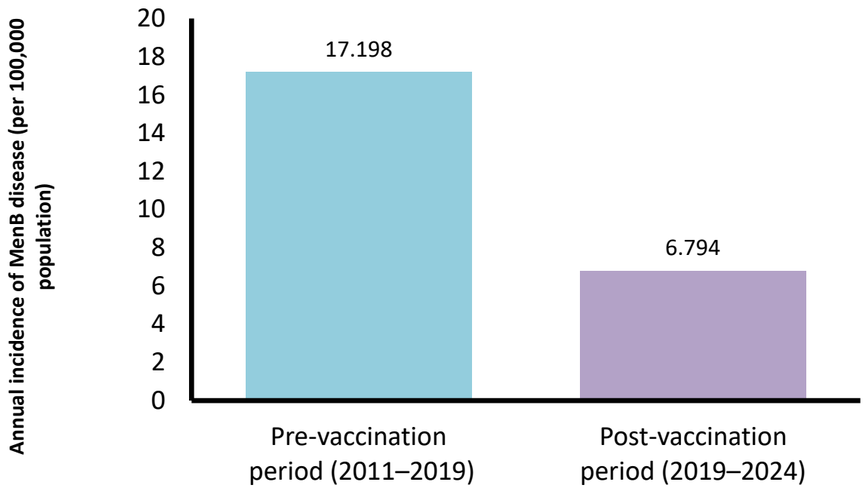
1. McMillan et al. CID 2021;73(3):e609–19. 2. Marijic et al. npj vaccines 2026;11:153

Long term 4CMenB vaccine impact and effectiveness against MenB disease in **children** in South Australia 5 years post-program implementation[1]

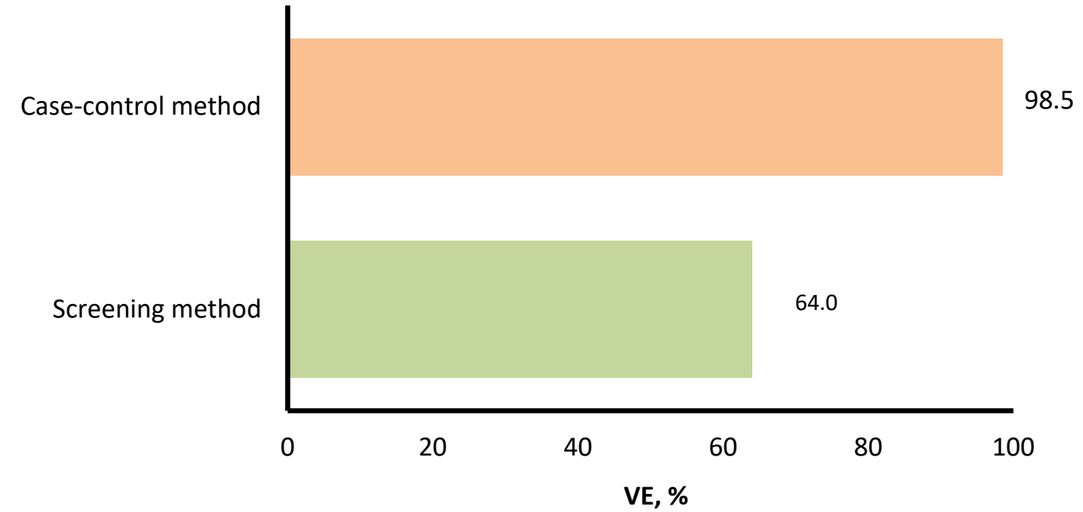


Bing Wang

Incidence of MenB Disease in infants aged < 1 year years: before and 5 years after program implementation



Two-dose VE 5 years after program implementation



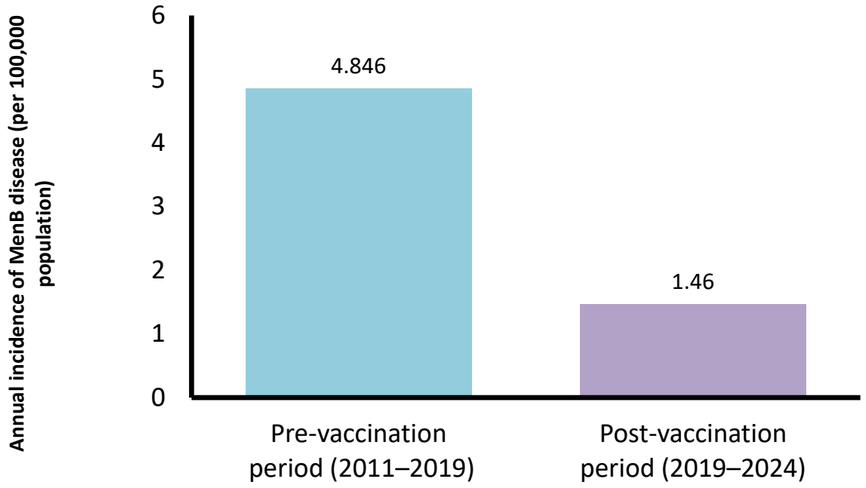
In infants, 5 years after program implementation (3 doses):

- **72.7%** (aIRR: 0.273; 95% CI: 0.120–0.620) **reduction in the incidence of MenB disease**
- **98.5%** (95% CI 81.9-99.9%) **VE of 4CMenB against MenB disease**

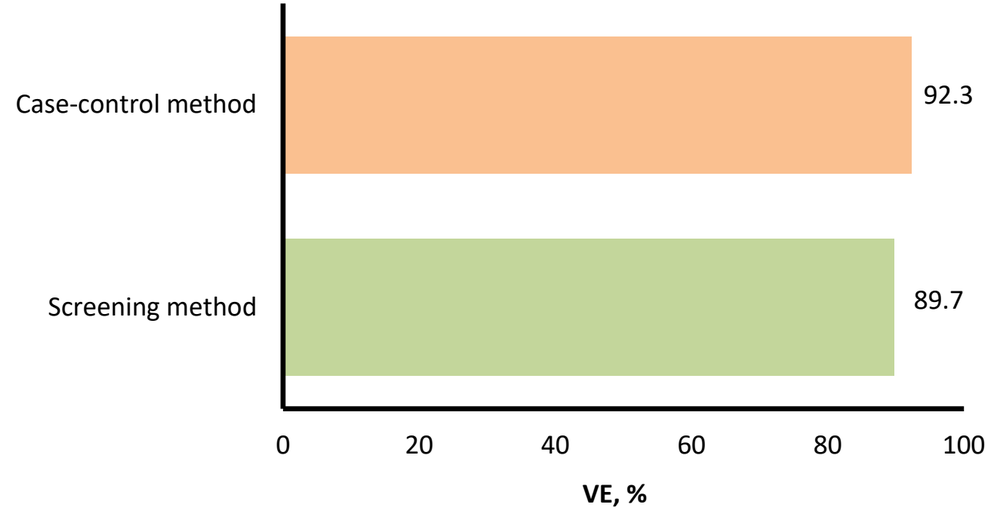
At 7 years VE=57.3% (95%CI: -39.9% to 86.9%; p=0.160)

4CMenB vaccine impact and effectiveness against MenB disease in **adolescents** in South Australia 5 years post-program implementation[1]

Incidence of MenB Disease in adolescents aged 15–18 years: before and 5 years after program implementation



Two-dose VE 5 years after program implementation



In adolescents, 5 years after program implementation:

- **76.2%** (aIRR: 0.238; 95% CI: 0.097–0.584) **reduction in the incidence of MenB disease**
- **92.3%** (95% CI 34.4-99.1%) **VE of 4CMenB against MenB disease**

At 7 years VE=85.4% (95%CI: 48.0% to 95.9%; p=0.003)

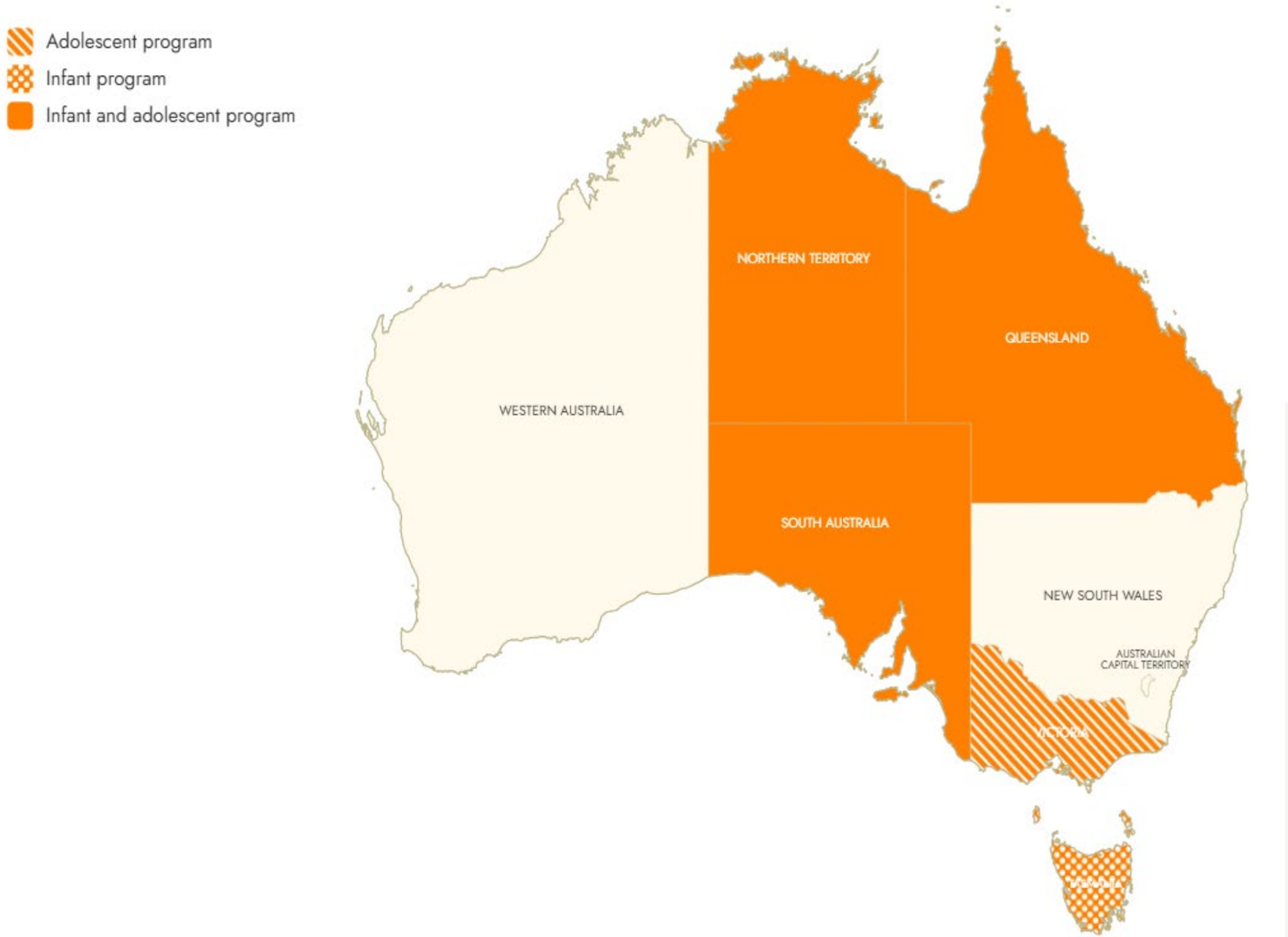
MenB vaccine programs in Australia

4CMenB

National Immunisation Program for Aboriginal and Torres Strait Islander infants

State programs

- ~regional epidemiology
- advocacy
- ~50% of the infant and adolescent population



https://studio.ultimaps.com/editor?create=australia

National Immunisation Program Schedule; Dept. of Health Disability and Ageing, Australian Government https://www.health.gov.au/sites/default/files/2026-06/national-immunis ation-program-schedule.pdf 2. Australian Immunisation Handbook https://immunisationhandbook.health.gov.au/contents/vaccine-preventable-diseases/meningococcal-disease.

4CMenB strain coverage against non-MenB strains due to expression of OMPs in other serogroups

Serogroup	No. of strains	Percentage (95% CI)
C	50	64.0 (46.0, 86.0)
W-135	27	63.0 (40.7, 92.6)
Y	30	36.7 (26.7, 43.3)

Australian meningococcal non-B strains expressing 4CMenB Antigens in MATS

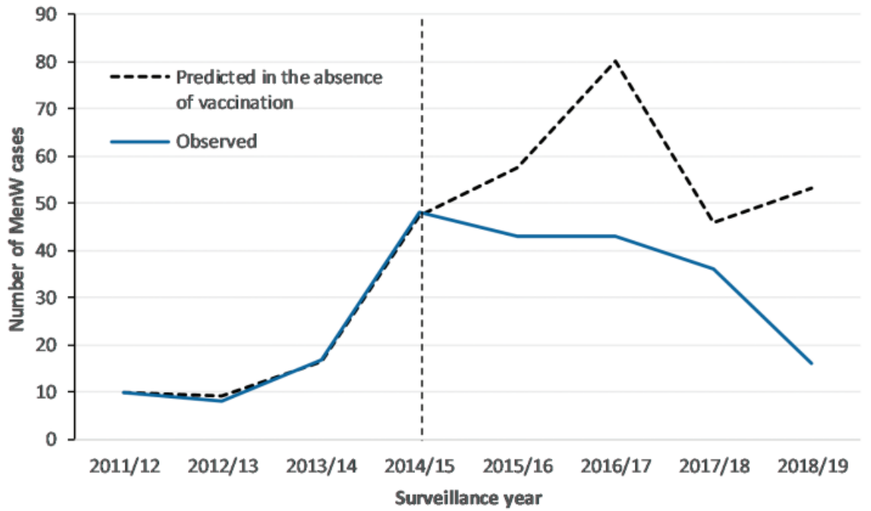


Figure 2. Observed MenW cases* in children under 5 years and predicted cases based on MenW disease trends in unvaccinated childhood cohorts aged ≤12 years in England during 2011/2012 to 2018/2019 surveillance years (September through August). *There were 679 000 children in each age group of 0, 1, 2, 3, and 4 years, so 10 cases would represent an incidence of 14.7 per million; similarly, there were 5.20 million children aged 5–12 years, so 10 cases would represent an incidence of 1.9 per million. Abbreviation: MenW, meningococcal group W.

Impact of 4CMenB vaccine on serogroup W in the UK

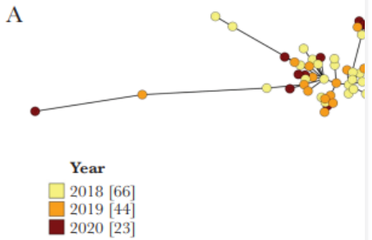
1. Tozer S. et.al. IPNC Wurtzberg, Germany 2012 2. Ladhani et al Clinical Infectious Diseases 2021;73(7):e1661–8

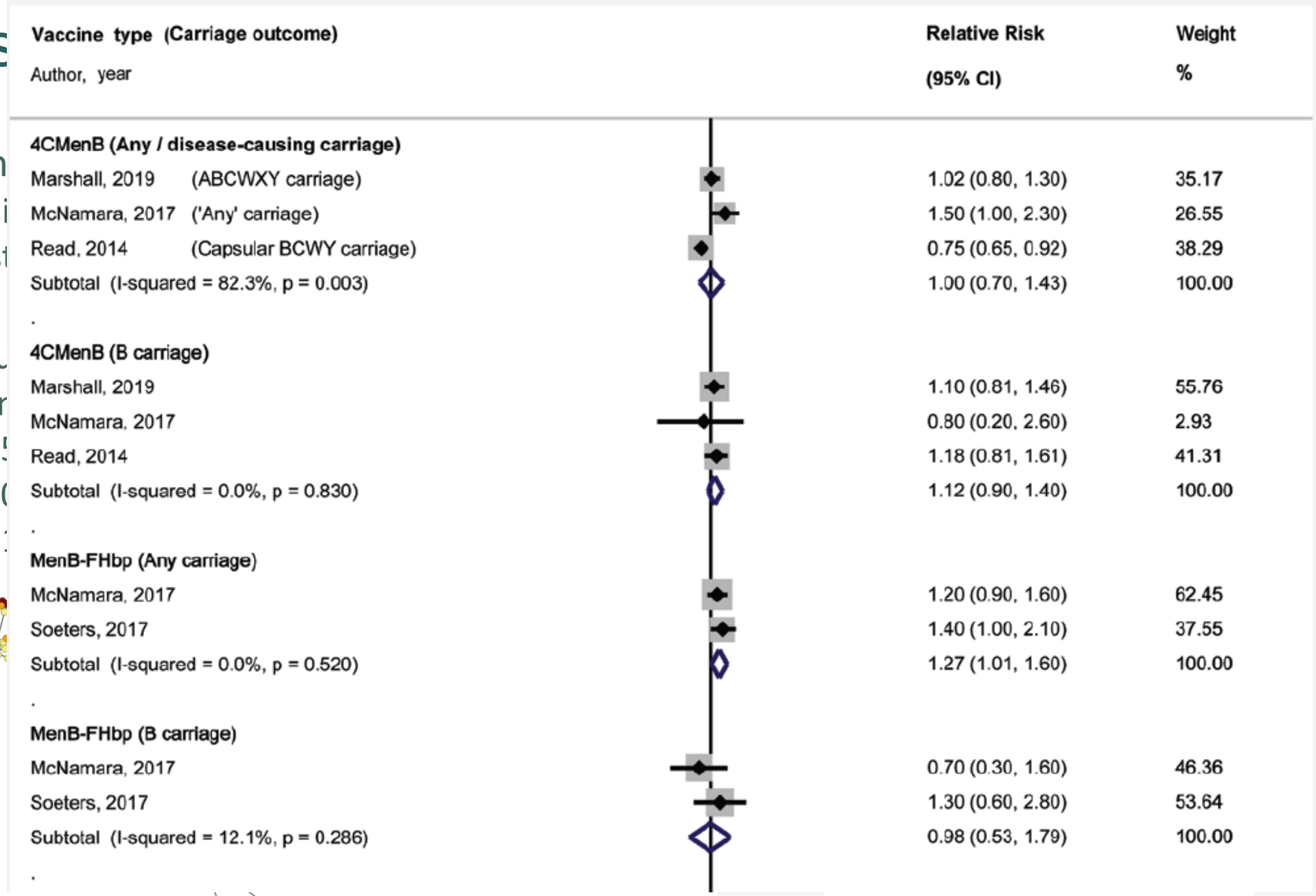
No impact … al strains ass…

21st International Pathogenic Neisseria Conference
September 23 – 28, 2018
IPNC 2018
Asilomar, California

MenB impact on …
- No short-term i… carriage in clust…

School leaver stu…
- No long-term ir…
  - Year 1 - 5.5…
  - Year 2 - 5.(…
  - year 3 - 5.…





	aOR (95% CI)
3	0.85 (0.70, 1.04)
3	1.02 (0.8, 1.31)
3	1.10 (0.81, 1.47)
3	0.81 (0.56, 1.18)
5	0.89 (0.43, 1.85)
5	1.87 (0.63, 5.55)
5	-

95% CI	ap-value
.54, 0.91)	0.008

Dr McMillan



1. Marshall H et al. NEJM 2020;382:318-27. 2. McMillan et al. IID 2022;225(4):637-649 3. McMillan et al. CID 2021;73(3):e609–19

Next generation pentavalent meningococcal vaccines

ABCWY – licensed in the US (Pfizer, GSK)

Vaccine

journal homepage: www.elsevier.com/locate/vacci

Breadth of coverage against a panel of 110 invasive disease immunogenicity and safety for 2 and 3 doses of an investig MenABCWY vaccine in US adolescents – Results from a ranc controlled, observer-blind phase II study

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Neisseria meningitidis
MenABCWY
Meningococcal vaccine

ABSTRACT

Background: Neisseria meningitidis serogroups A, B, C, W and Y wide. An investigational MenABCWY vaccine combining ser ACWY CRM_{197}-glycoconjugate vaccine (MenACWY-CRM) co ogroups. Complement mediated bactericidal activity induced of 110 randomly-selected serogroup B strains causing invasive breadth of coverage (BoC).

Methods: We conducted this observer-blind study (NCT02140762) and its extension (NCT02285777) in 8 centers in the US. Adolescents aged 10–18 years were randomized (1:1) to receive either 3 MenABCWY doses (MenABCWY group), on a 0, 2, 6-month (M) schedule or a single MenACWY-CRM dose at M2 and

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Immunogenicity and safety of a pentavalent meningococcal ABCWY vaccine in adolescents and young adults: an observer-blind, active-controlled, randomised trial

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Summary

Background Meningococcal serogroups A, B, C, W, and Y cause nearly all meningococcal disease, and comprehensive protection requires vaccination against all five serogroups. We aimed to assess the immunogenicity and safety of a pentavalent MenABCWY vaccine comprising two licensed vaccines—meningococcal serogroup B-factor H binding protein vaccine (MenB-FHbp) and a quadrivalent meningococcal serogroup ACWY tetanus toxoid conjugate vaccine (MenACWY-TT)—compared with two doses of MenB-FHbp and a single dose of quadrivalent meningococcal serogroup ACWY CRM_{197}-conjugate vaccine (MenACWY-CRM) as the active control. We previously reported the primary safety and immunogenicity data relating to the two-dose MenB-FHbp schedule. Here we report secondary outcomes and ad-hoc analyses relating to MenABCWY immunogenicity and safety.

ACWYX – other potential pentavalent vaccines

Safety and immunogenicity of a pentavalent meningococcal conjugate vaccine versus a quadrivalent meningococcal conjugate vaccine in adults in India: an observer-blind, mised, active-controlled, phase 2/3 study

rni, Anand Kawade, Sunil Kohli, Renuka Munshi, Chetna Maliye, Nithya J Gogtay, Ravish H S, Kiranjit Singh, K Vengadakrishnan, r Panigrahi, Jyotiranjan Sahoo, Ashish Bavdekar, B S Garg, Abhishek Raut, Jeffrey P Raj, Unnati Saxena, Vijaya L Chaudhari, pari Venkatarao, Nitu Kumari, Jithin Surendran, Varsha Parulekar, Luc Gagnon, Tania Gensale, Abhijeet Dharmadhikari, ameer Kale, Sambhaji S Pisal, Rajeev M Dhere, Asha Mallya, Cyrus S Poonawalla, Dhananjay Kapse

Meningococcal disease remains an important public health problem globally. We assessed the non- nd the lot-to-lot consistency of a pentavalent meningococcal ACYWX conjugate vaccine (NmCV-5; Serum India, Pune, India) versus a quadrivalent meningococcal ACWY conjugate vaccine (MenACWY-D) in lts.

this observer-blind, randomised, active-controlled, phase 2/3 study, healthy adults aged 18–85 years were om nine hospitals across seven cities in India. Participants were grouped by age (age 18–29, 30–60, and), and within each age group they were randomly assigned (3:1) to receive either NmCV-5 or MenACWY-D eur). In the age 18–29 years group, participants were additionally randomly assigned (1:1:1:1) to either lot lot C of NmCV-5 or MenACWY-D. Block randomisation was used (block sizes of 4, 8, and 12). Study and study personnel were masked to treatment assignment. Participants received either a 0·5 mL dose of ntaining 5 µg each of conjugated A, C, W, Y, and X polysaccharides, or 0·5 mL MenACWY-D, containing h of conjugated A, C, W, and Y polysaccharides. Vaccinations were administered intramuscularly in the scle. The primary outcomes were seroresponse (non-inferiority margin of –10%) and geometric mean s; non-inferiority margin of 0·5) in all participants, and lot-to-lot consistency of NmCV-5 (in participants years; consistency was shown if the geometric mean ratio [GMR] 95% CIs were within the limit interval For non-inferiority, serogroup X immune response in the NmCV-5 group was compared with the lowest sponse among serogroups A, C, W, and Y in the MenACWY-D group. Immunogenicity was assessed with ctericidal activity assay that used baby rabbit serum as the complement (rSBA) on days 1 and 29 in the er-protocol population (including all participants who were randomly assigned, received vaccine, had a tion rSBA measurement up to 121 days after vaccination, and no major protocol violations). Solicited collected for 7 days and serious adverse events were collected for 180 days, and assessed in the safety population (all participants who received vaccination). This study is registered with ClinicalTrials.gov, NCT04358731, and CTRI, CTRI/2019/12/022436, and is now complete.

Findings Between Dec 27, 2019, and Sept 19, 2020, 1712 individuals were screened, of whom 1640 were randomly assigned and received NmCV-5 (n=1233) or MenACWY-D (n=407; mean age 26·4 years [SD 12·2], 551 [33·6%] of 1640 were female, and 1089 [66·4%] were male). 1441 participants were aged 18–29 years (362 received lot A, 360 received lot B, and 361 received lot C of NmCV-5 and 357 received MenACWY-D, with one participant mis-randomised by age group and excluded from lot-to-lot consistency analysis). Non-inferiority of NmCV-5 against MenACWY-D was met in terms of seroresponse rates and GMT ratios for all five serogroups. The seroresponse rates were 84·3% (97·5% CI 81·7 to 86·7; serogroup A) or higher in the NmCV-5 group and 54·5% (48·5 to 60·3; serogroup A) or higher in the MenACWY-D group, with the difference in the seroresponse rate between vaccine groups ranging from 0·2 (97·5% CI –2·2 to 2·6) for serogroup W to 29·8 (24·4 to 35·2) for serogroup A. GMTs on day 29 were 7016·9 (97·5% CI 6475·7 to 7603·4; serogroup Y) or higher in the NmCV-5 group and 3646·8 (3188·2 to 4171·5; serogroup Y) or higher in the

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neiscre.com.au

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