

Update on gonococcal and chlamydial vaccine development

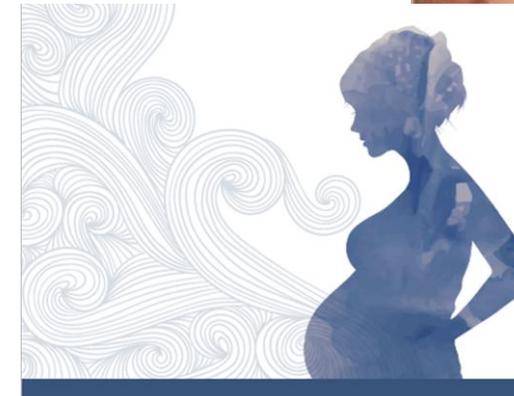
Dr Sami Gottlieb

WHO PDVAC Meeting

7 October 2025

Gonococcal infection: range of adverse effects on sexual and reproductive health

- Gonorrhoea: **common bacterial STI** caused by *Neisseria gonorrhoeae*
 - Genital symptoms: urethritis, cervicitis
 - Often few or no symptoms
- Disease consequences **disproportionately affect women and their neonates**
 - Pelvic inflammatory disease, infertility, ectopic pregnancy, chronic pelvic pain
 - Adverse pregnancy outcomes and neonatal conjunctivitis
 - Increased risk of HIV acquisition and transmission



~82 million new cases of gonococcal infection globally

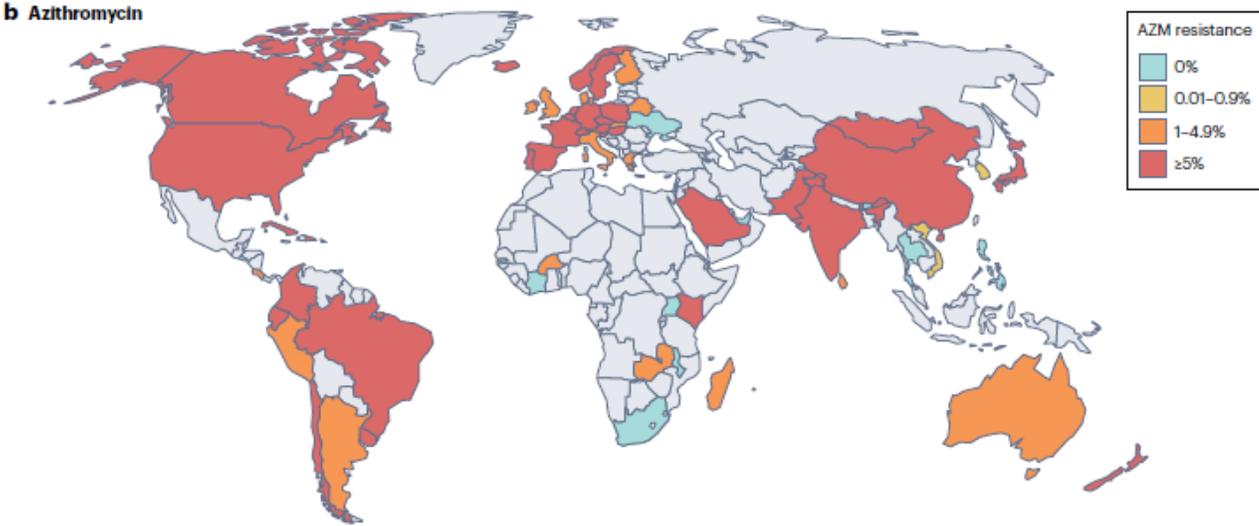
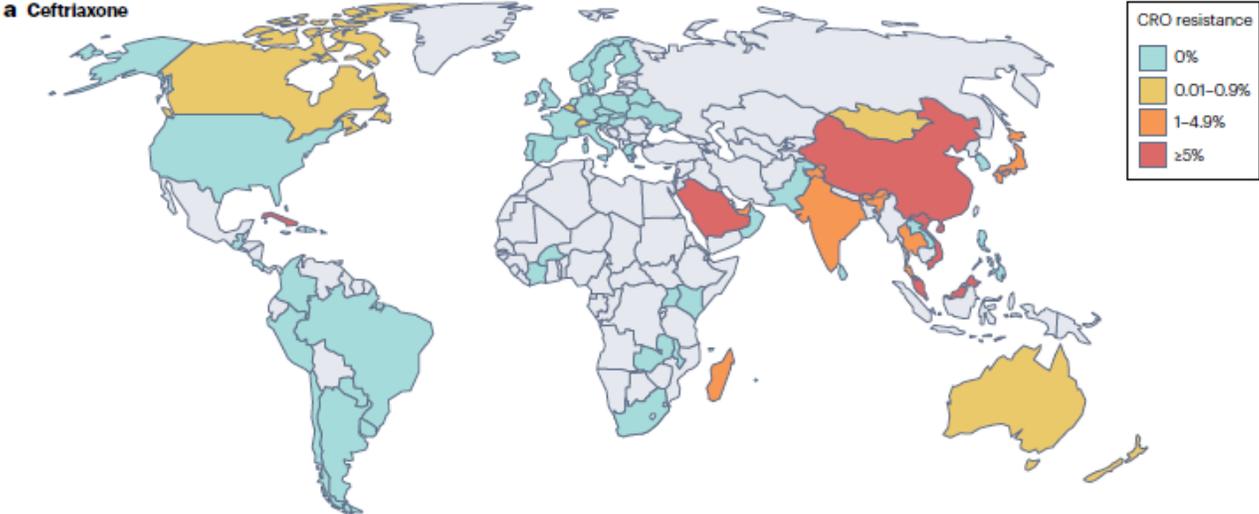
WHO estimates for 2020, among 15-49 year-olds



- Greatest burden in LMICs
- Higher in specific sub-populations, eg men who have sex w/ men (MSM)

Source: WHO 2021; <https://www.who.int/publications/i/item/9789240027077>

Gonorrhoea control threatened by AMR



- Increasing resistance to 3rd generation cephalosporins – last first-line drugs
- Increasing multidrug resistance – eg, with macrolides

Decreased susceptibility/resistance to ceftriaxone and azithromycin in *N. gonorrhoeae*, WHO Gonococcal Antimicrobial Surveillance Project

Explore the full findings in EGASP's 2023 report.



Source: Jensen and Unemo, 2024. WHO GASP data through 2020

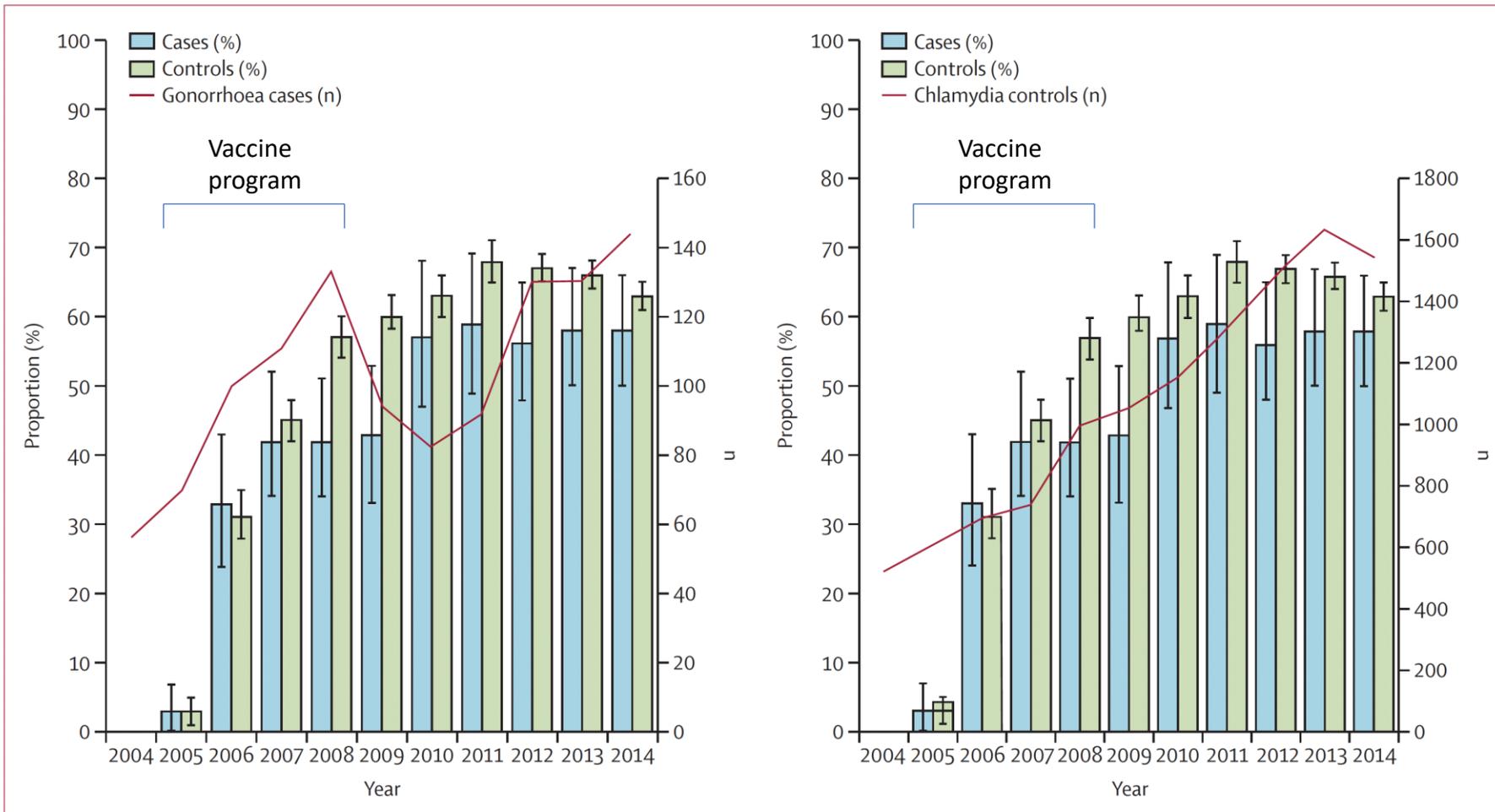
Historically, gonococcal vaccine development has been challenging

- Antigenic variability of *N. gonorrhoeae*
- Repeated infections without natural immunity



Limited focus on the field until some fortuitous epidemiologic observations

Neisseria meningitidis serogroup B (MenB) outer membrane vesicle (OMV) vaccines and gonorrhoea

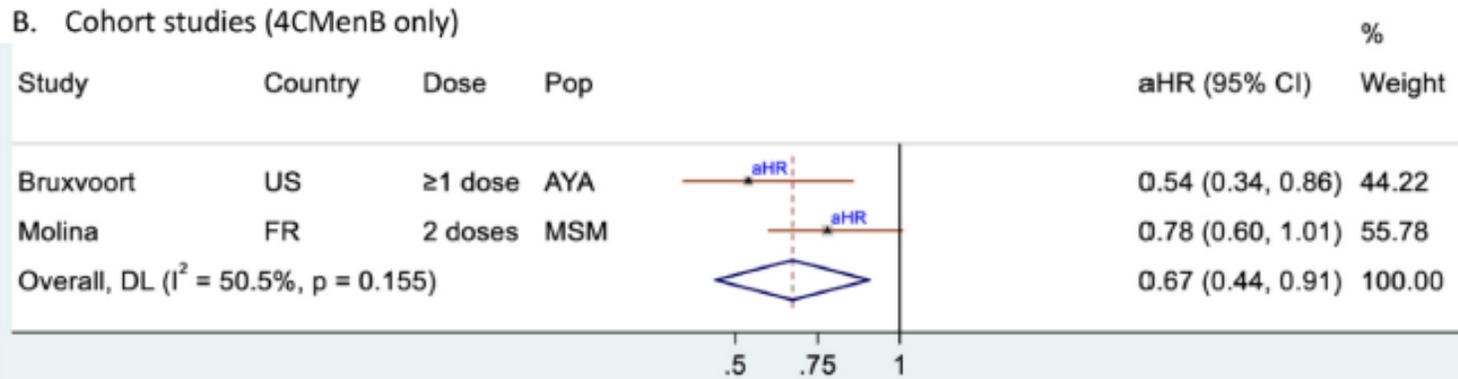
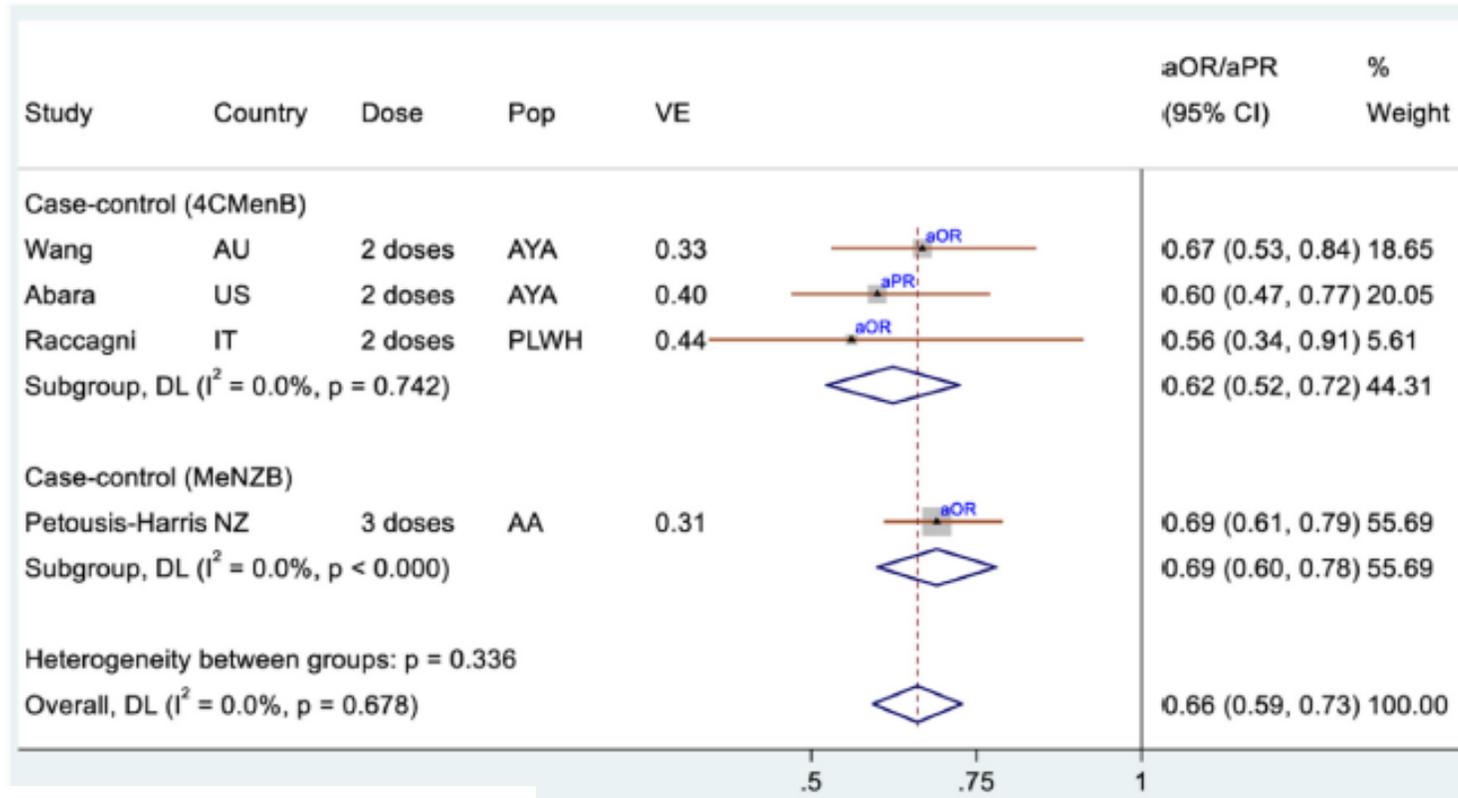


In New Zealand, after mass vaccination with MenB OMV vaccine, reported gonorrhoea cases appeared to decline

N. meningitidis has 80-90% homology with *N. gonorrhoeae*

Source: Petousis-Harris et al, Lancet, 2017

Evidence for MenB vaccine cross-protection



- At least 8 case-control or cohort studies and 1 small RCT
- Evaluating OMV-based MenB vaccines vs gonorrhoea
- 3 meta-analyses in last year

**Pooled estimates
~30 - 35% vaccine
effectiveness
against
gonorrhoea***

*Wang et al, 2024; Abara et al, 2025; Giorgiadis et al, 2025.

Long-Term Protection Against Invasive Meningococcal B Disease and Gonococcal Infection 5 Years After Implementation of Funded Childhood and Adolescent 4CMenB Vaccination Program in South Australia: An Observational Cohort and Case-Control Study

Bing Wang,^{1,2} Lynne Giles,^{2,3,⊙} Prabha Andraweera,^{1,2,⊙} Mark McMillan,^{1,2,⊙} Rebecca Beazley,⁴ Sara Almond,⁴ Noel Lally,⁴ Charlotte Bell,⁴ Louise Flood,^{4,⊙} James Ward,⁵ and Helen Marshall^{1,2}

¹Vaccinology and Immunology Research Trials Unit, Women's and Children's Health Network, Adelaide, South Australia, Australia; ²Robinson Research Institute and Adelaide Medical School, The University of Adelaide, Adelaide, South Australia, Australia; ³School of Public Health, The University of Adelaide, Adelaide, South Australia, Australia; ⁴Communicable Disease Control Branch, SA Health, Adelaide, South Australia, Australia; and ⁵UQ Poche Centre for Indigenous Health, University of Queensland, Brisbane, Queensland, Australia

Downloaded from <https://iaa>

Recent evidence related to duration of cross-protection

- Publicly funded adolescent MenB vaccination program in South Australia, started in 2018
- Evaluation published in July 2025:
 - 2-dose VE of 42% (34%-49%) within 5 years of vaccination
 - No significant protection thereafter (VE -6%, -45%-22%)

Wang B et al, CID, 2025.

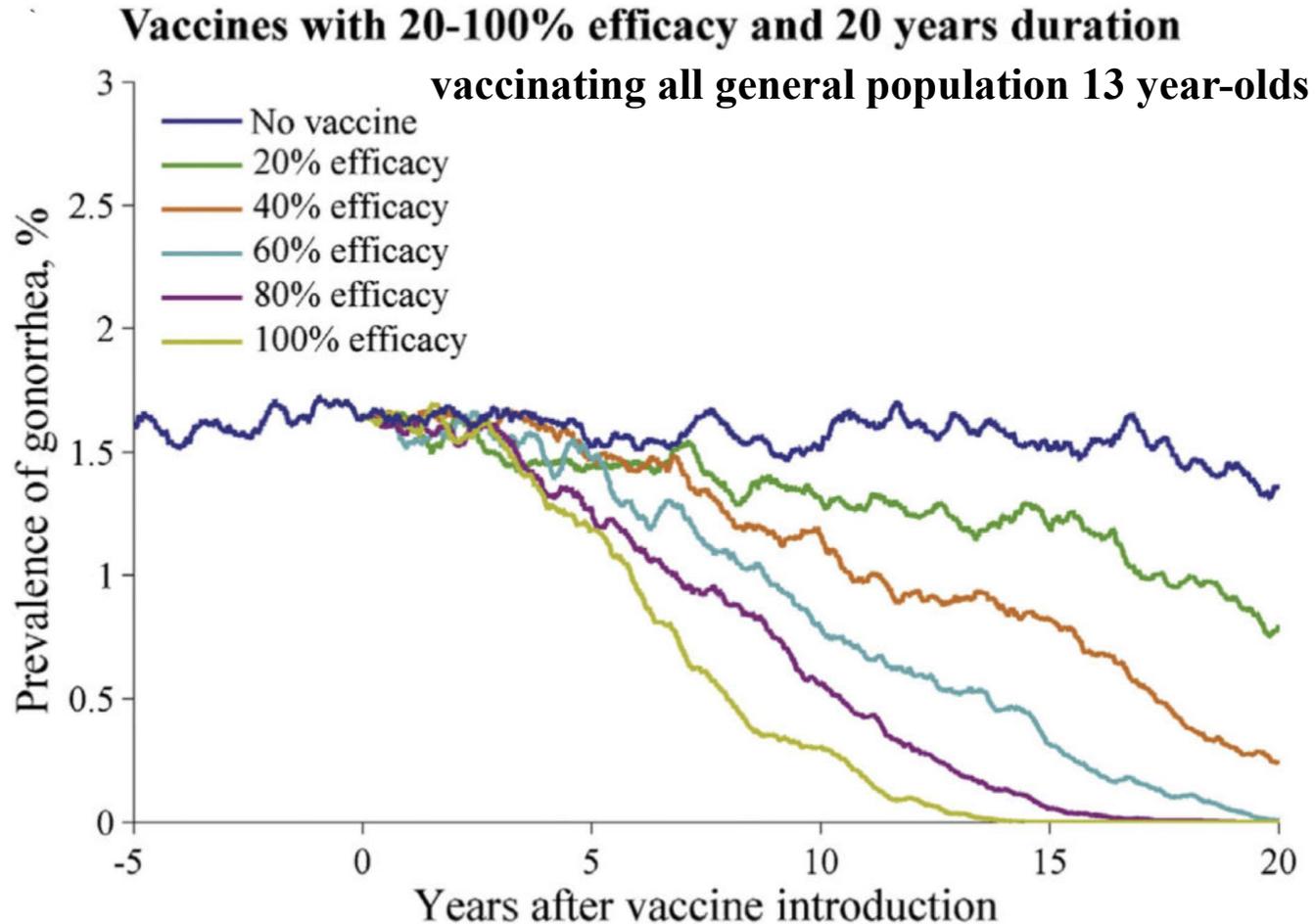
Ongoing clinical trials with 4CMenB

Trial number	Study name	Location, numbers	Expected completion
ACTRN126190 01478101	MenGO: Does the licensed meningococcal vaccine Bexsero® provide cross-protection against gonorrhoea?	Australia 130	2025
NCT04415424	GoGoVax: Efficacy study of 4CMenB Bexsero® to prevent gonorrhoea infection in gay and bisexual men	Australia 730	2025
NCT05766904	Efficacy Trial on Meningococcal B Vaccine for Preventing Gonorrhea Infections	Hong Kong 150	2025
NCT04350138	Safety and efficacy study of meningococcal group B vaccine rMenB+OMV NZ Bexsero to prevent gonococcal infection	USA, Thailand, (Malawi) 2,200	2026
NCT06446752	BIYELA: Efficacy of Bexsero in Preventing Gonococcal Infection Among South African Cis-Gender Women	South Africa 1100	2026
NCT05294588	Efficacy of Immunization With 4C-MenB in Preventing Experimental Urethral Infection With Neisseria Gonorrhoeae	USA 140	2028

4CMenB (Bexsero, GSK): commercially available vaccine with OMV component
+ 3 additional recombinant antigens

Source: <https://clinicaltrials.gov>
<https://www.anzctr.org.au/>

Models of gonococcal vaccine impact



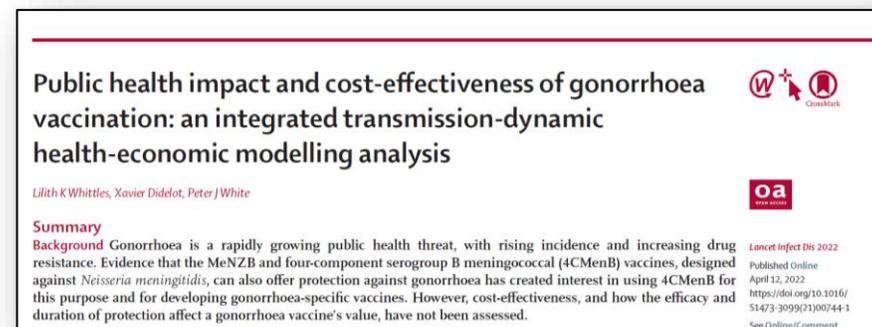
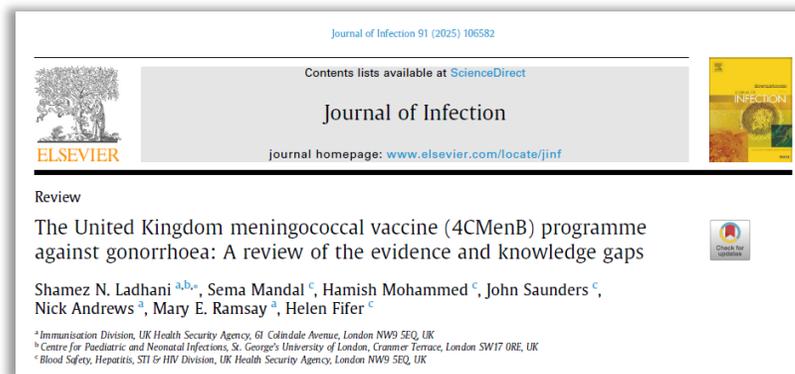
- Even vaccine with limited efficacy (~30%) could have substantial impact on gonorrhoea if high uptake
 - Targeted vaccination of MSM
 - Adolescent vaccination
- Depends on duration of protection: with shorter duration, need higher efficacy
- Vaccines can delay or prevent AMR

Figure: Craig et al, Vaccine, 2015.

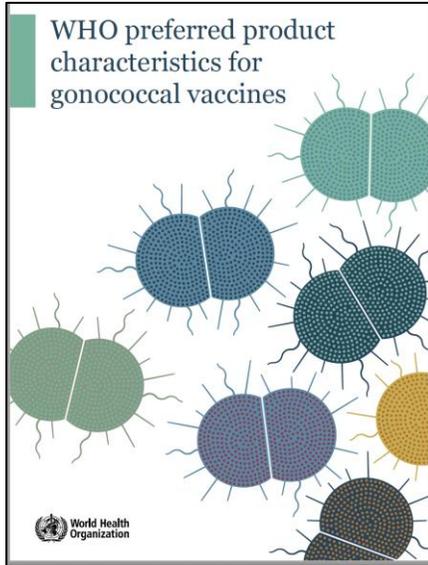
Review of models: Padeniya et al, Vaccine 2024.

UK recommends 4CMenB vaccine for people at highest risk

- In Aug 2025, UK began offering 4CMenB through sexual health services to small subset at high-risk (bact STI in last yr, >5 partners in past 3 mos)
 - 4CMenB already in UK National Immunization Programme
 - UK-specific modelling showed that given concentrated epidemic there, such a program could reduce pop-level incidence and be cost-effective
- Planned follow-up will assess vaccine uptake and effects on GC infection rates



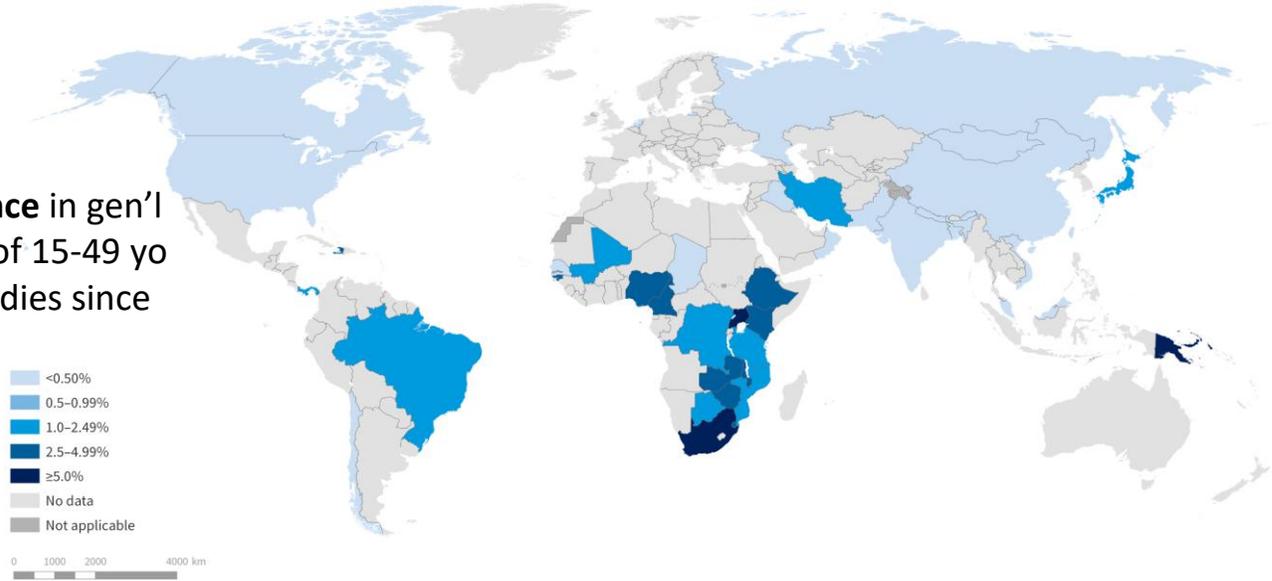
WHO PPCs for gonococcal vaccines



- **Target populations**
 - Young people = adolescents (10-19 yrs) and young adults (20-24 yrs)
 - Specific populations at higher risk for GC infection
- **Considerations for MenB use**
 - A lower efficacy could be acceptable for broadening use of existing MenB vaccines for GC infection versus standalone GC vaccines
 - Expanding indications of a MenB vaccine to include GC prevention could change cost-effectiveness and potentially affect decisions to introduce it in more countries and populations
 - Key consideration is overlap in epidemiology of the two conditions and where MenB OMV vaccines are already being used

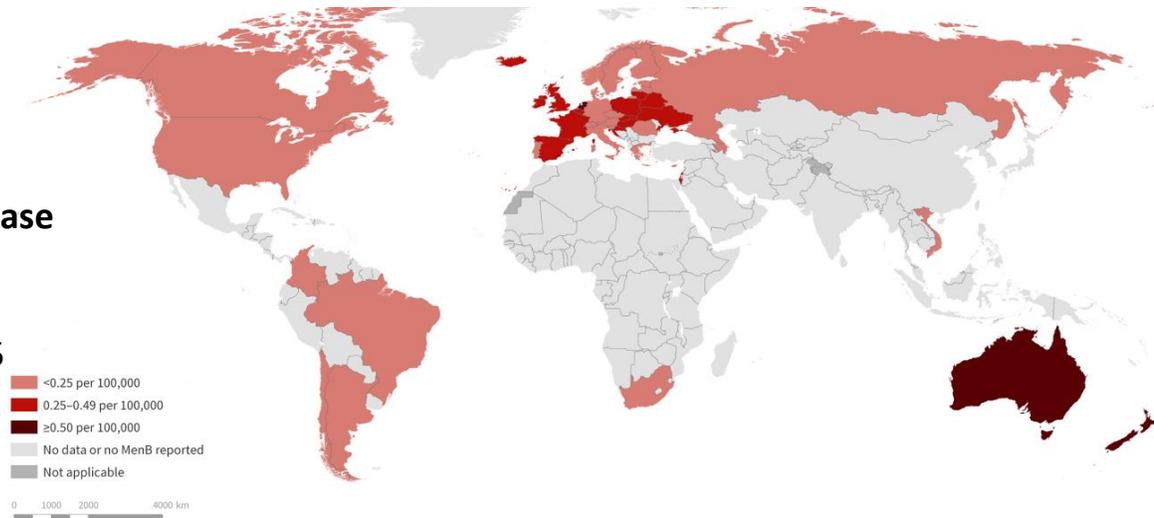
Epidemiology of gonorrhoea and MenB disease

GC prevalence in gen'l population of 15-49 yo women; studies since 2015



- HICs w higher MenB incidence have low gonorrhoea prevalence
- LMICs w higher gonorrhoea prevalence have no MenB data or low incidence
- Some settings w overlap (eg, Brazil, SA)
- Many countries lack data

Invasive MenB disease incidence/100,000
Most recent annual estimate since 2015



From reviews of country data for:

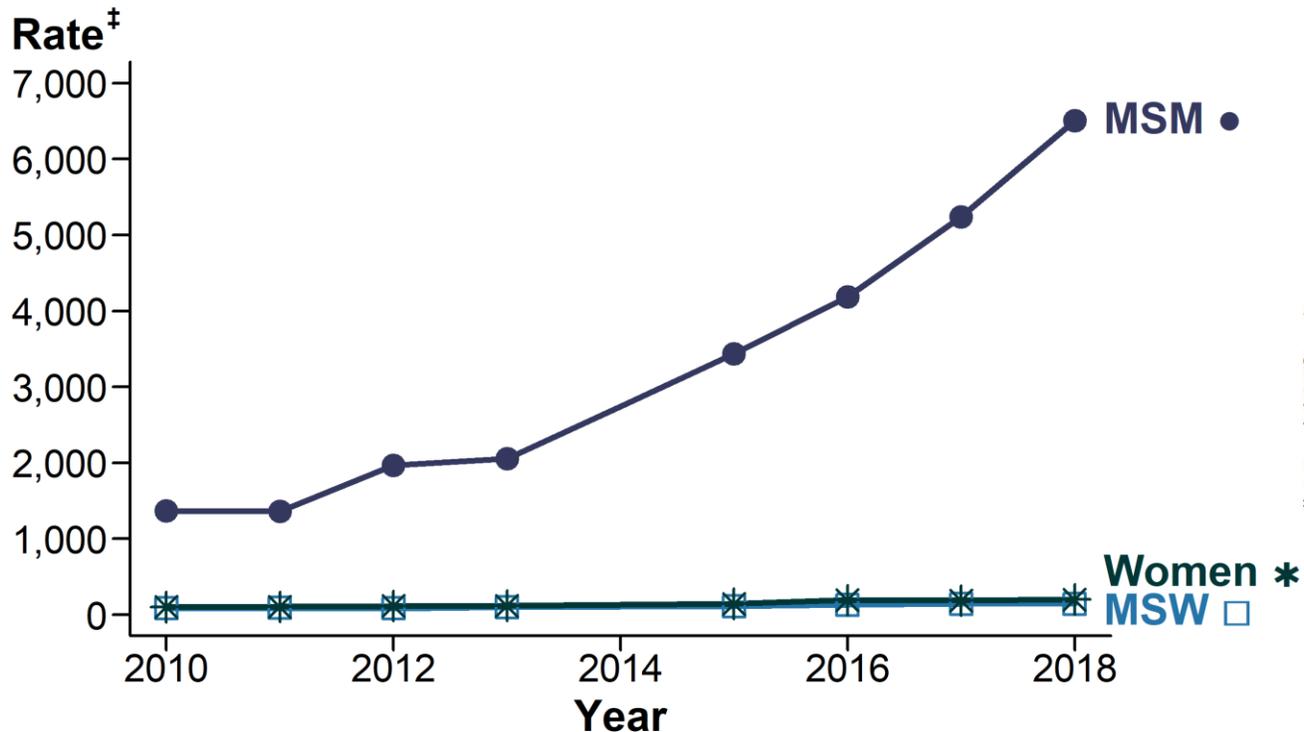
- WHO global estimates (Jane Rowley)
- Global Meningitis Initiative (Dominique Caugant)

Preliminary, unpublished data; please do not circulate

In many countries: low general population rates, but high rates in specific subpopulations

Figure 26. Gonorrhea — Estimated* Rates of Reported Gonorrhea Cases by MSM, MSW, and Women, STD Surveillance Network (SSuN)[†], 2010–2018 , USA

MSM = men who have sex with men
MSW = men who have sex with women



Source: <https://www.cdc.gov/std/stats18/default.htm>

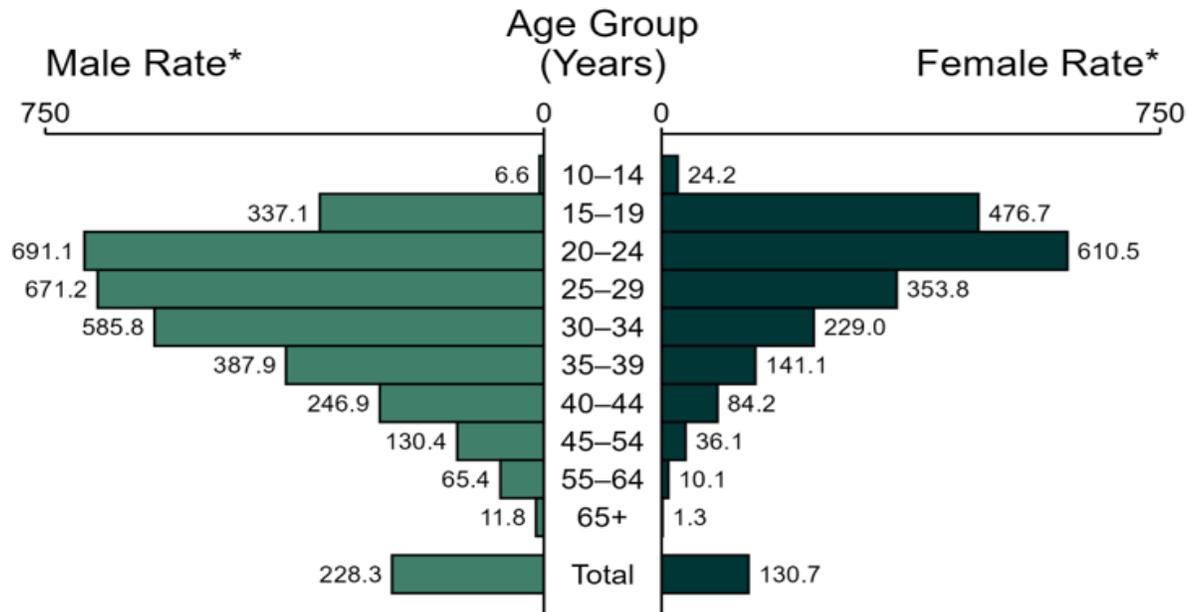
* Estimates based on interviews among a random sample of reported cases of gonorrhea (n=21,417); cases weighted for analysis. Data not available for 2014; 2013–2015 trend interpolated; trends lines overlap for MSW and women in this figure.

[†] Sites include Baltimore, Philadelphia, New York City, Washington State, San Francisco, and California (excluding San Francisco).

[‡] Per 100,000.

Age distribution of gonococcal infections

Gonorrhea — Rates of Reported Cases by Age Group and Sex, United States, 2023

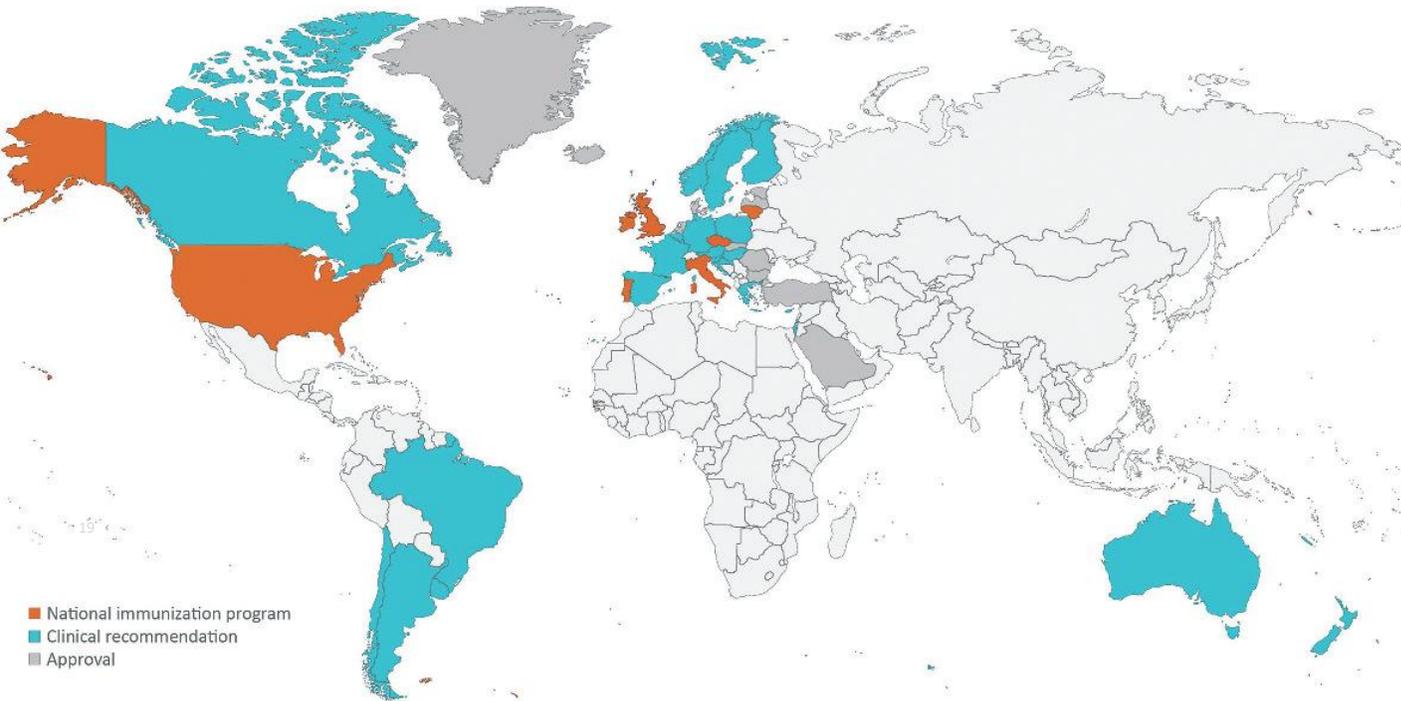


* Per 100,000

NOTE: In 2023, 4,005 gonorrhea cases among men (1.1%) and 2,293 cases among women (1.0%) had missing or unknown age. These cases are included in the total rates.

- In general populations, **peak GC incidence typically at age 20-24 yrs**
- Incidence can extend into older age groups for higher-risk populations
- For **MenB disease**, highest rates are **typically in infants**
- MenB disease in **adolescents/young adults** a concern in some countries

Countries with varying degrees of 4CMenB vaccine implementation, 2021



- Registered in 45 countries
- 33 countries: clinical recommendations
- 9 countries include in NIP

	Infant	Child	Adolescent	High risk	Outbreak control	Funding
Andorra	● □					Infant NIP
Argentina				● □		
Australia	● □	● □	● □	● □		RIP and high risk
Austria	● □	● □	● □	● □		
Belgium	○ □	○ □	○ □	● □		
Brazil	● △	● △	● △	● △		
Canada	○ □	○ □	○ □	● □	● □	High risk and outbreak control
Chile	● □			● □		High risk
Croatia				● □		
Cyprus	● △	● △	● △	● △		
Czech Republic	● □	● □	● □	● □	● □	Infant and adolescent NIP
Finland				● □	● □	
France	● □			● □	● □	High risk and outbreak control
Germany				● □	● □	High risk
Greece	● □			● □	● □	
Hungary	● □	● □	● □	● □		
Ireland	● □			● □	● □	Infant NIP and high risk
Israel	● □			● □	● □	High risk
Italy	● □	● △		● □		Infant NIP and high risk
Lithuania	● □			● □		Infant NIP
Luxembourg				● □	● □	
Malta	● □					Infant NIP
New Zealand				● □		
Norway				● □	● □	
Poland	● □			● □		High risk
Portugal	● □	○ △	○ △	● □	● □	Infant NIP and high risk
San Marino	● □			● □		Infant NIP and high risk
Slovenia				● □		High risk
Spain	● △			● □	● □	Infant RIP, high risk and outbreak control
Sweden				● □		
United Kingdom	● □			● □	● □	Infant NIP, high risk and outbreak control
Uruguay				● □	● □	
USA			☆ □	● □	● □	Adolescents, high risk and outbreak control

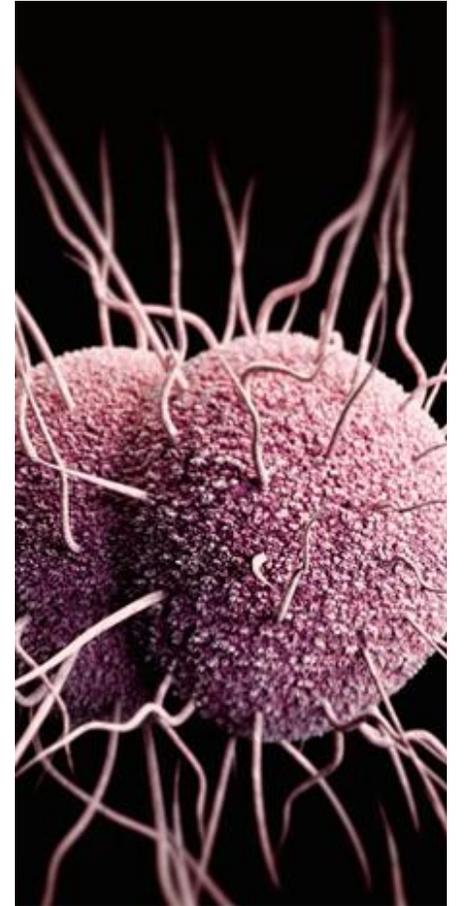
Legend ● NIP ☆ Vaccination based on shared clinical decision making ● Recommendation ○ Recommended on individual basis □ Recommended by government department of health △ Recommended by medical societies

Results of RCTs plus real-world assessments of MenB programs will inform value/cost-effectiveness of broader implementation

- In settings or subpopulations with high GC prevalence/incidence, MenB vaccines might be implemented for gonorrhoea alone, independent of MenB
- In settings with both GC and MenB, added protection against GC could tip the balance in terms of cost-effectiveness to decide to introduce
- Where MenB vaccine target populations might already include young people or key populations, vaccinating for both would be straightforward; duration of protection will be important
- Communication around vaccines clearly associated with an STI may be challenging; meningitis may be perceived as less stigmatizing

Immunologic data from MenB RCTs will also inform development of more efficacious GC-specific vaccine

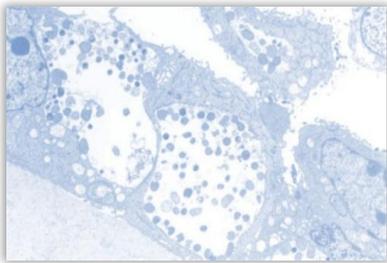
- Only one GC-specific vaccine has been in clinical development in recent years (NgG, GSK) but product not being taken forward
- Balance of using an imperfect MenB vaccine vs investing in a standalone GC vaccine may depend on increasing AMR, level of efficacy, cost of GC vaccine
- Ideally, would have combined gonococcal-chlamydial vaccine (or another adolescent vaccine)



Chlamydia trachomatis infection

- Urogenital (serovars D-K)
 - Similar disease outcomes and often co-infection with gonorrhoea
- Ocular (serovars A-C)
 - Trachoma responsible for blindness or visual impairment in 1.9 million people

Most common bacterial STI worldwide



Important cause of infertility



Leading infectious cause of blindness



103 million people live in trachoma endemic areas



Disproportionately affects adolescents



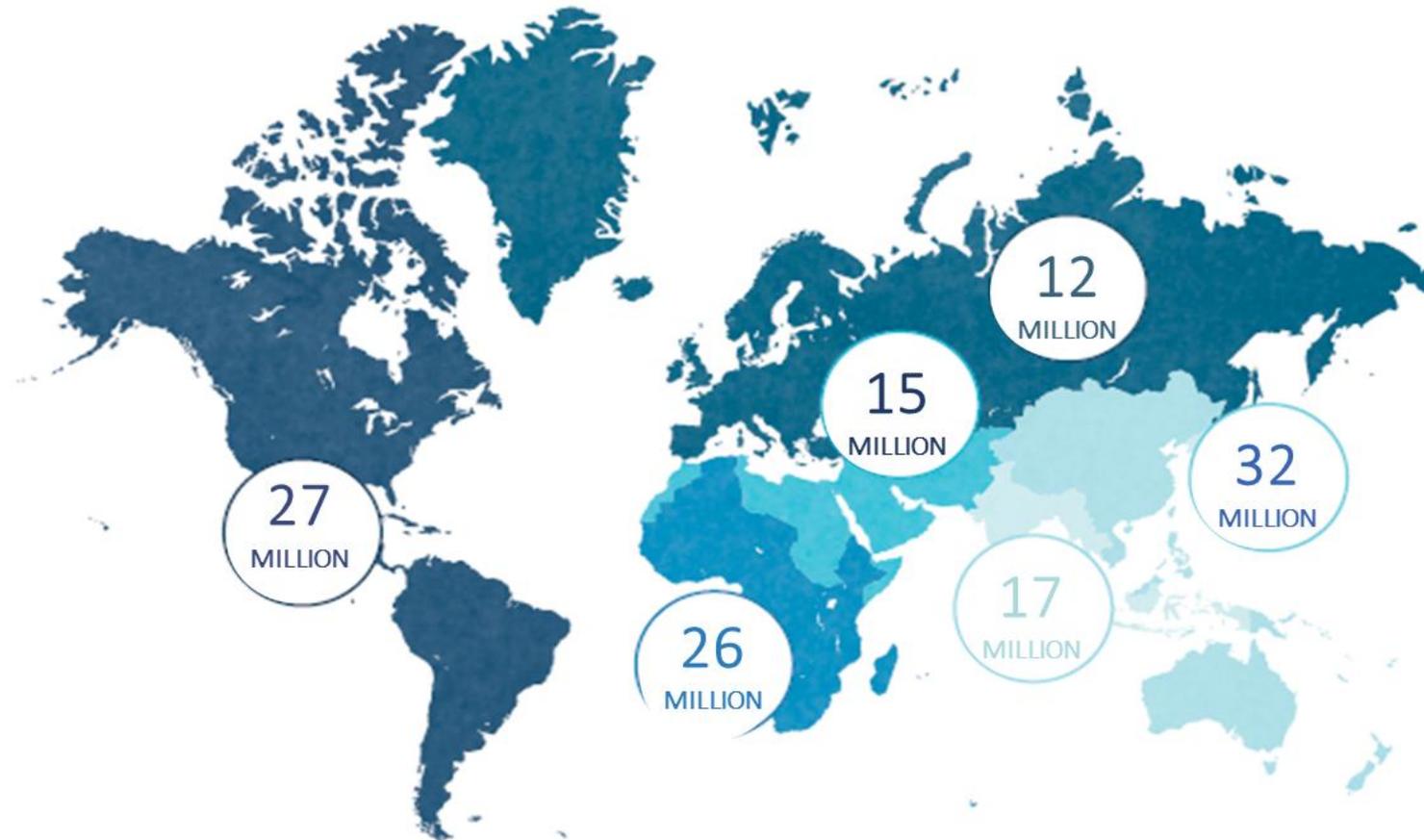
Control programs hard to bring to scale



- LGV (serovars L1-L3)
 - Lymphogranuloma venereum
 - Relatively uncommon

~129 million new cases of chlamydial infection globally

WHO estimates for 2020, among 15-49 year-olds



Source: WHO 2021; <https://www.who.int/publications/i/item/9789240027077>

Until this year, only one chlamydial vaccine candidate had been under clinical evaluation in the past decade

- CTH522 (Statens Serum Institut), based on the chlamydial MOMP, completed Phase 1 studies for both genital and ocular formulations
- Safe and induced significant levels of neutralizing antibodies
- Robust cellular response and levels of vaginal IgG and IgA; ocular IgA

Safety and immunogenicity of the chlamydia vaccine candidate CTH522 adjuvanted with CAF01 liposomes or aluminium hydroxide: a first-in-human, randomised, double-blind, placebo-controlled, phase 1 trial

Sonya Abraham*, Helene B Juel*, Peter Bang, Hannah M Cheeseman, Rebecca B Dohn, Tom Cole, Max P Kristiansen, Karen S Korsholm, David Lewis, Anja W Olsen, Leon R McFarlane, Suzanne Day, Sara Knudsen, Kjersti Moen, Morten Ruhwald, Ingrid Kromann, Peter Andersen, Robin J Shattock, Frank Follmann

An investigation of trachoma vaccine regimens by the chlamydia vaccine CTH522 administered with cationic liposomes in healthy adults (CHLM-02): a phase 1, double-blind trial



Katrina M Pollock*, Álvaro H Borges*, Hannah M Cheeseman, Ida Rosenkrands, Kirstine L Schmidt, Rie E Søndergaard, Suzanne Day, Abbey Evans, Leon R McFarlane, Jennifer Jaypooranachandran, Fahimah Amini, Per Skallerup, Rebecca B Dohn, Charlotte G Jensen, Anja W Olsen, Peter Bang, Tom Cole, Joanna Schronce, Nana-Marie Lemm, Max P Kristiansen, Peter L Andersen, Jes Dietrich, Robin J Shattock, Frank Follmann

Summary

Background There is no vaccine against the major global pathogen *Chlamydia trachomatis*; its different serovars cause trachoma in the eye or chlamydia in the genital tract. We did a clinical trial administering CTH522, a recombinant version of the *C trachomatis* major outer membrane molecule, in different dose concentrations with and without adjuvant, to establish its safety and immunogenicity when administered intramuscularly, intradermally, and topically into the eye, in prime-boost regimens.

Lancet Infect Dis 2024
Published Online
April 11, 2024
[https://doi.org/10.1016/S1473-3099\(24\)00147-6](https://doi.org/10.1016/S1473-3099(24)00147-6)
See Online/Comment

Chlamydial mRNA vaccine (Sanofi) fast-tracked by FDA and started Phase 1/2 trial in March 2025

Active, not recruiting ⓘ

Phase 1/2 Study of Chlamydia Trachomatis mRNA Vaccine in Adults Aged 18 to 29 Years

ClinicalTrials.gov ID ⓘ NCT06891417

Sponsor ⓘ Sanofi

Information provided by ⓘ Sanofi (Responsible Party)

Last Update Posted ⓘ 2025-07-20

- Evaluating safety, immunogenicity, and efficacy in seronegative and seropositive adults aged 18-29 years
- Expected completion Jan 2028

Summary

- Public health need for vaccines against gonococcal infection, particularly due to AMR
- Ongoing trials of MenB vaccines to prevent gonococcal infection will help define path forward for use of these vaccines for both infections
- Delineating public health value in terms of both pathogens is critical
 - Collecting better data on both conditions
 - Understanding community wishes and needs early on
 - Modelling impact, cost-effectiveness across both conditions
- Will also pave the way toward more efficacious gonococcal specific vaccines
- Chlamydia is an important problem for SRH/adolescent health in all settings and new clinical development activity for vaccines



Thank you!



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