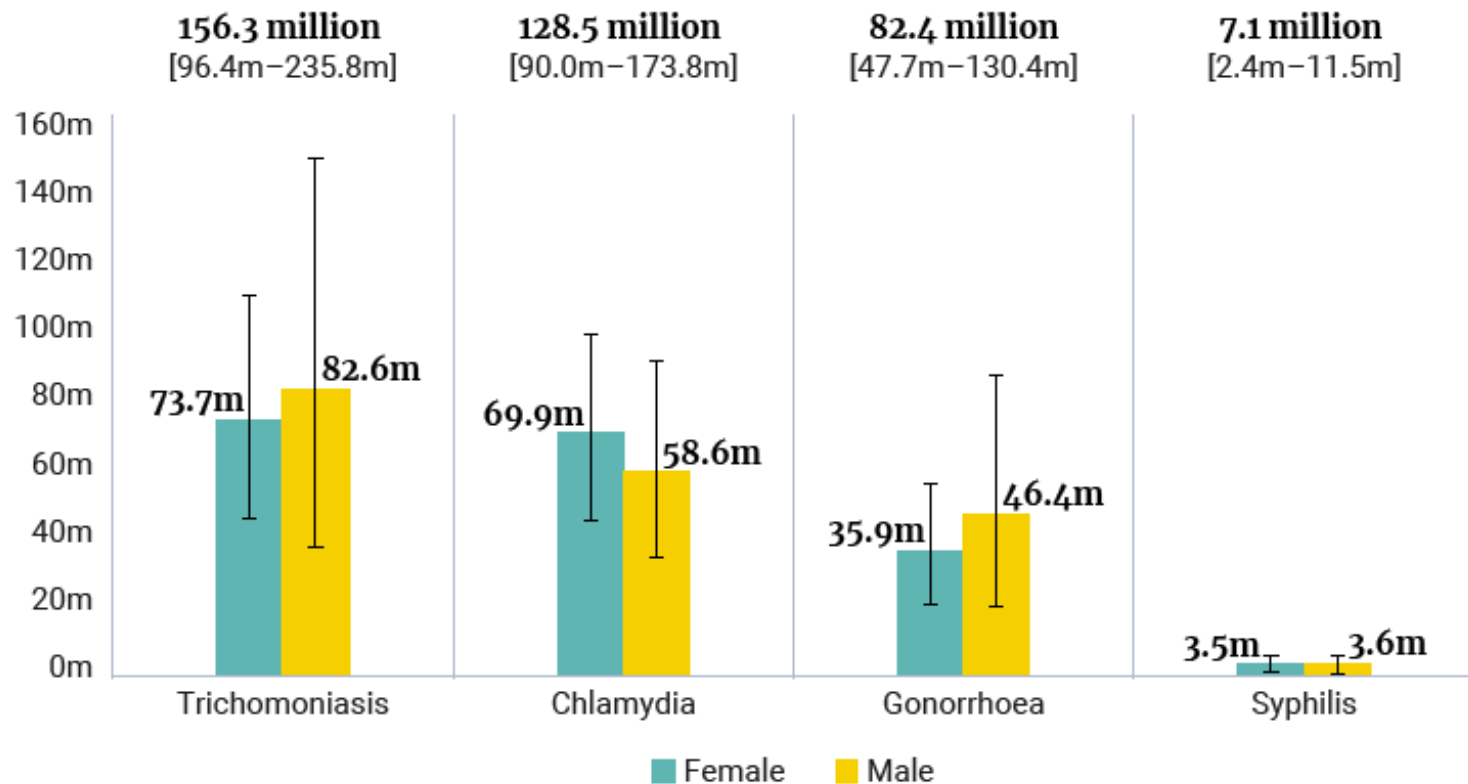


Vaccines for gonorrhoea

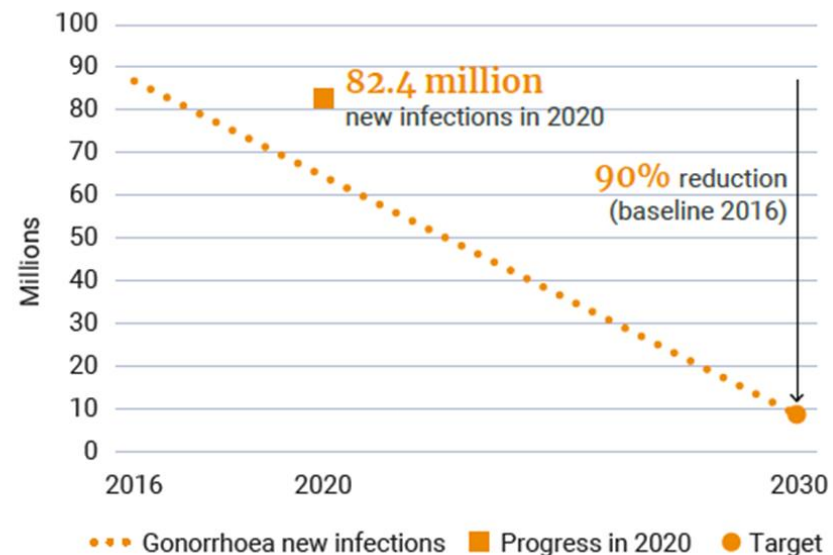
Sinead Delany-Moretlwe, MBBCh PhD DTM&H
University of the Witwatersrand
IAS webinar, May 2024

83 million new cases of gonorrhoea annually

TOTAL NEW INFECTIONS



INCIDENCE OF GONORRHOEA AMONG 15–49 YEARS OLD: 2030 TARGET AND PROGRESS IN 2020

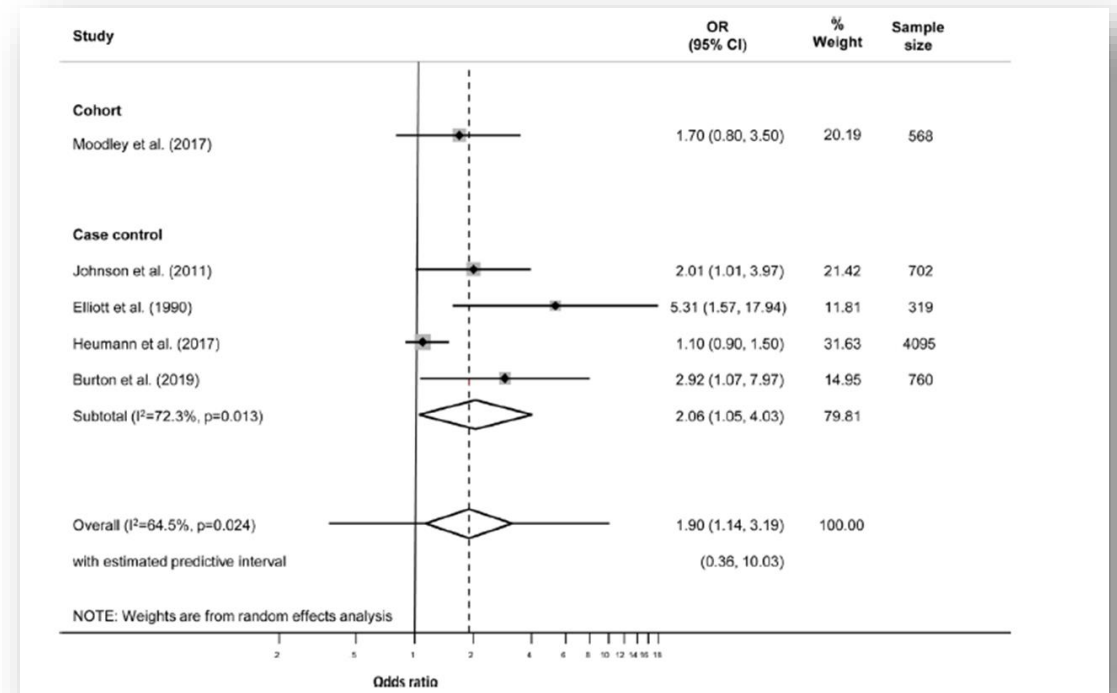


Source: WHO, 2021.

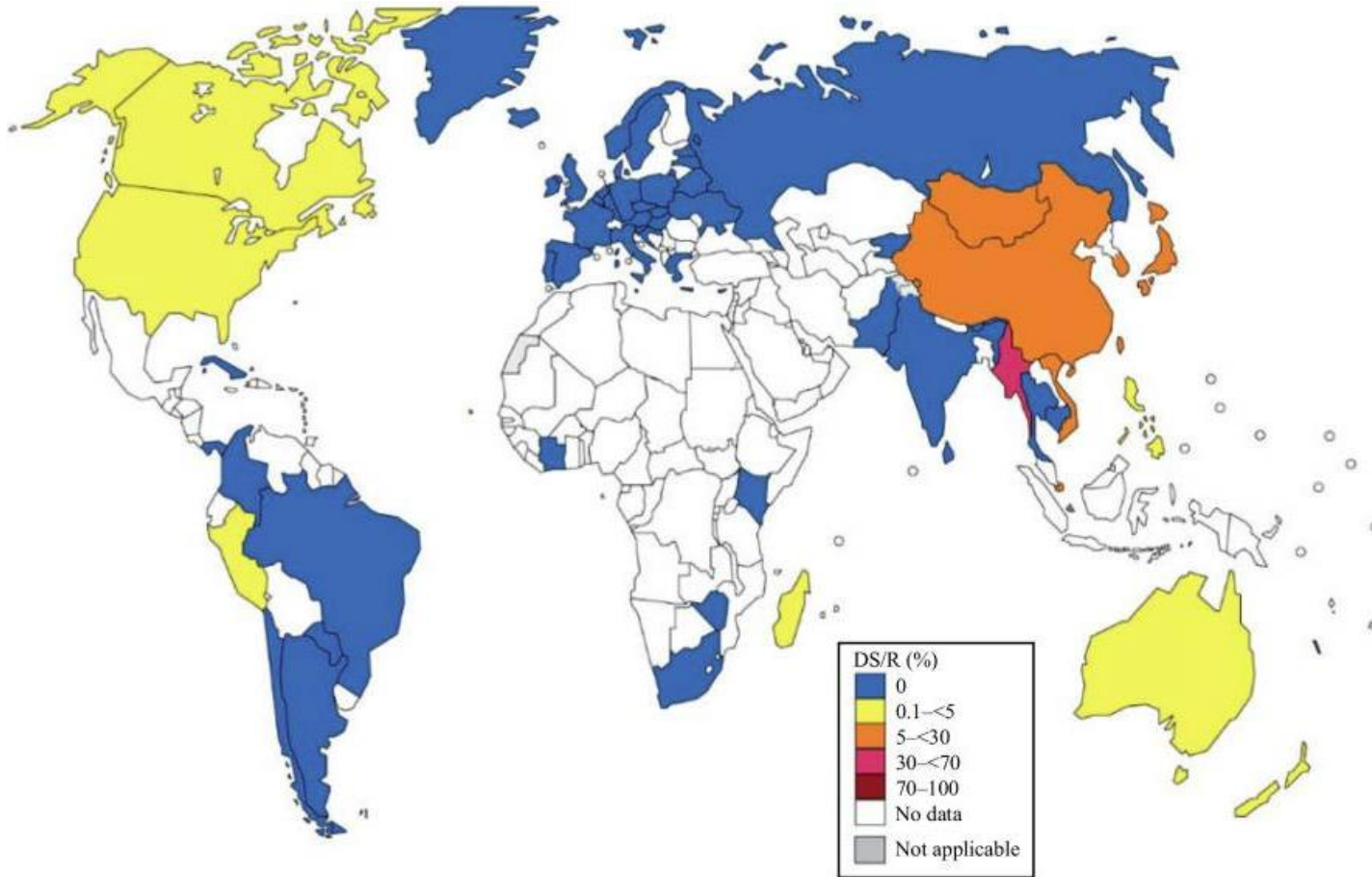
Source: WHO, 2021

Consequences of untreated gonorrhoea

- Untreated infection can lead to severe health consequences including
 - Pelvic inflammatory disease, infertility, ectopic pregnancy, chronic pelvic pain
 - Tubal Factor Infertility accounts for >85% of female infertility cases in regions of sub-Saharan Africa, compared to 33% of cases worldwide
 - GC prevalence higher in populations with TFI
 - Adverse pregnancy outcomes and neonatal conjunctivitis
 - ↑ pre-term birth, PROM, LBW, perinatal mortality
 - Stronger association in LMIC
 - Increased risk of HIV acquisition and transmission
 - DALYs, cost to health system
 - Stigma and reduced quality of life



Emerging threat of AMR



Percentage of isolates with decreased susceptibility or resistance to Ceftriaxone

- 21/68 (31%) of countries reported DS/R to ceftriaxone in 2018
- Confirmed clinical treatment failures with MDR strains
- Lack of new antibiotics
- *N. gonorrhoeae* included in top 10 WHO Priority Pathogens List, 2017

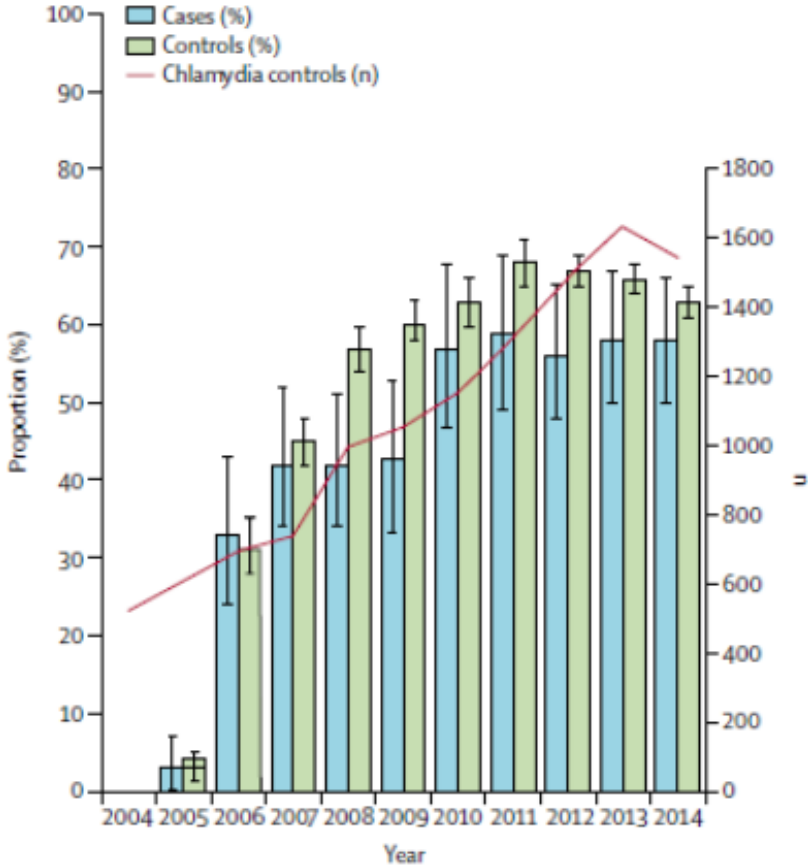
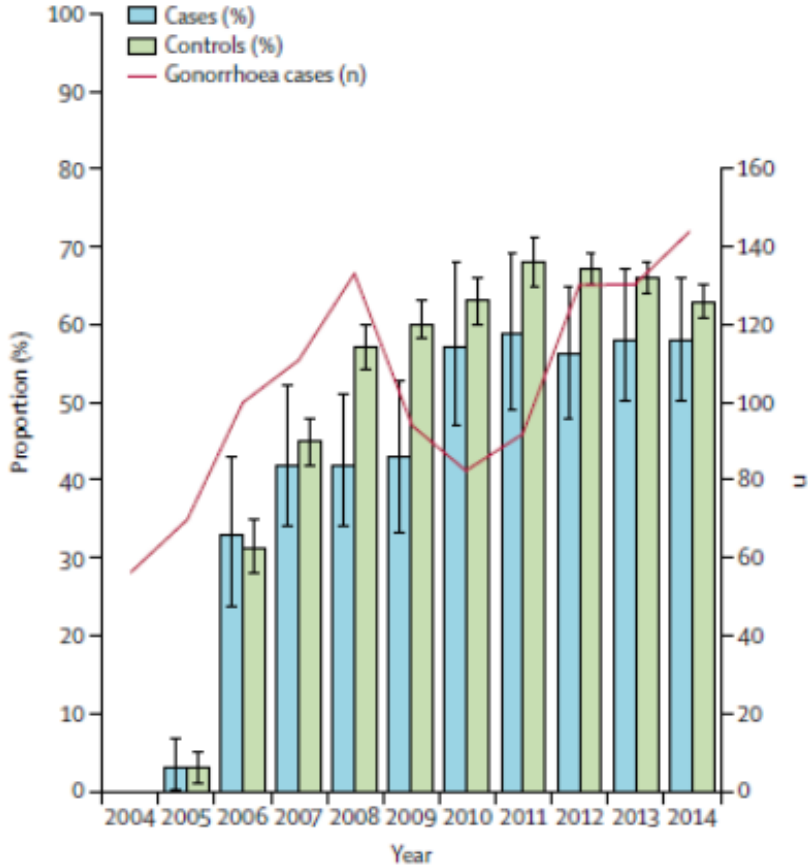


Home / News / WHO publishes list of bacteria for which new antibiotics are urgently needed

WHO publishes list of bacteria for which new antibiotics are urgently needed

Effectiveness of group B OMV meningococcal vaccine vs. gonorrhoea in New Zealand: a retrospective case-control

Vaccine effectiveness estimated 31% (95% 21-39, p<0.001)



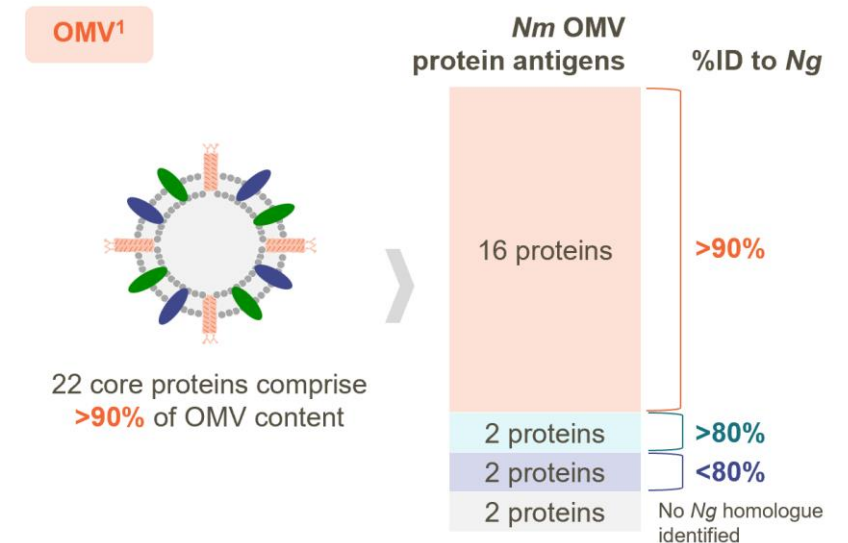
is, Lancet 2017; Paynter, 2019:

Observational evidence for MenB vaccine cross protection

Location	Study design	Vaccine	Effectiveness vs Ng
Cuba <i>Perez, 2009</i>	Ecological	VA-MENGOC-BC	
Norway <i>Whelan, 2016</i>	Ecological	MenBvac	40%
New Zealand <i>Petousis-Harris, 2017</i>	Case control	MeNZB	31%
Canada <i>Longtin, 2017</i>	Ecological	4CMenB	59%
USA <i>Abara, 2022</i>	Case control		40%
Australia <i>Wang, 2022</i>	Case control		32%
USA <i>Bruxvoort, 2022</i>	Matched cohort		46%
Italy MLHIV <i>Raccagni, 2023</i>	Case control		42%

Molecular and pre-clinical evidence for MenB cross-protection

- Ng and Nm genetically similar
- OMV and NHBA 4CMenB antigens present in both Nm and Ng
- Sera from vaccinated humans cross reacts with Ng
- In 4CMenB immunised mice
 - Antibodies from 4CMenB-immunised mice show functional activity vs Ng
 - 4CMenB accelerates clearance of Ng and reduces bacterial load in mouse models
 - Serum IgG and vaginal IgA and IgG cross react with Ng OMV
 - 4-fold increase in serum bactericidal₅₀ titers

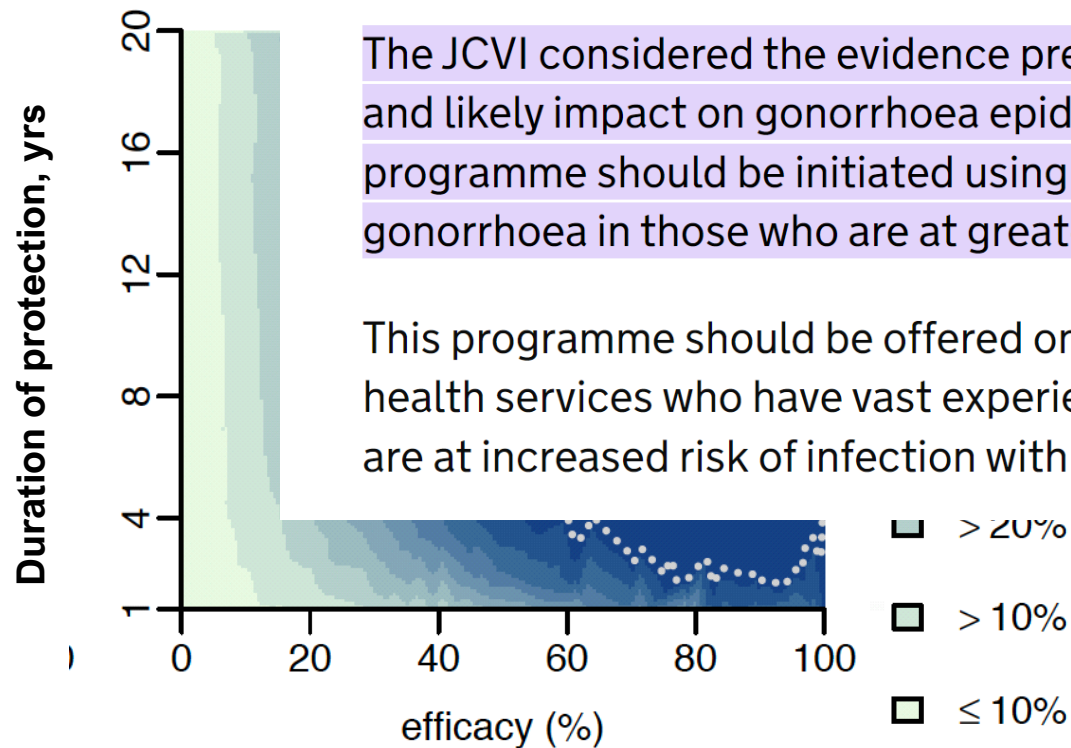


Gonococcal vaccine models: vaccinating all MSM attending UK sexual health clinics

Assuming untreatable infection due to AMR

JCVI advice

the group,
by and



The JCVI considered the evidence presented in terms of programme cost-effectiveness and likely impact on gonorrhoea epidemiology. The committee agreed that a targeted programme should be initiated using the 4CMenB vaccine for the prevention of gonorrhoea in those who are at greatest risk of infection.

ence by

This programme should be offered on an opportunistic basis through specialist sexual health services who have vast experience in assessment and identification of those who are at increased risk of infection with bacterial STIs.

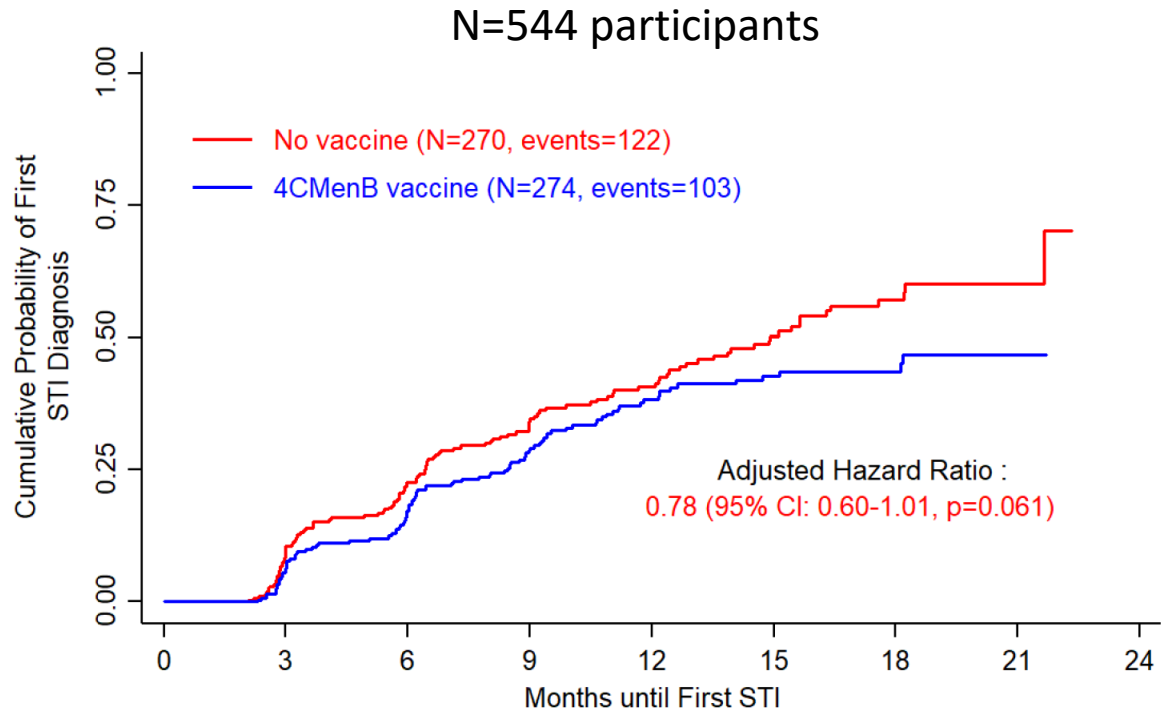
- Numbers needed to vaccinate may be lower

4CMenB Vaccine Time to First GC infection

No interaction between Doxy PEP and 4CMenB vaccine (p=0.82)

225 subjects infected
122 in No Vaccine arm
 (incidence: 77.1/100 PY),
103 in 4CMenB vaccine arm
 (incidence: 58.3/100 PY)


Interim analysis:
 49 subjects infected, aHR: 0.49
 (95%CI: 0.27 - 0.88)



Number at risk		0	3	6	9	12	15	18	21	24
No Vaccine	270	234	194	131	94	58	30	4	0	0
4CMenB vaccine	274	251	212	159	105	68	37	6	0	0

GC infections were considered from M3 visit (1 month after 2nd vaccine dose) and multi-sites infection = 1 single event

Trials of 4CMenB efficacy vs Ng

Trial number	Study name	Sponsor	Location, numbers	Expected completion
ACTRN12619001478101	MenGO: Does the licensed meningococcal vaccine Bexsero® provide cross-protection against gonorrhoea?	Gold Coast University Hospital	Australia 130	2024
NCT04415424	GoGoVax: Efficacy study of 4CMenB Bexsero® to prevent gonorrhoea infection in gay and bisexual men	Kirby Institute	Australia 730	2025
NCT04350138	MAGI: Safety and efficacy study of meningococcal group B vaccine rMenB+OMV NZ Bexsero to prevent gonococcal infection	NIAID	USA, Thailand, Malawi 2,200	2025
NCT05766904	Efficacy Trial on Meningococcal B Vaccine for Preventing Gonorrhea Infections	Chinese University of Hong Kong	Hong Kong 150	2025
NCT05294588	Efficacy of Immunization With 4C-MenB in Preventing Experimental Urethral Infection With Neisseria Gonorrhoeae	UNC	USA 140	2028
 Pending	BIYELA: efficacy 4CMenB vaccine for gonorrhoea prevention in individuals assigned female at birth	U of Washington	South Africa 1100	2026

Other gonorrhoea vaccine candidates in development

WHO preferred product characteristics for gonococcal vaccines

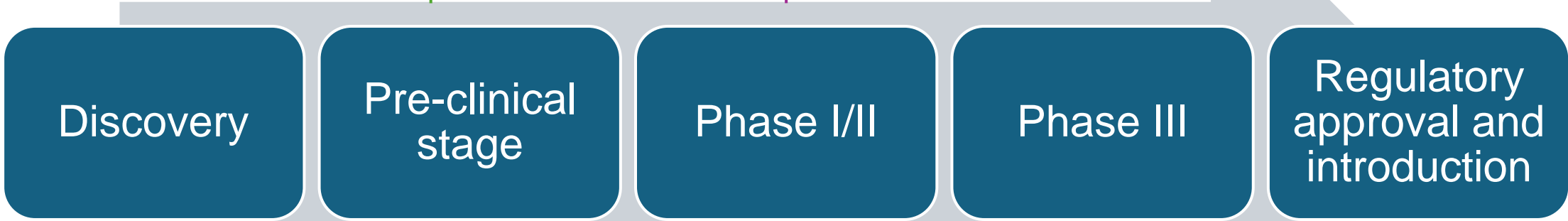


Purified protein subunit, peptide, lipooligosaccharide, mixed OMV and protein subunit

NIH/Intravax/Therapyx
OMV+IL2
NGoXIM

4CMen B trials

GSK GMMA
NCT05630859



Contents lists available at [ScienceDirect](https://www.sciencedirect.com)

Vaccine

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

Conclusions



- Urgent need for a vaccine to prevent gonorrhoea esp. in LMIC
- Observational studies show reductions in gonorrhoea of 30-59% in OMV-based MenB OMV vaccinated populations
- Molecular and pre-clinical studies of 4CMenB provide evidence of biological plausibility
- Trials in progress to evaluate 4CMenB for prevention of gonorrhoea
 - Results expected 2025-26
- Modelling suggests even a vaccine with relatively low efficacy could have a population impact
- Need to anticipate potential trial results and generate data on acceptability, demand, and potential 4CMenB implementation strategies in countries with overlapping epidemics

Acknowledgements

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