

Meningococcal Vaccine Does Not Significantly Reduce Gonorrhea Risk

While a small benefit can't be ruled out, the clinical relevance of the 4CMenB vaccine for gonorrhea prevention appears limited.

April 16, 2024 By [Liz Highleyman](#)

A vaccine that prevents meningococcal disease did not significantly lower the risk of gonorrhea in the DoxyVAC trial, according to updated study results presented at the [Conference on Retroviruses and Opportunistic Infections \(CROI 2024\)](#) last month in Denver.

“Although a small benefit cannot be ruled out, its clinical relevance seems very limited,” Jean-Michel Molina, MD, of the University of Paris Cité, reported. However, he noted that while the vaccine did not significantly reduce the likelihood of testing positive for gonorrhea, it may reduce the severity of illness for those infected.

DoxyVAC, conducted by the French National Agency for AIDS research (ANRS), tested two interventions in parallel to prevent sexually transmitted infections (STIs):

- [DoxyPEP](#), a single dose of the antibiotic doxycycline taken as post-exposure prophylaxis within 72 hours after sex;
- [Meningococcal B vaccine](#) (4CMenB, brand name Bexsero), which prevents bacterial meningitis and other illnesses caused by *Neisseria meningitidis*; prior research suggests it may also prevent gonorrhea, caused by the related bacteria *Neisseria gonorrhoeae*.

The study included more than 500 gay and bisexual men in the ANRS Prevenir HIV pre-exposure prophylaxis (PrEP) trial. The participants were taking tenofovir disoproxil fumarate/emtricitabine (Truvada or generic equivalents) for PrEP and had an STI within the past year. Most were white men born in France, and the median age was approximately 40 years.

The participants were randomly assigned to doxyPEP or the standard of care (STI testing and treatment after diagnosis) and were separately randomized to receive two doses of the vaccine spaced two months apart or no vaccine. Roughly half used doxycycline PEP alone, half were

assigned to doxycycline plus the vaccine, a quarter received the vaccine alone and a quarter got neither. They were tested for [chlamydia](#), [gonorrhea](#) and [syphilis](#) every three months.

The study was stopped early in September 2022. At CROI 2023, Molina [reported interim results](#) showing that both interventions appeared to be effective. Over a median nine months of follow-up, chlamydia and syphilis declined by 89% and 79%, respectively. Gonorrhea fell by about 50% in the doxyPEP group and in the vaccine group; the effects of the two interventions were independent, and men assigned to both doxycycline and the vaccine appeared to benefit from both. These findings were [similar to those of the DoxyPEP trial](#), conducted in San Francisco and Seattle, in which PrEP users assigned to doxyPEP saw a reduction in all three STIs (by 88%, 87% and 55%, respectively); that trial did not include a vaccine component.

However, follow-up DoxyVAC findings presented at this year's CROI were less promising. Due to a discrepancy between the interim and final data, ANRS decided to conduct further analysis before releasing the final results. With 21 months of follow-up, doxyPEP was less effective against gonorrhea than it previously appeared, though its effectiveness against the other two STIs remained robust.

Gonorrhea incidence was 33% lower in the doxyPEP group versus the standard care group, which was still a statistically significant difference. What's more, there was evidence of an increase in high-level antibiotic resistance among doxyPEP users who contracted gonorrhea. This doesn't necessarily mean that doxyPEP caused resistance, but rather that men exposed to resistant gonorrhea were less likely to benefit from doxycycline.

The vaccine was also less effective in the later analysis. Gonorrhea incidence was numerically lower in the vaccine group compared with the unvaccinated group (58.3 versus 77.1 cases per 100 person-years, respectively). Although the vaccine group had a 22% lower risk of gonorrhea, the difference fell short of the threshold for statistical significance, meaning it could have been due to chance.

In his [CROI 2024 review for The New England Journal of Medicine](#), Paul Sax, MD, of Brigham and Women's Hospital, wrote, "When a result is this close, the most conservative conclusion is that 'a small benefit cannot be excluded.' Even if that benefit is real, a better gonorrhea vaccine would be of great use."

Though disappointing, the DoxyVAC results are not the end of the line for a gonorrhea vaccine. Over the past decade, observational studies in several countries have seen meningococcal B vaccine effectiveness against gonorrhea in the 30% to 50% range.

Last August, researchers with the Oregon Public Health Division [analyzed gonorrhea incidence](#) among more than 30,000 students and staff who received the 4CMenB vaccine, which targets outer membrane vesicles (OMVs) common to both *Neisseria meningitidis* and *Neisseria gonorrhoeae*, or another non-OMV-based meningococcal B vaccine following meningitis outbreaks at two universities in 2015 and 2016. The study participants were ages 18 to 29 and 55% were

women. 4CMenB vaccine recipients were 47% less likely to be diagnosed with gonorrhea than those who received a non-OMV-based vaccine. Among those ages 18 or 19, 4CMenB vaccine effectiveness rose to 59%.

A Phase II trial ([NCT04350138](#)) of the Bexsero 4CMenB meningococcal vaccine for gonorrhea prevention is currently underway at several sites in the United States and in Malawi and Thailand.

“Vaccines represent a crucial path forward to ensuring the health of the population in the United States, and a vaccine for this infection could enhance the reproductive and sexual health of millions of people globally,” Jeanne Marrazzo, MD, MPH, director of the National Institutes of Allergy and Infectious Diseases, said in a University of Alabama at Birmingham [news release](#).

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