



## Review

# The United Kingdom meningococcal vaccine (4CMenB) programme against gonorrhoea: A review of the evidence and knowledge gaps



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## SUMMARY

On 01 August 2025, the United Kingdom became the first country in the world to implement a targeted immunisation programme using a meningococcal vaccine (4CMenB) for protection against gonorrhoea. 4CMenB is a recombinant, protein-based vaccine licensed for prevention of serogroup B meningococcal disease but, because *Neisseria meningitidis* is genetically closely related to *Neisseria gonorrhoeae*, observational studies estimate that the vaccine also provides some (30–41%) protection against gonorrhoea. Given the rising incidence of gonorrhoea and increasing antimicrobial resistance, the UK programme will offer 4CMenB through specialist sexual health services clinics primarily to gay, bisexual and other men who have sex with men (GBMSM) who are at high risk of infection. A comprehensive national surveillance programme is in place to assess vaccine uptake as well as effectiveness and impact of vaccination on symptomatic disease, asymptomatic infection, recurrent infections, co-infections with other sexually transmitted infections and duration of protection. Microbiological surveillance will monitor trends in antimicrobial resistance and help elucidate mechanisms of vaccine protection, including identification of potential antigenic targets for next-generation vaccines. It is hoped that the data collected will provide an evidence base for other countries considering implementing a similar immunisation programme for their populations at high risk of gonorrhoea.

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## The UK immunisation programme against gonorrhoea

The United Kingdom is the first country to implement a targeted national immunisation programme against gonorrhoea for populations at high risk of infection. From 01 August 2025, gay, bisexual and other men who have sex with men (GBMSM) at high risk of gonorrhoea are offered two doses of the 4CMenB (Bexsero®) vaccine.<sup>1</sup> The programme is being offered on an opportunistic basis through specialist sexual health services (SHS) alongside the other vaccines (hepatitis A, hepatitis B, human papillomavirus (HPV) and mpox) already offered in SHS.<sup>2</sup> In England, GBMSM at high risk of gonorrhoea are defined as those with a bacterial sexually transmitted infection (STI) in the previous 12 months and/or reporting

five or more sexual partners in the previous three months.<sup>2</sup> Other UK nations are using similar criteria to identify eligible GBMSM for their programmes.<sup>2</sup> Although there are no other groups with similarly high gonorrhoea incidence as the eligible GBMSM, sexual health clinic professionals may perform individual risk assessment and consider the offer of 4CMenB to individuals with a similar incidence; this may include some sex workers and transgender women.<sup>2</sup> Health economic modelling estimates that, even with moderate efficacy for a short duration, a vaccine programme targeting populations at high risk could be cost-saving to the UK National Health Service (NHS).<sup>3</sup> This programme has been highly anticipated by the community, healthcare professionals, professional bodies and sexual health charities.<sup>4</sup>

Here we review gonococcal disease, the vaccine, and the potential impact of the proposed immunisation programme. We also discuss the evidence gaps that the programme will aim to address to support national guidance, health economic modelling, potential expansion to other risk-groups and the long-term sustainability of the programme.

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## Search methodology

References for this review were identified through a literature search conducted through PubMed using the search terms “gonorrhoea”, “gonorrhea”, “gonorrhoeae”, “gonococcal”, “Neisseria”, “gonococcal vaccine”, “meningococcal vaccine”, “outer membrane vesicle”, “OMV” and “4CMenB”. Relevant articles published in English until 15 July 2025 were included and references within the articles were also reviewed. The websites of the World Health Organization (WHO), UK Health Security Agency (UKHSA) and NHS England were also reviewed, along with an online search for news articles and press releases relating to gonorrhoea and prevention through vaccination.

## Gonorrhoea

Gonorrhoea is a bacterial STI caused by the Gram-negative diplococcus, *Neisseria gonorrhoeae*, that affects the urethra, cervix, rectum, pharynx and eyes.<sup>5</sup> Humans are the only known host and reservoir. Gonorrhoea typically spreads through condomless vaginal, oral or anal sex, or mucosal exposure to infected secretions. The infection may be asymptomatic or symptoms may develop from 1 to 10 days following exposure.<sup>5,6</sup> Symptoms are more common with penile urethral infections, while endocervical, rectal and pharyngeal infections are more likely to be asymptomatic. Urogenital symptoms include thick green or yellow discharge from the penis or vagina and pain on urination.<sup>6</sup> Anorectal infections may be associated with purulent discharge, bleeding, itchiness, soreness and painful bowel movements. Left untreated, complications may include scrotal swelling, urethral stricture, pelvic inflammatory disease, ectopic pregnancy and infertility. Rarely, localised infection can extend systemically to cause disseminated disease.<sup>6</sup> Gonococcal infection can also increase the risk of acquiring other STIs, including HIV.<sup>5</sup> Concerningly, gonococci are becoming increasingly resistant to all classes of antibiotics used to treat the infection, with some countries already reporting emergence of extensively-drug resistant gonococcal strains.<sup>7</sup> Current empiric treatment for gonorrhoea includes once dose of intramuscular ceftriaxone.<sup>8</sup> Oral cefixime in combination with oral azithromycin is a second line option. Most cases of gonorrhoea can be prevented with consistent and correct condom use during every sexual encounter.<sup>9</sup>

In 2020, the WHO estimated that there were more than 82 million new gonorrhoea infections in adults aged 15 to 49 years.<sup>10</sup> In England, new gonorrhoea diagnoses have increased nearly three-fold in the last decade, peaking at more than 85,000 cases in 2023, with cases declining by 15.9% to 71,802 in 2024. This compares with 9535 infectious syphilis diagnoses, 168,889 chlamydia diagnoses, 25,056 first episode genital warts diagnoses and, overall, 364,750 new STI diagnoses in 2024.<sup>11</sup> GBMSM account for around half the diagnosed gonorrhoea cases in England. Globally, gonorrhoea incidence may be up to 10 times higher in GBMSM than WHO estimates for adult men aged 15–49 years.<sup>12</sup> Among GBMSM, risk factors for rectal gonorrhoea include number of male partners, receptive and insertive condomless anal sex acts as well as the number of anal receptive acts, while urethral gonococcal infections are associated with both insertive and receptive anal sex (vs. receptive only) and number of male partners. Given the growing global problem of rising gonorrhoea incidence alongside increasing antimicrobial resistance, the WHO has set ambitious targets to reduce the global burden of gonorrhoea by 90% by 2030, compared to 2020 baseline, through prevention, diagnosis, and treatment strategies.<sup>13</sup>

## Prevention through vaccination

There are currently no licensed vaccines for prevention of gonorrhoea, despite decades of intensive research and clinical trials.<sup>14</sup>

Reasons for the lack of success in developing an effective gonococcal vaccine include the high surface antigen variability and expression, thus complicating the identification of target vaccine antigens, and the ability to suppress host immune responses, meaning that recurrent infections are common.<sup>15</sup> Consequently, defining correlates of protection using immunological methods has been challenging.<sup>14</sup> Additionally, being an exclusively human pathogen, there have been no established animal infection models to study natural infection, immunity and responses to investigational vaccine candidates.<sup>14</sup> Despite this, anecdotal reports from countries, such as Norway and Cuba, where vaccines developed from the outer membrane vesicles (OMV) of the outbreak-associated group B (MenB) meningococcal strain were used to control local outbreaks of meningococcal disease, suggested that these vaccines might also provide some protection against gonorrhoea.<sup>16</sup> *Neisseria meningitidis* is genetically closely related to *Neisseria gonorrhoeae* and, therefore, the meningococcal OMV vaccines likely possessed common antigens that also provided some protection against gonorrhoea. These observations were subsequently confirmed in a retrospective observational case-control study in New Zealand where the MenB OMV vaccine (MenNZB) used to control their local MenB outbreak was reported to be 31% protective against gonorrhoea in 15–30 year-olds attending sexual health clinics.<sup>17</sup>

## 4CMenB and protection against gonorrhoea

MenNZB is one of the four components of a novel, broad-spectrum, recombinant protein-based MenB vaccine, which was licensed in 2013 for prevention of MenB invasive meningococcal disease (IMD). The other three components of 4CMenB include *Neisseria* adhesin A (NadA), factor H binding protein (fHbp), and *Neisseria* Heparin Binding Antigen (NHBA). 4CMenB has been safely given to millions of children and adults worldwide,<sup>18</sup> and is highly effective in preventing IMD caused by MenB and other meningococcal serogroups.<sup>19</sup> The vaccine is currently part of the UK infant immunisation programme which began in 2015, so the oldest vaccinated children will be 10 years old in 2025.<sup>20</sup> 4CMenB is not licensed for protection against gonorrhoea but the vaccine induces antibodies in humans that recognise gonococcal proteins.<sup>21</sup> In particular, NHBA is expressed on the surface of both *N. meningitidis* and *N. gonorrhoeae* and anti-NHBA antibodies induced by 4CMenB cross-react with gonococcal NHBA and contribute to the bactericidal response against *N. gonorrhoeae*.<sup>22</sup> Importantly, too, another licensed MenB vaccine (MenB-fHbp, Trumenba®), which is composed solely of recombinant fHbp protein without a meningococcal OMV, is not protective against gonorrhoea.<sup>23</sup> In terms of real-world data, regional 4CMenB immunisation programmes against meningococcal disease in different countries have consistently reported some protection against gonorrhoea in vaccinated compared to unvaccinated adolescents and young adults.<sup>16</sup> A 2024 systematic review and meta-analysis of published studies estimated a pooled vaccine effectiveness (VE) of meningococcal OMV vaccines against gonorrhoea of 34% (95%CI, 27–41%) in case-control studies and 33% (95%CI, 9–56%) in cohort studies.<sup>24</sup> The strongest real-world evidence comes from prospective surveillance in South Australia, where two 4CMenB doses in adolescents conferred 46.0% (95%CI, 36.3–54.2%) protection against gonorrhoea for at least 4 years.<sup>25</sup> More recently, the five-year VE against gonorrhoea was reported to be 41.8% (95%CI, 34.0–48.7%).<sup>26</sup> The only RCT evaluating 4CMenB protection against gonorrhoea involved GBMSM in France and estimated a 22% VE (95%CI, –1% to 40%;  $P=0.06$ ) against the first episode of gonorrhoea.<sup>27</sup> The trial was, however, powered for detection of 30% VE and was stopped prematurely, thus reducing its power.<sup>28</sup> Notably, a lower VE of even 20% would still achieve cost-effectiveness thresholds in the UK programme.<sup>28</sup> Additionally, health economic evaluations indicate

that targeted 4CMenB vaccination of GBMSM is cost-saving at any vaccine uptake level.<sup>29</sup>

### General population vs high risk populations

The French RCT involving GBMSM<sup>27</sup> does, however, raise important questions about whether the higher vaccine effectiveness reported in the South Australian adolescent programme<sup>25</sup> can be extrapolated to populations at higher risk.<sup>30</sup> By virtue of the eligibility criteria for the UK 4CMenB programme, GBMSM, especially those reporting multiple sexual partners in the previous three months, will have more frequent STI exposures, including gonorrhoea, than those reporting a single or fewer partners.<sup>31</sup> Since 4CMenB is only partially protective, there is an expectation that some vaccinated GBMSM will acquire gonorrhoea over time.<sup>31</sup> In the French RCT, for example, the incidence of first gonorrhoea episode was 58.3/100 person-years (103 events in 274 participants) in vaccinated participants and 77.1/100 person-years (122 events in 270 participants) in unvaccinated participants.<sup>27</sup> Rather than VE against first gonococcal infection, therefore, differences in the number of infections in vaccinated and unvaccinated participants might be a better measure of vaccine effectiveness in GBMSM. In south Australia, a second episode of gonococcal infection was 36.5% (95%CI, 4.3–57.9%) lower in vaccinated compared gonococcal cases during the first four years after vaccination,<sup>25</sup> and 27.0% (95%CI, 1.2–46%) during the first five years after vaccination,<sup>26</sup> highlighting the importance of monitoring the number of infections (rather using the first episode at the end-point) over a reasonably long time-period to allow capture of multiple infections in the same individuals.

### Natural infection, reinfection and vaccine-induced immunity

Natural infection does not appear to provide immunity, as *N. gonorrhoeae* is able to suppress adaptive immune responses and the killing mechanisms of innate immune cells,<sup>32</sup> which may explain why recurrent gonorrhoea is common.<sup>5</sup> At the same time, it remains unclear how natural gonococcal infection does not appear to provide any protection against reinfections, yet 4CMenB provides significant and measurable *albeit* moderate protection against gonorrhoea and reinfections, lasting for several years and beyond that predicted by measuring vaccine-induced antibodies.<sup>26</sup> Even more importantly, the interaction between natural infection, vaccination and immune responses remains poorly understood. In populations at high risk of gonorrhoea with frequent gonococcal exposure, such as the GBMSM eligible for the UK 4CMenB immunisation programme, VE might be lower because prior, recent and/or multiple exposures to *N. gonorrhoeae* may affect both risk of subsequent infections as well as vaccine-induced immune responses – and, consequently, vaccine effectiveness – compared to infection-naïve populations.<sup>14,33</sup> Additionally, the very high gonorrhoea incidence in populations at high risk increases the risk of active infection at the time of vaccination, which may also attenuate vaccine responses.<sup>12</sup> The UK programme recommends that eligible GBMSM should be offered vaccination even if attending SHS for diagnosis or treatment of STI, including gonorrhoea, on the basis that any reduction in vaccine responses with one vaccine dose should be countered by the other vaccine dose because of the two-dose schedule. The UK surveillance programme will aim to evaluate vaccine effectiveness in eligible GBMSM who are vaccinated during acute infection. However, vaccine immunogenicity studies in gonorrhoea-naïve, gonorrhoea-exposed and active gonorrhoea populations would provide a better understanding of infection immunology and help inform future vaccine recommendations. There are, however, no validated 4CMenB immunogenicity or bactericidal assays against gonorrhoea, although work is progressing in this field.<sup>34,35</sup>

As well as studies on immunogenicity and bactericidal activity, microbiological surveillance including comparison of strain types and genetic sequences of vaccine-associated antigens in gonococci isolated from vaccinated and unvaccinated individuals could also provide an insight into the mechanisms of protection provided by 4CMenB and potentially identify novel surface antigen targets for next-generation gonococcal vaccines.

### Vaccine perception, risk behaviour and vaccine uptake

Estimation of VE will also be affected by who takes up the offer of vaccination, vaccine perception and risk behaviour post vaccination. Measured VE will be lower if vaccine uptake is higher among those with the highest risk of gonorrhoea exposure unless this can be adjusted for by using prior STI infection rates. Additionally, despite clear messaging to continue to use condoms to protect against all STIs, vaccination may provide false reassurance of protection, potentially resulting in increased risk behaviour, which would increase their risk of gonorrhoea and reduce measured VE. Such risk compensation behaviour may be compounded by the contemporaneous rollout of doxycycline post-exposure prophylaxis (doxyPEP). Although doxyPEP is anticipated to primarily reduce syphilis and chlamydia infections by 70–80%, it may also prevent some gonococcal infections despite high tetracycline resistance among gonococcal strains,<sup>36</sup> which could complicate 4CMenB vaccine evaluation.

As well as assessing VE, the overall impact of the programme can be assessed by comparing gonorrhoea rates in the target population to the rates before implementation, to rates in other non-targeted groups who are not eligible for 4CMenB and to rates of other STIs with similar epidemiological patterns. This impact assessment could, however, be complicated by doxyPEP implementation disproportionately impacting chlamydia and syphilis incidence. High vaccine uptake would facilitate the assessment of vaccine impact should vaccine effectiveness against gonorrhoea be lower in eligible GBMSM. Reassuringly, in an online survey of >1000 GBMSM in November/December 2023, two-thirds of participants reported intention to have the vaccine and, notably, participants with markers of sexual risk and with uptake of other preventative interventions were more likely to take up the vaccine.<sup>37</sup>

Another concern is that, since 4CMenB only prevents around one in three infections, vaccinated individuals will likely still acquire gonorrhoea, albeit less frequently, and this experience could compromise vaccine confidence. This could potentially adversely affect uptake not only of 4CMenB but also of other vaccines that are offered through SHS. Studies that assess changes in risk behaviour, sexual activity and antimicrobial use after 4CMenB vaccination would provide useful insights to aid programme evaluation.

### Symptomatic vs asymptomatic infection

An important question that remains unanswered is whether 4CMenB also protects against asymptomatic infection in addition to symptomatic gonococcal disease. It is, for example, possible that vaccination transitions symptomatic disease to become paucisymptomatic or asymptomatic, which would allow for continued transmission. The primary objective of vaccination, however, is to prevent symptoms, which will reduce healthcare utilisation, in terms of the need for clinical assessment, diagnostic investigations and antibiotic prescriptions. In a recent study of gonococcal infections among 473 GBMSM (including 451 living with HIV) who had previously received two 4CMenB doses during 2017–23, the percentage of nucleic acid amplification test (NAAT) positive rectal gonococcal swab samples was 7.7% (76/957) after 4CMenB vaccination compared to 11.1% (51/456%) before vaccination. Those with rectal gonococcal infection were younger, more likely to have had a previous STI and had more sexual partners ( $P < 0.001$ ).<sup>31</sup> Notably, too,

rectal gonococcal infections in vaccinated individuals were less frequently symptomatic (34.2% vs 66.7%;  $P=0.001$ ) and more likely to have a negative gonococcal-specific culture (55.3% vs 19.6%;  $P<0.001$ ) compared with before vaccination.<sup>31</sup> A higher proportion with asymptomatic infection in vaccinated GBMSM could potentially lead to increased opportunities for transmission to others because symptomatic disease would usually prompt treatment and curtailment of infection. Conversely, the high proportion of infections that failed to produce a positive culture could indicate a lower bacterial load and, potentially, lower transmissibility.<sup>38</sup>

### Site of infection

*N. gonorrhoeae* can colonise the oropharynx, rectum, urethra or any combination of these sites, and infection can be symptomatic (especially at the urethral site) or asymptomatic (especially at the pharyngeal site). In the French RCT involving GBMSM, for example, 58% of the 302 gonorrhoea infections were pharyngeal, 56% were rectal and 11% were urethral, with a substantial proportion having infection at multiple anatomical sites,<sup>27</sup> but none of the published studies so far have been powered to assess VE by anatomical site of infection.<sup>24,39</sup> Pharyngeal infection, for example, is known to be more difficult to eradicate, even with effective antibiotics, compared to urethral or anorectal infection.<sup>40</sup> This has important implications for broadening the offer of vaccination to a wider population and achieving a sustainable reduction in gonococcal infection, transmission and symptomatic disease across the population.<sup>41</sup>

### Direct vs indirect protection

Studies to evaluate the effect of vaccination on gonococcal acquisition and/or elimination from oropharyngeal, anorectal or genitourinary sites in humans, in addition to studies assessing the severity and duration of symptoms in vaccinated individuals, would provide useful insight into the potential of the programme to induce direct and indirect (herd) protection. Interestingly, in a well-established mouse vaginal infection model, 4CMenB vaccination significantly accelerated clearance and reduced the gonococcal bacterial burden compared placebo.<sup>42</sup> The authors also found that 4CMenB administered subcutaneously induced vaginal and serum IgG1, IgG2a and IgA that cross-react with several gonococcal OMV proteins. In a large South Australian RCT in adolescents, too, 4CMenB had no effect on oropharyngeal carriage of disease-causing meningococci.<sup>43</sup> Notably, however, a significant reduction in carriage of non-encapsulated (usually commensal) meningococci was observed in vaccinated compared to unvaccinated adolescents.<sup>43</sup> It is postulated that the lack of polysaccharide capsule allows 4CMenB-induced bactericidal antibodies easier access to meningococcal surface antigens. Since *N. gonorrhoeae* is also non-encapsulated, it is possible that 4CMenB-induced antibodies will also eliminate gonococci from mucosal surfaces, such as the oropharynx and anorectum. Additionally, in Cuba, a meningococcal OMV vaccine developed to target a local MenB outbreak strain was implemented into their national immunisation programme in 1989 and, in contrast with other STIs, was associated with large declines in gonorrhoea incidence in vaccinated and unvaccinated age groups, postulated to be due to herd immunity.<sup>44</sup> These indirect observations have particularly important implications for the UK immunisation programme which primarily focuses on GBMSM, where reduction in carriage and interruption of transmission within sexual networks of men who have sex with men exclusively could have a much larger impact on disease rates in the target population beyond the individual direct protection offered by vaccination.

The large UK GBMSM cohort eligible for 4CMenB is also ideally placed to evaluate site-specific VE against gonorrhoea because of their high incidence of oropharyngeal, rectal and urethral infection.

In the UK, GBMSM with multiple sexual partners are offered three-monthly STI screening, which includes NAAT testing of anal swabs, throat swabs and urine for gonorrhoea.<sup>45</sup> The on-going testing recommendations when 4CMenB is implemented, will provide a unique opportunity to assess VE against symptomatic and asymptomatic gonococcal infection by anatomical site.<sup>41</sup>

### Duration of protection

A key question that can only be answered through long-term follow-up is the duration of protection, which will then inform the need for any boosters. Early 4CMenB immunogenicity RCTs identified rapid waning of vaccine-induced antibodies, suggesting limited duration of protection, even in adolescents.<sup>46</sup> Real-world surveillance, however, has shown that clinical protection continues for several years even after antibody waning. In South Australia, the adolescent programme remains highly effective against MenB IMD, whilst protection against gonorrhoea continues for at least five years after vaccination, although there is some evidence of waning protection over time. The large UK cohort of GBMSM who will be eligible for 4CMenB, estimated to account for around 15% of all GBMSM,<sup>3</sup> will not only allow VE estimates stratified by risk-groups within the eligible cohort but also duration of protection to help inform decisions about the need for and timing of any booster doses.

### Impact on antimicrobial resistance

A major concern in addition to rising gonorrhoea incidence is the increasing resistance to all classes of antibiotics used to treat the infection, with extensively-drug resistant gonorrhoea cases being reported in many parts of the world. Vaccination, even with partial protection, will reduce the burden of disease and, therefore, decrease antimicrobial use and contribute to antimicrobial stewardship. Whether vaccination of populations at high risk has any impact on overall gonococcal antibiotic resistance rates remains to be established. The UK 4CMenB programme for GBMSM will be sufficiently large to allow assessment of VE against antibiotic-susceptible and antibiotic-resistant strains. Such information could play an important part in decisions on future outbreak control strategies, where 4CMenB may provide additional protection during outbreaks associated with specific antibiotic-resistant gonococcal strains that are known to be susceptible to 4CMenB-induced antibodies.

### Protection against meningococcal disease

In addition to protection against gonorrhoea, the prevention of IMD by 4CMenB cannot be undervalued.<sup>26</sup> Although IMD is much less common in adults than in children, it is a very severe disease with high case fatality ratios and risk of long-term complications among survivors. Large IMD outbreaks associated with significant morbidity and mortality have occurred among GBMSM, with IMD incidence reaching 4–30 times higher than the general population.<sup>47–49</sup> Because most cases and outbreaks among GBMSM have been due to serogroup C, many countries recommend MenC or MenACWY, but not MenB, vaccination for GBMSM.<sup>48</sup> Although 4CMenB is licensed specifically for prevention of MenB disease, the vaccine can protect against other meningococcal serogroups if the strains possess 4CMenB-associated antigens on their cell surface.<sup>19</sup>

### Protection against sexually transmitted *N. meningitidis*

Over the past decade, there have been increasing reports of sexually transmitted *N. meningitidis*, including in England.<sup>50,51</sup> Sexually transmitted *N. meningitidis* is generally under-recognised and under-reported because the organism can cause syndromes, including urethritis and proctitis, that are clinically indistinguishable



from gonococcal infections.<sup>50</sup> Identification of Gram-negative diplococci on microscopy of urethral discharge from symptomatic individuals usually leads to the presumptive diagnosis of gonococcal disease and first line treatment for gonorrhoea is equally effective for both infections. Some meningococcal strains have adapted to colonise and infect the anorectal and urogenital tract by acquiring critical genes from gonococci that allow them to survive in anaerobic environments as well as their ability to lose their polysaccharide capsule and become increasingly resistant to common antibiotics.<sup>50</sup> Such strains are increasingly being detected as the cause of genital symptoms in different parts of the world, including the UK.<sup>52</sup> Further studies are needed to determine whether 4CMenB might also reduce STIs caused by such strains,<sup>53</sup> given that they – like the gonococci – no longer possess a polysaccharide capsule, thus potentially making them more susceptible to killing by vaccine-induced bactericidal antibodies.

### Future implications

The scale of the UK immunisation programme against gonorrhoea will allow collection of real-world data to help assess the protection offered by 4CMenB and answer important scientific, social and public health questions that go beyond the direct protection in vaccinated individuals. Demonstrating a significant impact on disease burden and healthcare utilisation in the target population could provide the data needed to inform the need for and timing of any boosters to provide longer-term protection. The UK programme could also potentially be widened to include other populations at high risk attending SHS, including but not limited to heterosexuals with a gonorrhoea or syphilis diagnosis in the previous 12 months, and sex workers irrespective of gender identity. The vaccine could also be used as part of the public health responses to gonococcal outbreaks where the circulating strain is known to be preventable by 4CMenB. Additionally, phenotypic and genomic surveillance of gonococcal strains in vaccinated compared to unvaccinated individuals could provide insight into antigens that are critical for protection, thus contributing to the development of more effective next-generation gonococcal vaccines.

The data collected through the UK programme can help to inform decisions to implement a similar vaccine programme in other countries. For example, the Galicia region of Spain has already used the UK advice to recommend a similar programme for GBMSM at high risk of infection in their region.<sup>54</sup>

### Conclusions

Concerns about rising incidence and increasing antimicrobial resistance mean that we must not delay taking action to control gonorrhoea now. Whilst 4CMenB is not licensed for protection against gonorrhoea, there is consistent real-world evidence of protection, with health economic modelling indicating that even moderate protection for a limited duration would be a cost-effective strategy to reduce the burden of gonorrhoea in populations at high risk of infection. The UK national 4CMenB immunisation programme for GBMSM at high risk of infection will not only provide critical, real-world data on the protection offered by the vaccine and associated reductions in healthcare utilisation and antibiotic use, but also contribute to our understanding of natural infection and immunity, vaccine immunity, breadth of protection and duration of protection in a population with a very high incidence of gonorrhoea. It is hoped that the data collected will provide an evidence base for other countries considering implementing a similar immunisation programme for their populations at high risk of infection. The UKHSA has developed a range of resources to support for

programme for healthcare professionals and the public (<https://www.gov.uk/government/collections/meningococcal-b-menb-vaccination-programme-for-gonorrhoea>).

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