Off target protection of MenB-OMV vaccines against *Neisseria gonorrhoea*

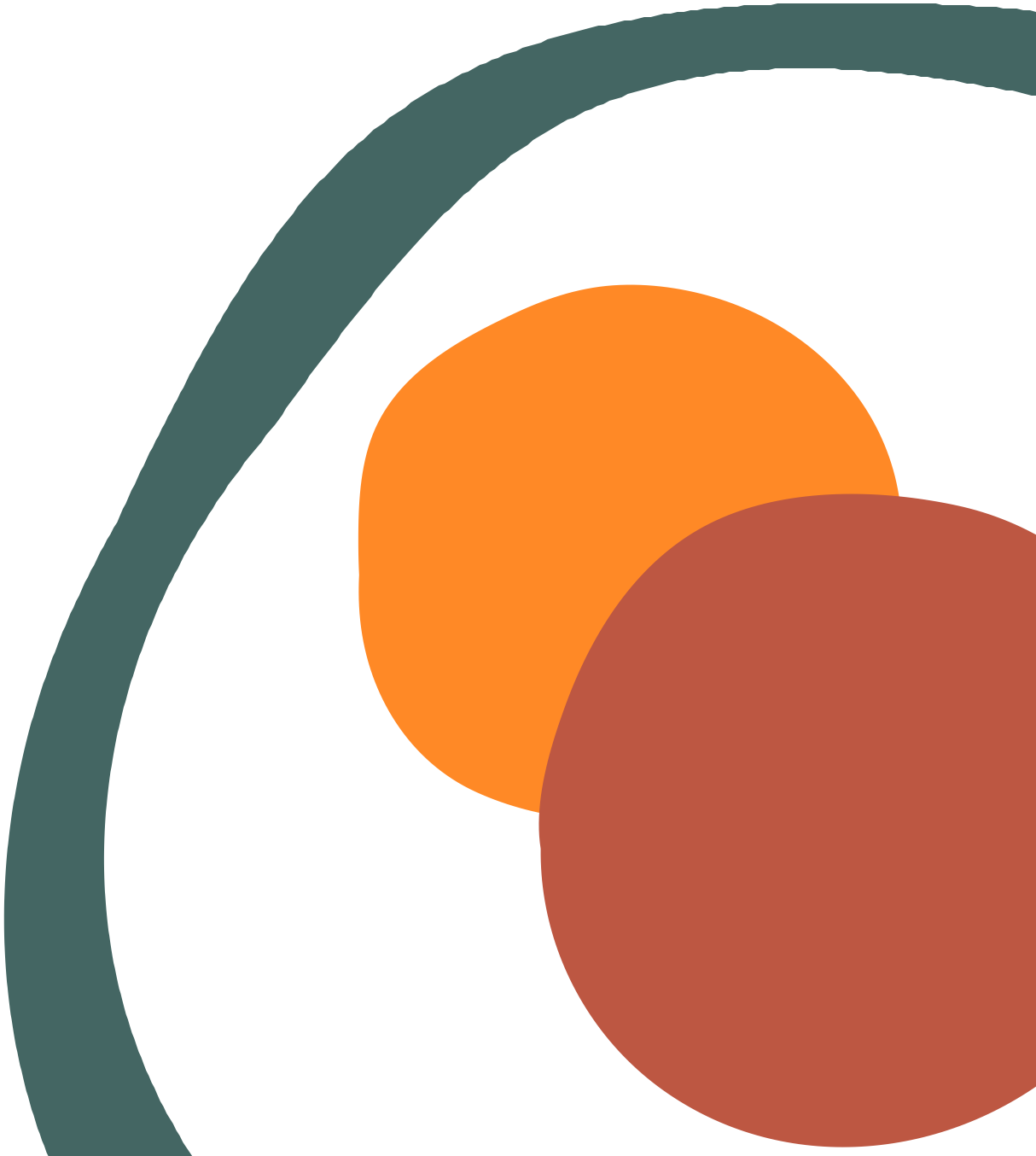
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neis CRE Centre for Research Excellence in Neisseria disease control

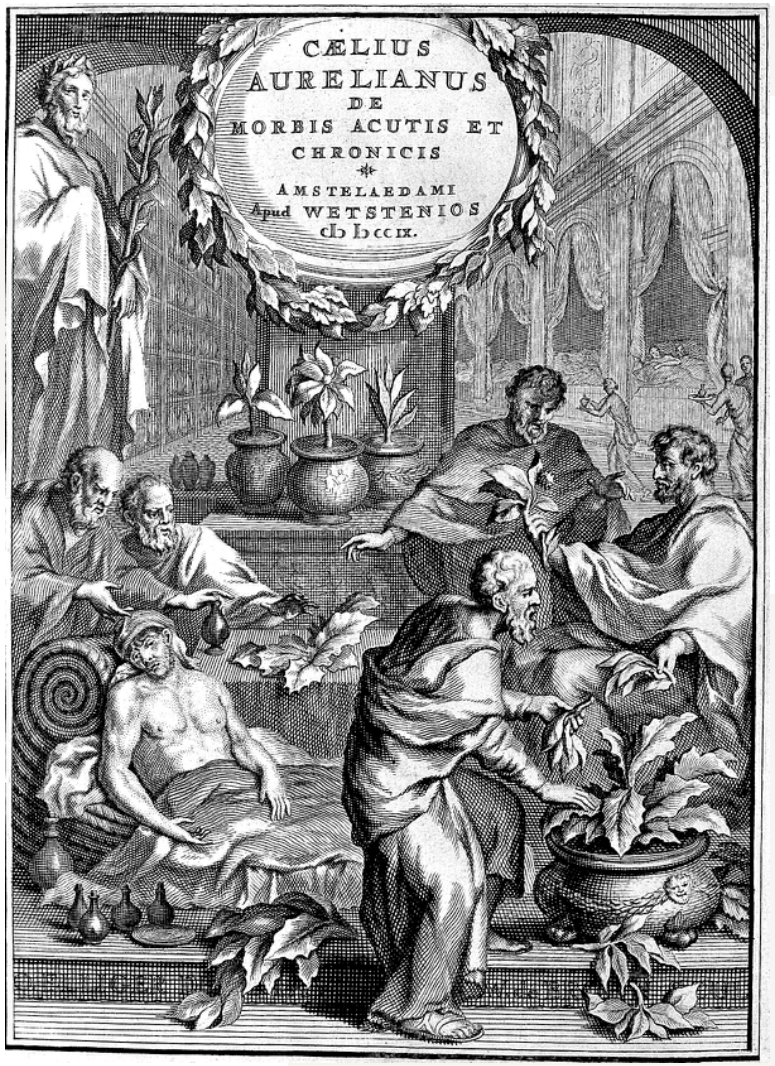
Adelaide University

IPNC 2026



Gonorrhoea

- One of the oldest sexually transmitted infections in human history, at least 3500 years ago
- Roman physician Galen described the disease as an “involuntary escape of semen”
- Derived from the Greek meaning “the flow of seed” *There is an involuntary, permanent flow of seed without pleasure*
- Predominance of description in relation to men (implication was females were not affected) showing the hidden burden for women with most disease asymptomatic resulting in scarring and infertility
- Fall of civilisations such as the Roman Empire were due to infertility in rulers which may have resulted from gonorrhoea



Caelius Aurelianus, *De morbis acutis & chronicis.* Amstelaedami, ex officina Wetsteniana, 1709.

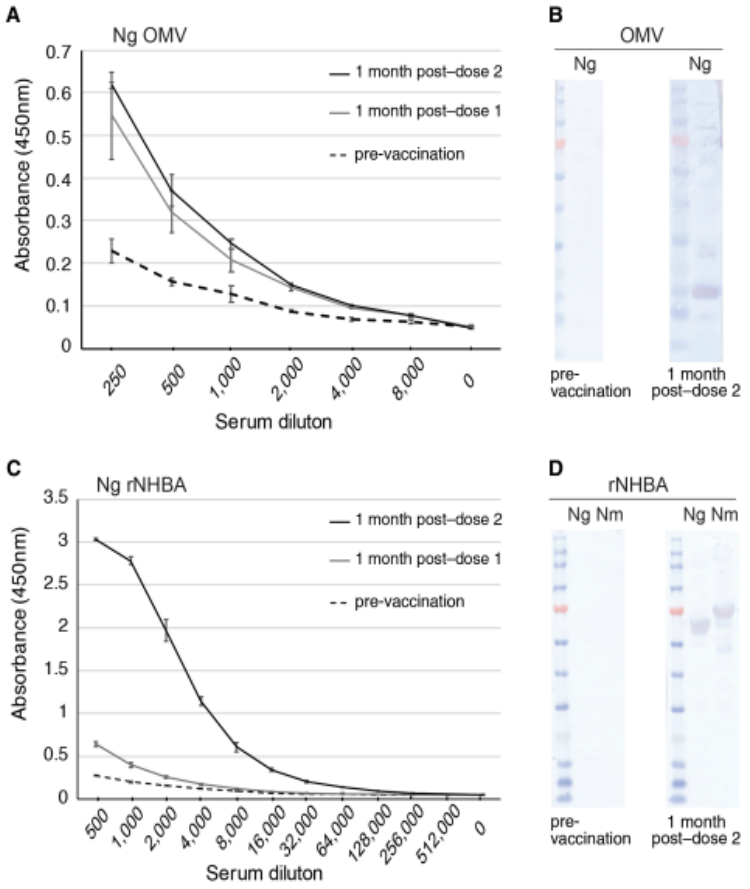
1. Chiara Beatrice Vicentini et al. Le Infezioni in Medicina, 2019; 2, 212-221. 2. The hidden affliction. edited by Simon Szeter 2019

MenB vaccine cross protection against gonorrhoea



Evgeny Semchenko

- 80-90% genetic homology between *N. meningitidis* and *N. gonorrhoeae*[1]
- MenB-OMV vaccines showed a post vaccine program reduction in gonorrhoea [2] [3]
- 4CMenB vaccine induced antibodies have been shown to recognise gonococcal proteins [1]
- reduction in carriage of unencapsulated meningococci in the vaccinated group[5]
  - vaccine-type outer membrane proteins are potentially more exposed without a capsule
  - the gonococcus is an unencapsulated Neisseria bacteria
- proteins targeted by 4CMenB vaccine expressed on *N. meningitidis* as well as *N. gonorrhoeae (*OMV, NHBA) and have high homology [4]



1. Semchenko EA et al. CID 2019;69(7):1101-11 2. Petousis-Harris H et al. Lancet 2017;390:1603-1610. 3. Wang B et al. JID 2023;87(2):95-102. 4. Marshall H et al. NEJM 2020;382(4):318-327

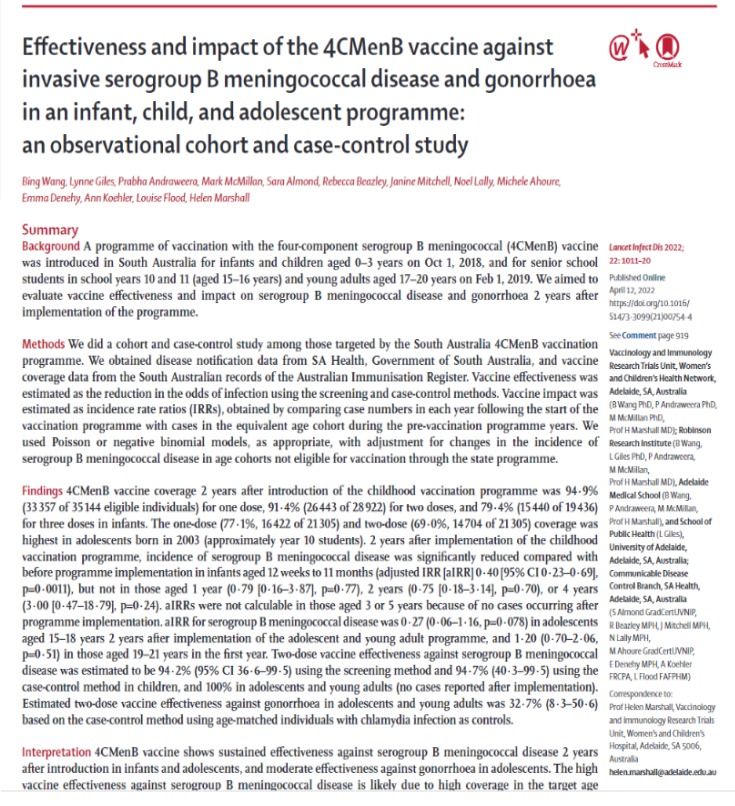
Moderate effectiveness of 4CMenB against gonorrhoea at 2 years post 4CMenB vaccine introduction

Previous evidence of VE against gonorrhoea with OMV vaccines

- MenB-OMV vaccines showed a post vaccine program reduction in gonorrhoea in Cuba
- MeNZB vaccine showed VE=31%[1]

Cohort and case control study in SA assessing effect of 4CMenB against gonorrhoea [2]

- Population: 15-20 yr olds in SA, 2 years post-introduction of 4CMenB
- VI=24% (aIRR=0.76 (0.48, 1.22) reduction in gonorrhoea incidence
- VE=33% (8.3, 50.6) against gonorrhoea



Effectiveness and impact of the 4CMenB vaccine against invasive serogroup B meningococcal disease and gonorrhoea in an infant, child, and adolescent programme: an observational cohort and case-control study

Bing Wang, Lynne Giles, Prabha Andraweera, Mark McMillan, Sara Almond, Rebecca Beazley, Janine Mitchell, Noel Lally, Michele Ahoure, Emma Denehy, Ann Koehler, Louise Flood, Helen Marshall

Summary

Background A programme of vaccination with the four-component serogroup B meningococcal (4CMenB) vaccine was introduced in South Australia for infants and children aged 0–3 years on Oct 1, 2018, and for senior school students in school years 10 and 11 (aged 15–16 years) and young adults aged 17–20 years on Feb 1, 2019. We aimed to evaluate vaccine effectiveness and impact on serogroup B meningococcal disease and gonorrhoea 2 years after implementation of the programme.

Methods We did a cohort and case-control study among those targeted by the South Australia 4CMenB vaccination programme. We obtained disease notification data from SA Health, Government of South Australia, and vaccine coverage data from the South Australian records of the Australian Immunisation Register. Vaccine effectiveness was estimated as the reduction in the odds of infection using the screening and case-control methods. Vaccine impact was estimated as incidence rate ratios (IRRs), obtained by comparing case numbers in each year following the start of the vaccination programme with cases in the equivalent age cohort during the pre-vaccination programme years. We used Poisson or negative binomial models, as appropriate, with adjustment for changes in the incidence of serogroup B meningococcal disease in age cohorts not eligible for vaccination through the state programme.

Findings 4CMenB vaccine coverage 2 years after introduction of the childhood vaccination programme was 94·9% (33 357 of 35 144 eligible individuals) for one dose, 91·4% (26 443 of 28 922) for two doses, and 79·4% (15 440 of 19 436) for three doses in infants. The one-dose (77·1%, 16 422 of 21 305) and two-dose (69·0%, 14 704 of 21 305) coverage was highest in adolescents born in 2003 (approximately year 10 students). 2 years after implementation of the childhood vaccination programme, incidence of serogroup B meningococcal disease was significantly reduced compared with before programme implementation in infants aged 12 weeks to 11 months (adjusted IRR [aIRR] 0·40 [95% CI 0·23–0·69], p=0·0011), but not in those aged 1 year (0·79 [0·16–3·87], p=0·77), 2 years (0·75 [0·18–3·14], p=0·70), or 4 years (3·00 [0·47–18·79], p=0·24). aIRRs were not calculable in those aged 3 or 5 years because of no cases occurring after programme implementation. aIRR for serogroup B meningococcal disease was 0·27 (0·06–1·16, p=0·078) in adolescents aged 15–18 years 2 years after implementation of the adolescent and young adult programme, and 1·20 (0·70–2·06, p=0·51) in those aged 19–21 years in the first year. Two-dose vaccine effectiveness against serogroup B meningococcal disease was estimated to be 94·2% (95% CI 36·6–99·5) using the screening method and 94·7% (40·3–99·5) using the case-control method in children, and 100% in adolescents and young adults (no cases reported after implementation). Estimated two-dose vaccine effectiveness against gonorrhoea in adolescents and young adults was 32·7% (8·3–50·6) based on the case-control method using age-matched individuals with chlamydia infection as controls.

Interpretation 4CMenB vaccine shows sustained effectiveness against serogroup B meningococcal disease 2 years after introduction in infants and adolescents, and moderate effectiveness against gonorrhoea in adolescents. The high vaccine effectiveness against serogroup B meningococcal disease is likely due to high coverage in the target age

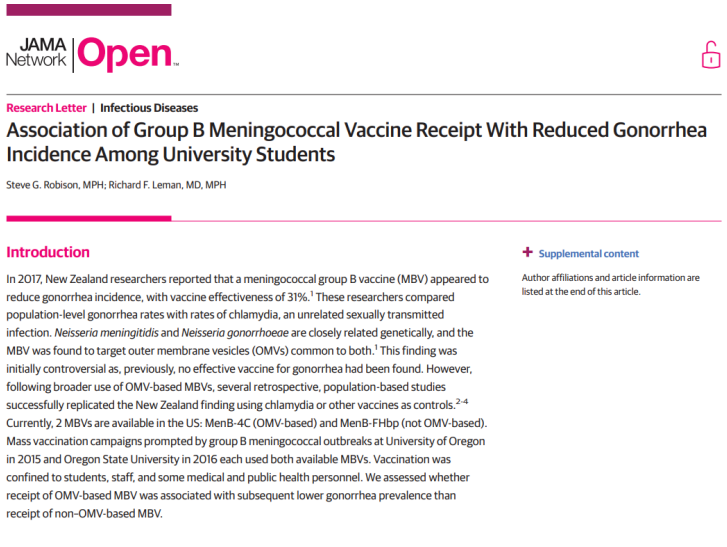
Lancet Infect Dis 2022; 22: 1011–20
Published Online April 12, 2022 https://doi.org/10.1016/S1473-3099(21)00754-4
See Comment page 919

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There is currently no indication for 4CMenB to be used for protection against gonorrhoea

1. Petousis-Harris H. et al Lancet 2017;390:1603-1610. 2. Wang B, Marshall H Lancet ID 2022;22(7):1011-20

Global real-world evidence for a moderate effectiveness of 4CMenB against gonorrhoea



JAMA Network Open

Research Letter | Infectious Diseases

Association of Group B Meningococcal Vaccine Receipt With Reduced Gonorrhea Incidence Among University Students

Steve G. Robison, MPH; Richard F. Leman, MD, MPH

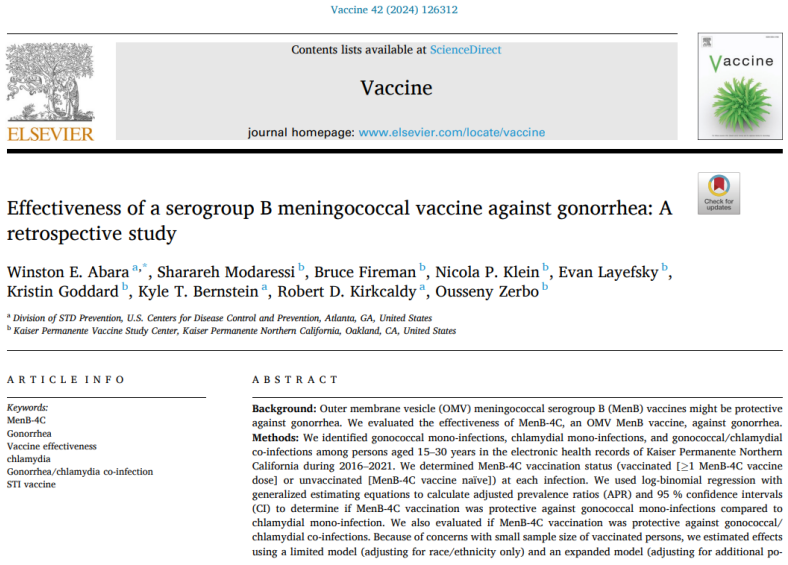
Introduction

In 2017, New Zealand researchers reported that a meningococcal group B vaccine (MBV) appeared to reduce gonorrhea incidence, with vaccine effectiveness of 31%.[1] These researchers compared population-level gonorrhea rates with rates of chlamydia, an unrelated sexually transmitted infection. *Neisseria meningitidis* and *Neisseria gonorrhoeae* are closely related genetically, and the MBV was found to target outer membrane vesicles (OMVs) common to both.[1] This finding was initially controversial as, previously, no effective vaccine for gonorrhea had been found. However, following broader use of OMV-based MBVs, several retrospective, population-based studies successfully replicated the New Zealand finding using chlamydia or other vaccines as controls.[2-4] Currently, 2 MBVs are available in the US: MenB-4C (OMV-based) and MenB-FHbp (not OMV-based). Mass vaccination campaigns prompted by group B meningococcal outbreaks at University of Oregon in 2015 and Oregon State University in 2016 each used both available MBVs. Vaccination was confined to students, staff, and some medical and public health personnel. We assessed whether receipt of OMV-based MBV was associated with subsequent lower gonorrhea prevalence than receipt of non–OMV-based MBV.

+ Supplemental content

Author affiliations and article information are listed at the end of this article.

- 18-19 year olds,
- 4CMenB and MenBfhbp available
- 4CMenB VE= 47% (95% CI, 13%-68%) effective in preventing gonorrhea among recipients aged 18 to 29 years
- University Oregon, USA



Vaccine 42 (2024) 126312

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

Effectiveness of a serogroup B meningococcal vaccine against gonorrhea: A retrospective study

Winston E. Abara [a,*], Sharareh Modaressi [b], Bruce Fireman [b], Nicola P. Klein [b], Evan Layefsky [b], Kristin Goddard [b], Kyle T. Bernstein [a], Robert D. Kirkcaldy [a], Ousseny Zerbo [b]

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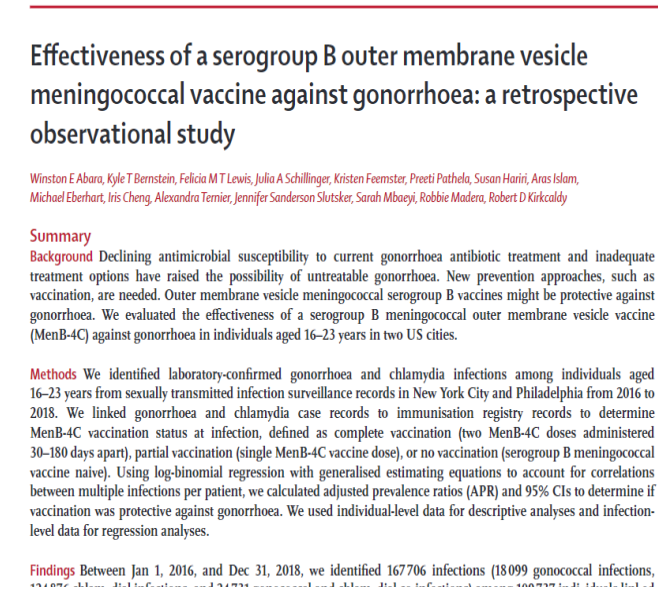
ARTICLE INFO

Keywords:
MenB-4C
Gonorrhea
Vaccine effectiveness
chlamydia
Gonorrhea/chlamydia co-infection
STI vaccine

ABSTRACT

Background: Outer membrane vesicle (OMV) meningococcal serogroup B (MenB) vaccines might be protective against gonorrhea. We evaluated the effectiveness of MenB-4C, an OMV MenB vaccine, against gonorrhea. **Methods:** We identified gonococcal mono-infections, chlamydial mono-infections, and gonococcal/chlamydial co-infections among persons aged 15–30 years in the electronic health records of Kaiser Permanente Northern California during 2016–2021. We determined MenB-4C vaccination status (vaccinated [≥1 MenB-4C vaccine dose] or unvaccinated [MenB-4C vaccine naïve]) at each infection. We used log-binomial regression with generalized estimating equations to calculate adjusted prevalence ratios (APR) and 95 % confidence intervals (CI) to determine if MenB-4C vaccination was protective against gonococcal mono-infections compared to chlamydial mono-infection. We also evaluated if MenB-4C vaccination was protective against gonococcal/chlamydial co-infections. Because of concerns with small sample size of vaccinated persons, we estimated effects using a limited model (adjusting for race/ethnicity only) and an expanded model (adjusting for additional po-

- N= 68,454 persons, 15-30 yrs
- 0.8 % received MenB-4C vaccinated persons with13,000 gonococcal mono-infections, 68,008 chlamydial mono-infections
- 4CMenB aVE=23 % protective against gonococcal mono-infection compared to chlamydial mono-infection.
- Kaiser Permanente, California, **USA**



Effectiveness of a serogroup B outer membrane vesicle meningococcal vaccine against gonorrhoea: a retrospective observational study

Winston E Abara, Kyle T Bernstein, Felicia M T Lewis, Julia A Schillinger, Kristen Feemster, Preeti Pathela, Susan Hariri, Aras Islam, Michael Eberhart, Iris Cheng, Alexandra Ternier, Jennifer Sanderson Slutsker, Sarah Mbaeyi, Robbie Madera, Robert D Kirkcaldy

Summary

Background Declining antimicrobial susceptibility to current gonorrhoea antibiotic treatment and inadequate treatment options have raised the possibility of untreatable gonorrhoea. New prevention approaches, such as vaccination, are needed. Outer membrane vesicle meningococcal serogroup B vaccines might be protective against gonorrhoea. We evaluated the effectiveness of a serogroup B meningococcal outer membrane vesicle vaccine (MenB-4C) against gonorrhoea in individuals aged 16–23 years in two US cities.

Methods We identified laboratory-confirmed gonorrhoea and chlamydia infections among individuals aged 16–23 years from sexually transmitted infection surveillance records in New York City and Philadelphia from 2016 to 2018. We linked gonorrhoea and chlamydia case records to immunisation registry records to determine MenB-4C vaccination status at infection, defined as complete vaccination (two MenB-4C doses administered 30–180 days apart), partial vaccination (single MenB-4C vaccine dose), or no vaccination (serogroup B meningococcal vaccine naive). Using log-binomial regression with generalised estimating equations to account for correlations between multiple infections per patient, we calculated adjusted prevalence ratios (APR) and 95% CIs to determine if vaccination was protective against gonorrhoea. We used individual-level data for descriptive analyses and infection-level data for regression analyses.

Findings Between Jan 1, 2016, and Dec 31, 2018, we identified 167706 infections (18099 gonococcal infections,

- Retrospective case-control study (CDC), 2016-2018
- 167,706 gonorrhoea infections, 16-23 yrs
- VE=40%(23, 53) against gonorrhoea (2 dose)

  VE=26% (12, 37) (1 dose)
- Philadelphia, USA

1. Robison SG, Leman RF. JAMA Network Open 2023; 6:e2331742. 2. Abara WE et al. 2024;42(26): 126312 3. Abara WE et al. Lancet ID 2022;22(7):1021-9

Global real-world evidence for a moderate effectiveness of 4CMenB against gonorrhoea

ORIGINAL STUDY

Meningococcus B Vaccination Effectiveness Against *Neisseria gonorrhoeae* Infection in People Living With HIV: A Case-Control Study

Angelo Roberto Raccagni, MD, Laura Galli, MSc,† Vincenzo Spagnuolo, MD,† Elena Bruzzesi, MD,* Camilla Muccini, MD,† Simona Bossolasco, MD,† Martina Ranzenigo, MD,* Nicola Gianotti, MD,† Riccardo Lolatto, MSc,† Antonella Castagna, MD,*† and Silvia Nozza, MD†*

Background: We assessed the vaccination effectiveness (VE) of multicomponent meningococcal serogroup B (4CMenB) vaccine against gonorrhea among people living with HIV (PLWH) with a previous diagnosis of sexually transmitted infection.

Methods: Unmatched case-control study on men who have sex with men living with HIV, in care at San Raffaele Scientific Institute, Milan, Italy, with gonorrhea, syphilis, chlamydia, or anal human papillomavirus between July 2016 (beginning of 4CMenB vaccination) and February 2021 (date of freezing). For the analysis, cases were people with ≥1 gonorrhea infection since July 2016, and controls were people with ≥1 syphilis, chlamydia, or anal human papillomavirus infection since July 2016. Logistic regression was used to provide the estimate of 4CMenB VE against gonorrhea.

Results: Included people living with HIV were 1051 (103 cases, 948 controls); 349 of 1051 (33%) received 2 doses of 4CMenB vaccination. The median follow-up was 3.8 years (2.1–4.3 years). The unadjusted estimate for VE against gonorrhea was 42% (95% confidence interval, 6%–64%; $P = 0.027$). Logistic regression showed that VE against gonorrhea remained significant (44%; 95% confidence interval, 9%–65%; $P = 0.020$) after adjusting for some factors that might have a potential influence on VE or those with significant unbalanced distributions between cases and controls at univariable analysis.

Conclusions: 4CMenB vaccination is associated with a lower risk of gonorrhea in the setting of men who have sex with men living with HIV with a previous sexually transmitted infection.

Gonorrhea, a sexually transmitted infection (STI), is a major

However, the feasibility of developing a vaccine primarily targeting *Neisseria gonorrhoeae* has been historically questioned as all previous vaccine candidates failed at reducing gonorrhea cases. The high antigenic variability, the lack of natural protection following infection, and the ability to subvert the immune system are challenges for vaccine development.[4–6]

Although several gonococcal antigens showed promise in different preclinical stages, a new vaccine would be available for clinical use in several years.[7] Therefore, expanding the current indications of accessible vaccines might be the most effective solution in a short-term scenario. Antiserogroup B *Neisseria meningitidis* vaccines have been identified as the ideal candidate, after having demonstrated a cross-protective immune response.[8,9] Ecologic evidence from Cuba and Norway highlighted a possible reduction of cases after vaccination with outer membrane vesicle (OMV)–based serogroup B antimeningococcal vaccines.[10,11] In New Zealand, MeNZB has shown to decrease both gonorrhea cases by 31% and gonococcal-related hospitalizations by 24%.[8,12,13] Currently, multicomponent meningococcal serogroup B (4CMenB) is the most used vaccine against serogroup B *N. meningitidis* worldwide. Recent evidence from the United States and Australia, by means of surveillance or medical records, supports its effectiveness against *N. gonorrhoeae*.[14–16] Moreover, given the additional components of 4CMenB when compared with MeNZB, its effectiveness is expected to be higher; indeed, in different studies, 4CMenB effectiveness has been estimated to be between 32% and 46%.[12,14–16] Italian guidelines suggest routine vaccination with 4CMenB with a

- Unmatched case-control, (San Raffaele scientific institute)
- 2016-2021
- 103 cases in 1051 MSM living with HIV
- 37-51 yrs
- VE=44% (95%CI 9, 65%)
- Italy

About CROI Abstracts Presenters CROI Conference on Retroviruses and Opportunistic Infections Attendees Scholarships Program

Final Results of ANRS 174 DOXYVAC: A Randomized Trial to Prevent STI in MSM on PrEP

4CMenB Vaccine Secondary Efficacy Outcomes

Positive	4CMenB vaccine (N=274) Events (Incidence per 100 p-y)	No vaccine (N=270) Events (Incidence per 100 p-y)	Adjusted hazard ratio (95% CI)	p-value
First episode				
Gonorrhea (all sites)	103 (58.3)	122 (77.1)	0.78 (0.60-1.01)	0.06
Anal Gonorrhea	61 (29.7)	64 (33.1)	0.90 (0.64-1.28)	0.57
Pharyngeal Gonorrhea	58 (27.6)	74 (37.7)	0.75 (0.53-1.05)	0.09
Urinary Gonorrhea	13 (5.4)	10 (4.3)	1.29 (0.56-2.94)	0.55
Symptomatic Gonorrhea	12 (5.0)	14 (6.1)	0.82 (0.38-1.78)	0.62
Culture Positive Gonorrhea	26 (14.7)	25 (15.8)	0.95 (0.55-1.65)	0.86
Cumulative incidence			**Adjusted IRR (95% CI)**	
Gonorrhea (all sites)	132 (52.6)	151 (62.4)	0.84 (0.67-1.07)	0.16
Anal Gonorrhea	88 (35.1)	82 (33.9)	1.04 (0.77-1.40)	0.82
Pharyngeal Gonorrhea	80 (31.9)	92 (38.0)	0.84 (0.62-1.13)	0.25
Urinary Gonorrhea	18 (7.2)	12 (5.0)	1.45 (0.70-3.01)	0.32

- Randomised study with two different interventions: doxycycline and Bexsero®
- aHR: 0.78 (95%CI: 0.60-1.01) for a first episode of GC
- aIRR: 0.84 (0.67-1.07) for cumulative episodes p=0.06
- France

Clinical Infectious Diseases

MAJOR ARTICLE

IDSA Infectious Diseases Society of America hivma hiv medicine association OXFORD

Prevention of *Neisseria gonorrhoeae* With Meningococcal B Vaccine: A Matched Cohort Study in Southern California

Katia J. Bruxvoort,[1,2,0] Joseph A. Lewnard,[3,4,5] Lie H. Chen,[2] Hung Fu Tseng,[2,6] Jennifer Chang,[7] Jeanne Marrazzo,[8] and Lei Qian[2]

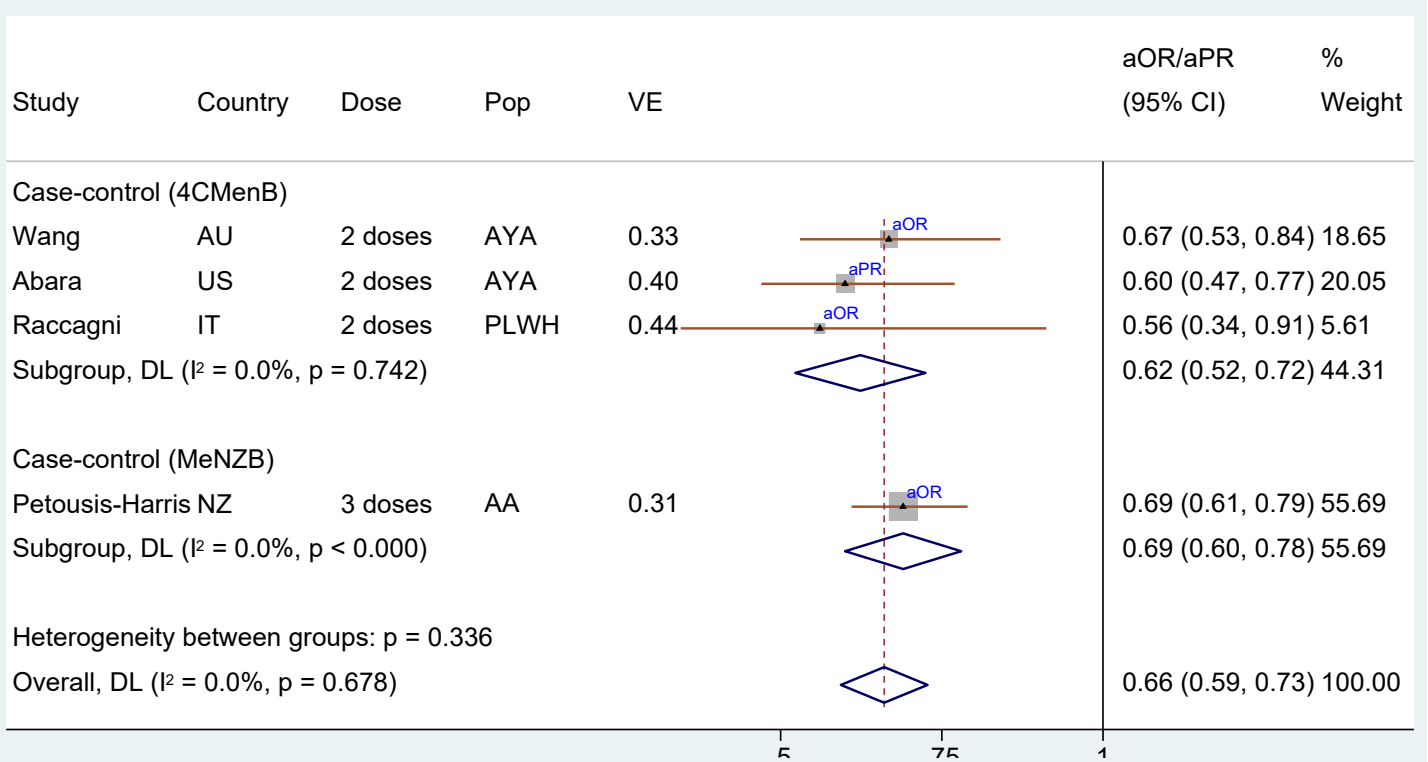
[1]Department of Epidemiology, University of Alabama at Birmingham, Birmingham, Alabama, USA; [2]Department of Research & Evaluation, Kaiser Permanente Southern California, Pasadena, California, USA; [3]Division of Epidemiology, School of Public Health, University of California–Berkeley, Berkeley, California, USA; [4]Division of Infectious Diseases & Vaccinology, School of Public Health, University of California–Berkeley, Berkeley, California, USA; [5]Center for Computational Biology, College of Engineering, University of California–Berkeley, Berkeley, California, USA; [6]Department of Health Systems Science, Kaiser Permanente Bernard J. Tyson School of Medicine, Pasadena, California, USA; [7]Department of Infectious Diseases, Los Angeles Medical Center, Southern California Permanente Medical Group, Los Angeles, California, USA; and [8]Division of Infectious Diseases, University of Alabama at Birmingham Heersink School of Medicine, Birmingham, Alabama, USA

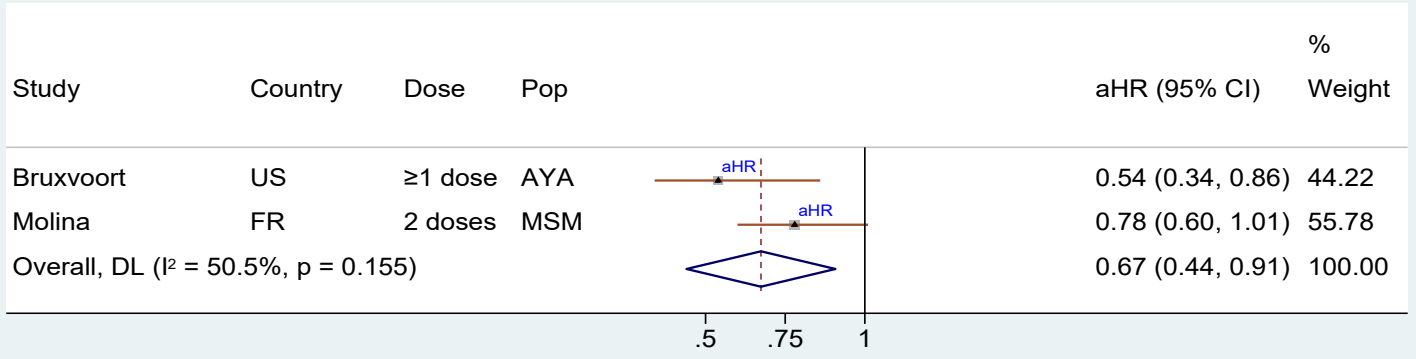
Background. *Neisseria gonorrhoeae* is acquiring increasing resistance to available oral antibiotics, and current screening and treatment approaches have not decreased gonorrhea incidence. Although a gonorrhea-specific vaccine does not exist, *N. gonorrhoeae* shares much of its genome with *Neisseria meningitidis*, notably critical antigenic determinants including outer

- Retrospective, matched cohort, (Kaiser-Permanente)
- 2016-2020
- 6641 MenB;26,471 MenACWY
- 15-20 yrs
- VI=46% (HR 0.54 (0.34, 0.86)) reduction in incidence of gonorrhoea
- Southern California, USA

1. Raccagni et al. Sexually transmitted Diseases 2023;50(5):247-251. 2. Molina J-M et al, Lancet ID . 3.Bruxvoort KJ et al. CID 2023;76:e1341-49.

Vaccine effectiveness of MenB OMV vaccines against gonorrhoea: systematic review





MenB-OMV[1]

- **VE = 33-34%**

MenB-fHbp[2]

- **VE=3%**

(Adjusted prevalence ratio=0.97 95%CI 0.79-1.19)

Bruxvoort KJ et al. CID 2023

- Kaiser Permanente cohort, USA (>30,000)
- 4CMenB vs MenACWY
- VI=46% 4CMenB

Robison et al. JAMA 2023

- Uni. Oregon, USA (N=39,000)
- 4CMenB vs MenB-FHbp
- VE=47% 4CMenB

1. Wang B et al. Journal of Infection 2024; 106225 2. Robison SG, Leman RF. JAMA Network Open 2023; 6:e2331742.

Duration of protection by year since vaccination in 6 year adolescent cohort in SA; subgroup analyses

Two-dose 4CMenB vs unvaccinated	Adjusted OR (95%CI)	Vaccine effectiveness (%) (95%CI)
> 3 months since vaccination	0.598 (0.539 to 0.633) p<0.001	40.2 (37.7 to 46.1)

VE by year since 4CMenB vaccination (subgroup analysis)				
1 year	3-12 months	VE=31.6% (2.9-51.9) p<0.001	>12 months	VE=40.7% (34.1-46.7) p<0.001
2 years	3-24 months	VE=51.7% (40.0-61.2) p<0.001	>24 months	VE=37.0 % (29.8-43.5) p<0.001
3 years	3-36 months p<0.001	VE=53.0% (45.0-59.9)	>36 months	VE=28.1% (18.9, 36.2) p<0.001
4 years	3-48 months	VE=45.2% (37.8-51.7) p<0.001	>48 months	VE=22.9% (10.2-33.8) p=0.001
≥ 5 years	3-60 months p<0.001	VE=32.3% (22.3-41.0)	>60 months	VE=4.1% (-17.8-21.9) p=0.690

Wang et al. 2026 Unpublished data

6 years post 4CMenB introduction in SA: Protection against repeat gonococcal infection (Cohort study: Time to event analysis)

- The risk of a **2nd episode** of gonococcal infection was lower in those who received **two doses**

  aHR=0.671 (95%CI 0.513, 0.878) p=0.004

- Risk of a **3rd episode** of gonococcal infection was lower in those who received **two doses**

  aHR=0.701 (95%CI 0.442, 1.110) p=0.130

No. of episodes	No. individual with infections
1	1,809
2	256
3	68
4	25
5	8
6	6
7	3
8	2
12	1
Total	2,178

Adjusted hazard ratio for second gonococcal infection (vaccinated vs unvaccinated), adjusted for sex and chlamydia co-infection, stratified by age and SEIFA

Wang et al. Unpublished data

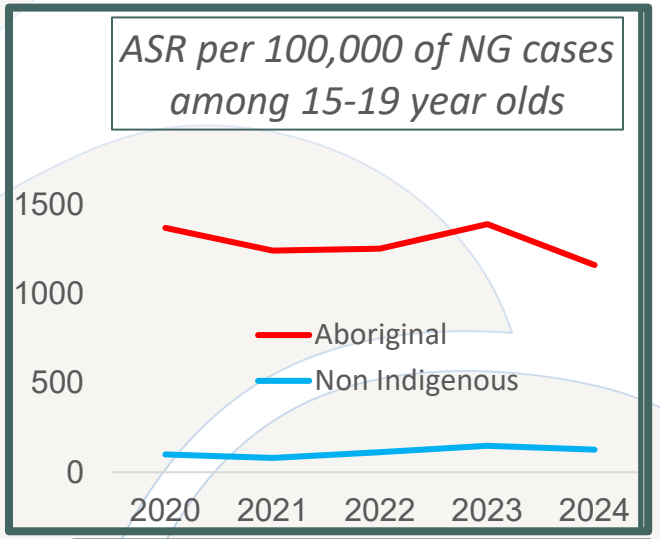
Impact of 4CMenB vaccine against gonorrhoea in First Nations young people in Australia: “B Part of It NT” study



- 14-19 year olds in urban, rural and remote regions of the NT (42.4% Aboriginal or Torres strait Islander)
- 10% received 2 doses of 4CMenB
- 97% gonococcal notifications were in Aboriginal young people

Cohort study N=30,650

- Time to infection analysis using a Cox proportional hazards model





VE =38.4% (95%CI: 18.6-53.4) against gonococcal infection

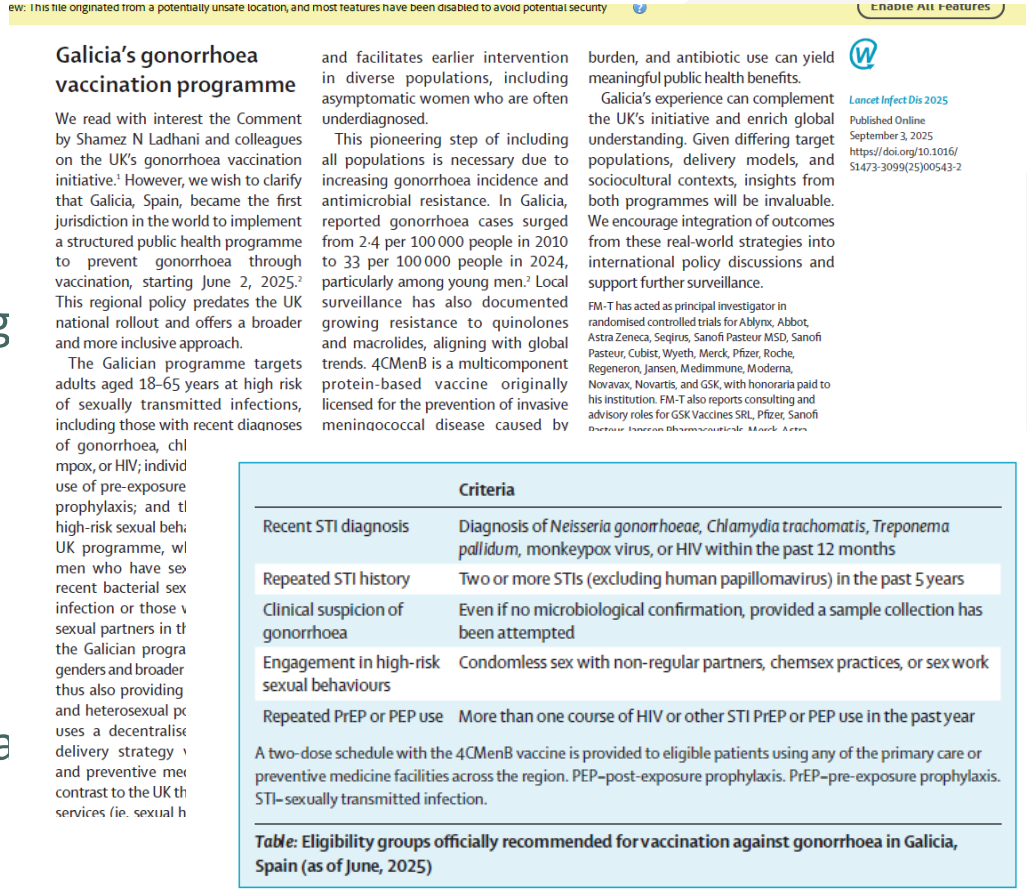
1. Marshall H et al. Vaccines 2022;10(2): 309. 2. McMillan M et al. Open Forum Infectious Diseases 2026;13(8):ofag409

Figure courtesy Prof James Ward

Policy recommendations for use of 4CMenB to reduce the risk of gonorrhoea in high-risk groups, UK and Spain

JCVI, UK recommendation, 10 November 2023 and funded program launched on 22nd May 2025.
Recommendation for a targeted programme using 4CMenB to prevent gonorrhoea among individuals at higher risk of infection attending sexual health services.

Galicia, Spain
became the first jurisdiction in the world to implement a structured public health progra to prevent gonorrhoea through vaccination, starting June 2, 2025.



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Galicia's gonorrhoea vaccination programme

We read with interest the Comment by Shamez N Ladhani and colleagues on the UK's gonorrhoea vaccination initiative.[1] However, we wish to clarify that Galicia, Spain, became the first jurisdiction in the world to implement a structured public health programme to prevent gonorrhoea through vaccination, starting June 2, 2025.[2] This regional policy predates the UK national rollout and offers a broader and more inclusive approach.

The Galician programme targets adults aged 18–65 years at high risk of sexually transmitted infections, including those with recent diagnoses of gonorrhoea, chl mpox, or HIV; individ use of pre-exposure prophylaxis; and tl high-risk sexual beh UK programme, wl men who have se recent bacterial sex infection or those v sexual partners in th the Galician progra genders and broader thus also providing and heterosexual p uses a decentralise delivery strategy and preventive me contrast to the UK th services (ie, sexual h and facilitates earlier intervention in diverse populations, including asymptomatic women who are often underdiagnosed.

This pioneering step of including all populations is necessary due to increasing gonorrhoea incidence and antimicrobial resistance. In Galicia, reported gonorrhoea cases surged from 2·4 per 100 000 people in 2010 to 33 per 100 000 people in 2024, particularly among young men.[2] Local surveillance has also documented growing resistance to quinolones and macrolides, aligning with global trends. 4CMenB is a multicomponent protein-based vaccine originally licensed for the prevention of invasive meningococcal disease caused by

burden, and antibiotic use can yield meaningful public health benefits.

Galicia's experience can complement the UK's initiative and enrich global understanding. Given differing target populations, delivery models, and sociocultural contexts, insights from both programmes will be invaluable. We encourage integration of outcomes from these real-world strategies into international policy discussions and support further surveillance.

FM-T has acted as principal investigator in randomised controlled trials for Ablynx, Abbot, Astra Zeneca, Seqirus, Sanofi Pasteur MSD, Sanofi Pasteur, Cubist, Wyeth, Merck, Pfizer, Roche, Regeneron, Jansen, Medimmune, Moderna, Novavax, Novartis, and GSK, with honoraria paid to his institution. FM-T also reports consulting and advisory roles for GSK Vaccines SRL, Pfizer, Sanofi

Lancet Infect Dis 2025
Published Online
September 3, 2025
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S1473-3099(25)00543-2

	Criteria
Recent STI diagnosis	Diagnosis of *Neisseria gonorrhoeae*, *Chlamydia trachomatis*, *Treponema pallidum*, monkeypox virus, or HIV within the past 12 months
Repeated STI history	Two or more STIs (excluding human papillomavirus) in the past 5 years
Clinical suspicion of gonorrhoea	Even if no microbiological confirmation, provided a sample collection has been attempted
Engagement in high-risk sexual behaviours	Condomless sex with non-regular partners, chemsex practices, or sex work
Repeated PrEP or PEP use	More than one course of HIV or other STI PrEP or PEP use in the past year

A two-dose schedule with the 4CMenB vaccine is provided to eligible patients using any of the primary care or preventive medicine facilities across the region. PEP–post-exposure prophylaxis. PrEP–pre-exposure prophylaxis. STI–sexually transmitted infection.

Table: **Eligibility groups officially recommended for vaccination against gonorrhoea in Galicia, Spain (as of June, 2025)**



Shamez Ladhani



Frederico Martinon-Torres

Selectively vaccinating high risk groups was the most cost-effective intervention.

Whittles et al. Lancet ID 2022

GOGOVAX: RCT of 4CMenB in men who have sex with men



Kate Seib

Eligibility: 18-50 years of age, sex with at least 1 man in past 6 months, gonorrhoea in past 18 months

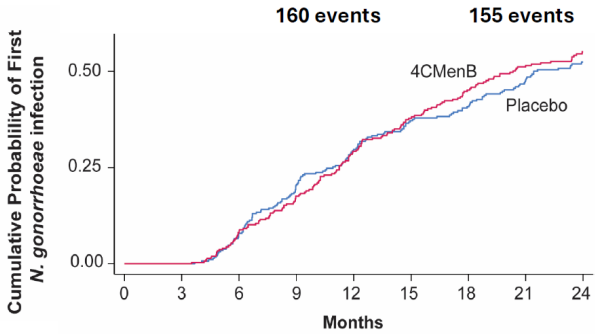
Results: N=620

- Incidence gonorrhoea 60 per 100 person years
- 60% > 10 partners
- Mean age 34 years

Results cannot be generalised to other populations including women, or people with lower gonorrhea incidence or previous exposure

Primary efficacy outcomes

Gonorrhea	4CMenB Incidence (per 100 PY)	Placebo Incidence (per 100 PY)	Incidence rate ratio (95% CI)	Vaccine Efficacy (%) (95% CI)
Per-protocol population (N=587)				
First-episode	48.1	47.8	**1.01** (0.80 to 1.26)	**-0.50 %** (-26.16 to 19.93)



4CMenB was not effective in reducing the incidence of gonorrhea

Subgroup	4CMenB	Placebo	Incidence rate ratio (95% CI)
	no. events/total PY (incidence/100 PY)		
Overall	160/330.0 (48.1)	155/324.2 (47.8)	1.01 (0.80-1.26)
HIV status			
HIV-negative	142/298.0 (47.6)	135/301.3 (44.8)	1.06 (0.84-1.35)
HIV-positive	18/34.9 (51.5)	20/22.9 (87.3)	0.59 (0.31-1.12)
Sexuality			
Gay/homosexual	147/307.1 (47.9)	143/286.3 (49.9)	0.96 (0.76-1.21)
Other	13/25.9 (50.2)	12/37.9 (31.7)	1.58 (0.69-3.66)
Number of sexual partners			
2-5	12/61.4 (19.5)	20/63.3 (31.6)	0.62 (0.30-1.28)
6-10	19/60.3 (31.5)	27/57.7 (46.8)	0.67 (0.37-1.22)
11-50	87/136.7 (63.6)	77/124.1 (62.0)	1.03 (0.76-1.38)
>50	23/27.3 (84.1)	12/16.3 (73.8)	1.14 (0.57-2.30)
History of gonorrhea			
No	8/36.5 (21.9)	15/44.3 (33.9)	0.65 (0.28-1.52)
Yes	152/296.5 (51.3)	140/279.9 (50.0)	1.02 (0.81-1.30)

Seib K et al. NEJM 2026 395;4:349-361

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Impact of 4CMenB in reducing the risk of gonorrhoea in different risk groups

	4CMenB population programs for MenB prevention in adolescents	4CMenB population programs in higher risk (NT)	4CMenB in very high risk e.g. MSM
Methods	Case control/cohort	Case control/cohort	RCT
Age (years)	15-18	15-18	18-50
Gender	All	All	Males only
Risk of gonorrhoea	low	moderate	high
Previous exposure (gonococcal infection)	2.8%	4.2%	90%
Force of infection	65% have 0-1 partner[1]	49% have 0-1 partner[2]	< 1% have 0-1 partner 50% 11-50 partners
Anatomical site	74% genital, 11.1% rectal, 6.2% pharynx	95% genital, 3% rectal, 2% pharynx [3] (AMR testing)	17% genital, 41.3% rectal, 41.7% pharynx
Results to date			
	11 studies overall VE~33% against gonorrhoea	1 Study VE = 38%	4 Studies showing non significant VE

1. National survey of Australian secondary students and sexual health: ssashsurvey.org.au 2. Ward T et al. The Goanna survey 2. https://youngdeadlyfree.org.au/wp-content/uploads/2021/09/GoannaSurvey2-FINAL-date.pdf 3. Lahra M et al. Commun Dis Intell. 2025;49. doi. 10.33321/cdi.2025.49.056

4CMenB program for UK adolescents

GOV·UK

Home > Health and social care > Public health > Health protection > Health surveillance and reporting programmes

Independent report

JCVI statement on meningococcal B vaccination in older children and young adults, 16 July 2026

In South Australia, a study based adolescent 4CMenB vaccination p.. vaccine effectiveness of 41.8% against go.. lasted out to 5 years, with vaccine waning evide.. study using sexually transmitted infection (STI) surveilla.. New York City and Philadelphia estimated a 4CMenB 2-dose vac.. effectiveness of 40% against gonorrhoea, with a vaccine effectiveness of 26% for one dose.

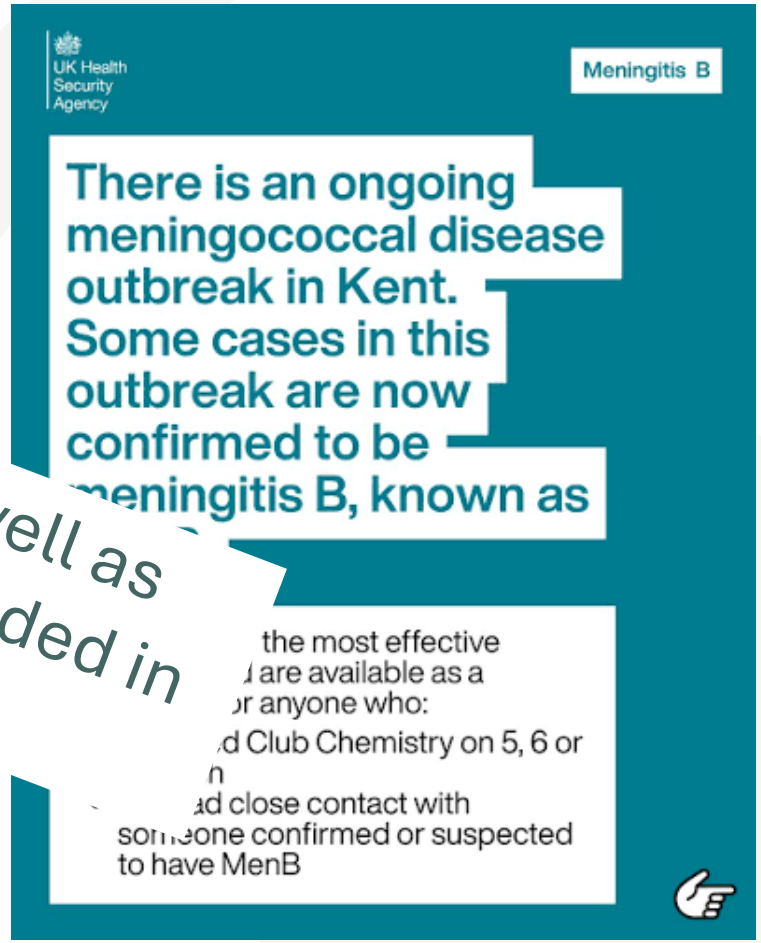
A recently published randomised controlled trial conducted in Australia concluded that 4CMenB vaccination in men who have sex with men (MSM) who were at high risk for gonorrhoea did not result in a lower level of gonococcal infection compared with those who had not received the vaccine. The trial population had very high rates of prior gonococcal infection and did not include women. JCVI considers that the trial population is unlikely to be reflective of the target population for a national adolescent MenB vaccination programme, who would largely have not had previous exposure to gonorrhoea.

Promotional material

A guide to the Meningococcal B vaccines that help to protect against meningitis ..nticaemia

First time impact on gonorrhoea as well as invasive meningococcal disease included in cost-effectiveness analysis

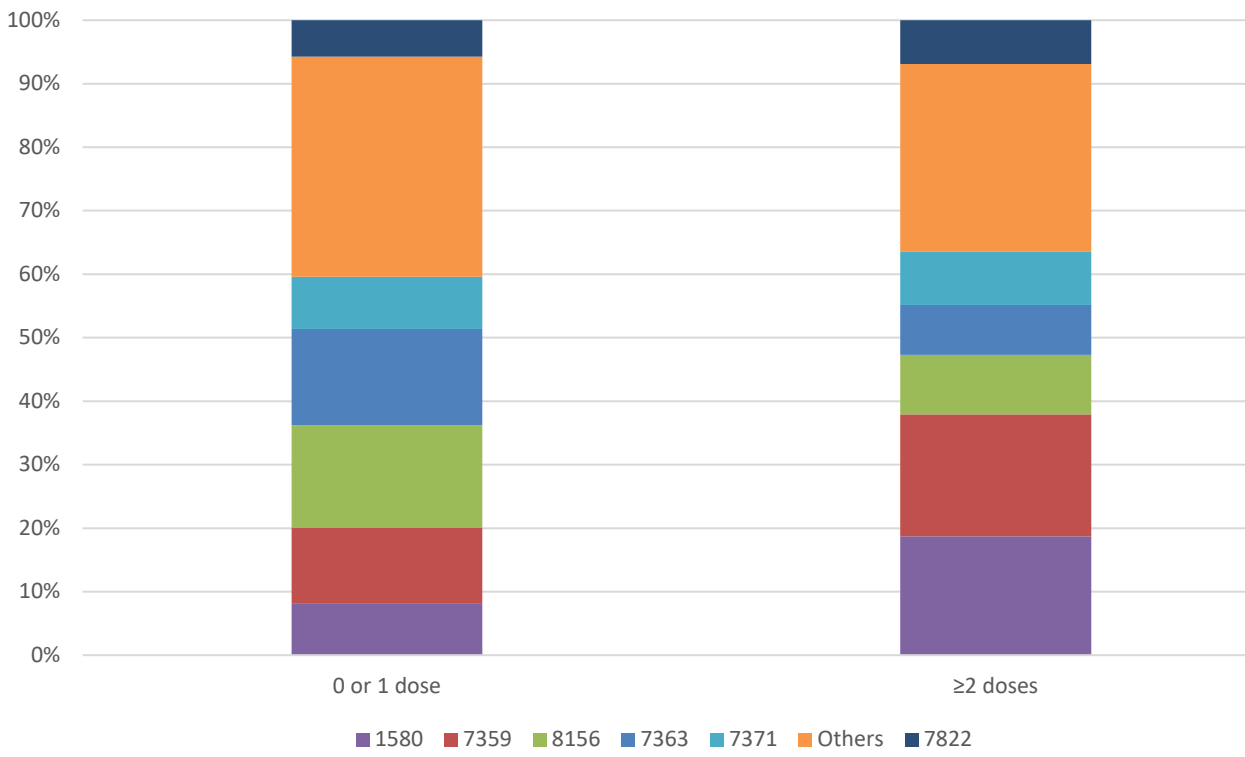




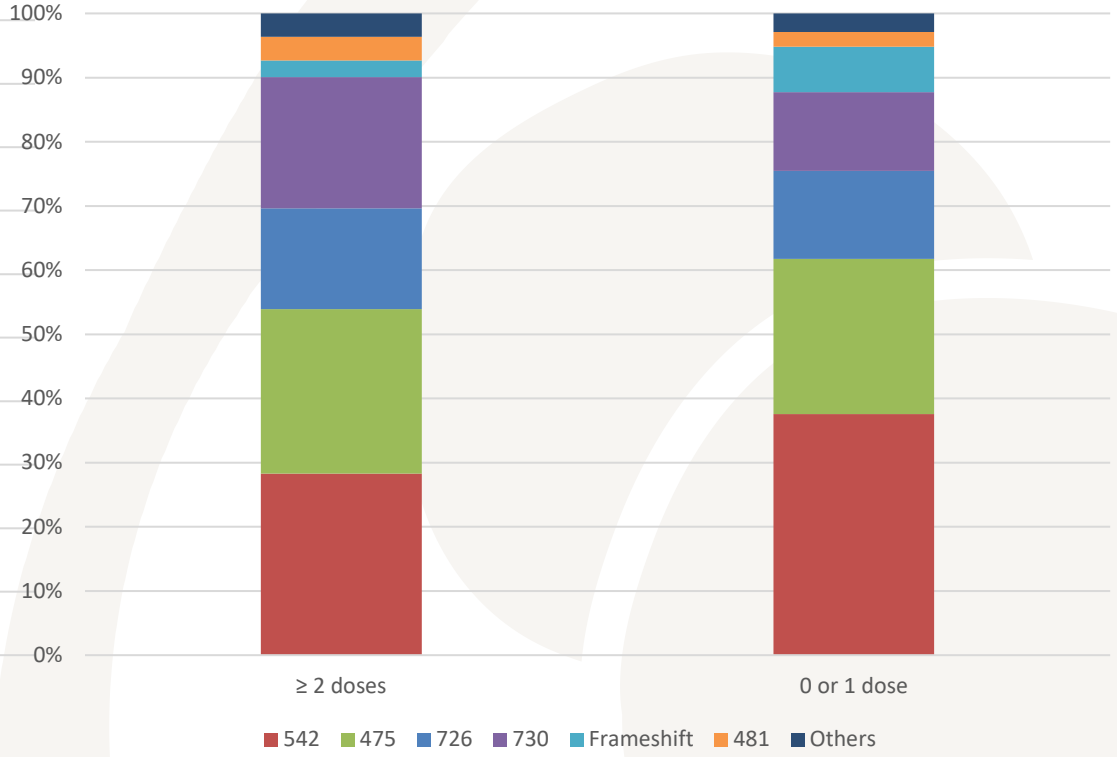
https://www.gov.uk/government/publications/jcvi-statement-on-meningococcal-b-vaccination-in-older-children-and-young-adults-16-july-2026.
UK Health security Agency

Differential impact on MLST and NHBA variants in vaccinated vs unvaccinated

Whole genome sequencing of gonococci: Differential impact of 4CMenB on MLST and NHBA variants: 1103 gonococcal isolates: SA (n=876) and the NT (n=227) (Oct. 2021-Jan 2026)



MLST by 4CMenB dose (n=265)



NHBA antigen by 4CMenB dose (n=265)

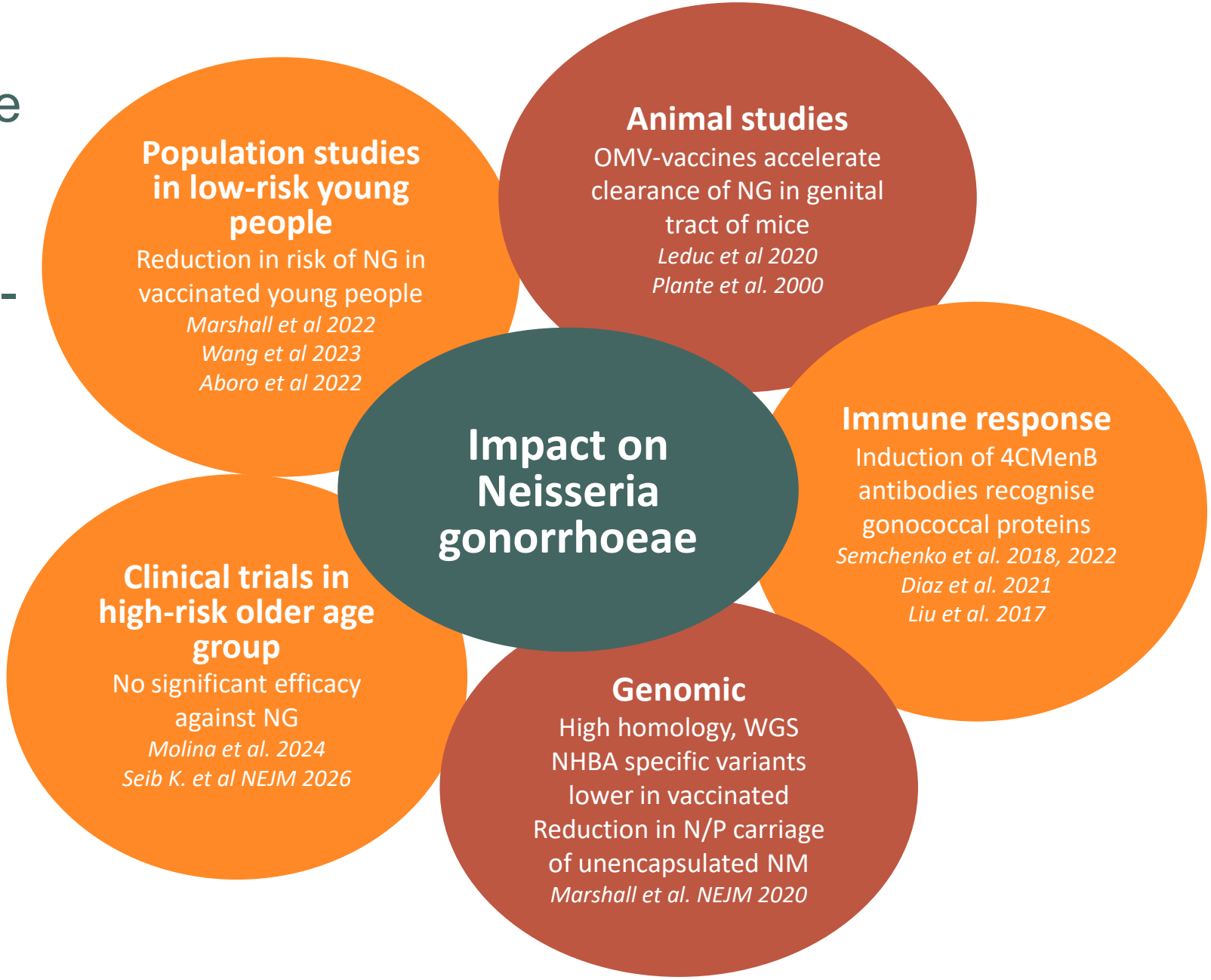
NHBA-542, 475, 481 each share 67% identity to NHBA-2 in 4CMenB

WGS Results for *N. gonorrhoeae*

N. Gonorrhoea sequencing MLST and NHBA antigen

Wang et al. Unpublished data

Summary of the evidence for MenB-OMV vaccines cross-protection against gonorrhoea



In summary

Cross-protection against gonorrhoea using OMV based vaccines

- could induce better control of Neisseria disease in population programs, with likely impact greatest in young, gonococcal naïve individuals (e.g. HPV vaccine)
- Vaccine Effectiveness against gonorrhoea may be different in low-risk vs high risk, exposed vs unexposed groups, low/high force of infection, younger vs older vaccine recipients and anatomical site
- inform gonococcal vaccine development

Wang et al. Unpublished data

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AIM is to determine the most effective immunisation program for prevention of meningococcal disease and gonorrhoea in Australia and globally

By 2030, the NEIS CRE will deliver a roadmap to eliminate meningitis and drive down gonorrhoea globally

https://neiscre.com.au

NEIS CRE Investigator team



Investigators: Helen Marshall, James Ward, Kate Seib, Peter Richmond, Monica Lahra, Bing Wang, Charlene Kahler, Sebastian van Hal, Jason. Ong, Mark McMillan, Martin Maiden, Shamez Ladhani, Ivo Vlaev, Louise. Flood, Stephen. Lambert, Sami Gottlieb, Nigel Crawford, Karen Quick, Jon Karnon

Thank you and a huge thanks to our partners





