Findings from three new studies presented at CROI2023 were encouraging for STI prevention in MSM and transgender women, but disappointing in cisgender women. IMAGE: Nick Youngson CC BY-SA 3.0 Pix4free

What new STI prevention findings mean for SA

News & Features

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Last year, Spotlight reported that taking a widely available antibiotic after condomless sex can reduce the risk of contracting three different sexually transmitted infections (STIs). The antibiotic, doxycycline, was found to significantly reduce the risk of men who have sex with men (MSM) and transgender women developing chlamydia, gonorrhoea, and syphilis in a study conducted in San Francisco and Seattle in the United States. (Spotlight previously reported on the state of gonorrhoea and syphilis in South Africa.)

Further findings from three studies into DoxyPEP have now been presented at the recent Conference on Retroviruses and Opportunistic Infections (CROI) in Seattle. DoxyPEP is short for the use of doxycycline as post-exposure prophylaxis (PEP).

Encouraging but mixed findings

Overall, the findings from the three new studies were encouraging for STI prevention in MSM and transgender women, but disappointing in cisgender women.

A combination of DoxyPEP and a vaccine (known as the Bexsero vaccine or 4CMenB) also demonstrated potential for preventing STIs. The vaccine is a multi-component vaccine

that provides protection against type B meningococcal disease – a disease caused by bacteria which can lead to meningitis and sepsis.

New short-term data on the development of drug resistance while using DoxyPEP is also promising, but as in other areas, longer-term data is needed.

Findings from three new studies were encouraging for STI prevention and experts say it should serve as a call to action to step up STI prevention research. IMAGE: Jernej Furman/Flickr

The new findings should serve as a "call to action to step up STI prevention research," according to Dr Tendesayi Kufa-Chakezha, a public health specialist and Senior Epidemiologist in HIV and STIs at the National Institute of Communicable Disease (NICD). She says that this should be done to translate the DoxyPEP research findings to our specific setting. The studies did not include any participants from South Africa, so it's not yet clear how well DoxyPEP will work as STI prevention in our context.

"I am hoping that all these discussions around DoxyPEP and [the] 4CMenB vaccine will stimulate the necessary discussions on how to improve STI prevention and care in South Africa," Kufa-Chakezha says. "This discussion is sorely needed given the limited investments made in these areas over the years. South Africa needs to invest in the human resources capacity, laboratory, and clinical resources needed for optimal STI care."

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Dr Nigel Garrett, head of HIV pathogenesis and vaccine research at the Centre for the AIDS Programme of Research in South Africa (CAPRISA), tells Spotlight that "this [DoxyPEP] is a very interesting intervention, particularly for MSM, and that's another good reason to strengthen our services for MSM and transgender people [in South Africa]." "I think overall we need to have a spotlight on STIs again, start with some diagnostic testing so that we actually can quantify the problem in South Africa better," he adds.

Disappointing findings in cisgender women

One of the studies on DoxyPEP looked at whether it was effective at preventing STIs in cisgender women. The open-label randomised controlled trial compared DoxyPEP (200mg of doxycycline given within 72 hours of sex, as in the initial study among MSM) with the standard of care among 449 cisgender women in Kenya.

"We did not see a reduction in STIs among cisgender women, which is in stark contrast to my colleagues' studies here amongst cisgender men and transgender women," said Dr Jenell Stewart, one of the study authors who presented the findings at CROI. Overall, 109 STIs were detected – 50 in the doxycycline arm and 59 in the standard-of-care arm. The difference between arms was not statistically significant.

In response to this Garrett says that the results are polarised, as the DoxyPEP studies in MSM and transgender women show that the strategy is working well in the short term as there isn't long-term data on it yet, but the results presented at CROI show it's not working in cisgender women.

He adds that more studies are needed to determine why this is the case. Many different things might impact the effectiveness of DoxyPEP in this population. These might include behavioural issues, such as poor adherence, or biological factors like the difference in anatomy or drug levels not being high enough. "I think there could be many different things and they [the study authors] need to guide us a bit. What have they looked at, have they looked at drug levels, have they done any causal studies?" he says.

Cisgender women make up about half of the STI burden in the country and STIs in this population affect fertility and infants but it is not clear if there are any concrete plans to adopt and roll out DoxyPEP in SA. IMAGE: Nick Youngson CC BY-SA 3.0 Pix4free

When asked how these results might affect any potential plans to provide DoxyPEP in South Africa, Kufa-Chakezha says that at this point she doesn't know if there are any concrete plans to adopt and roll out DoxyPEP yet. However, since cisgender women make up about half of the STI burden in the country and STIs in this population affect fertility and infants, effective prevention strategies are urgently needed. "Another consideration will also be how effective DoxyPEP is [in] men-who-have-sex-with-women only. If DoxyPEP effectiveness is limited in this group also, then DoxyPEP may have limited impact on STI transmission in South Africa," she says.

DoxyVac study findings

Another important study showcased at CROI looked at whether DoxyPEP in combination with the 4CMenB vaccine, which provides protection against meningococcal type B, could reduce gonorrhoea incidence. According to Prof Jean-Michel Molina, one of the study authors, the DoxyPEP study presented last year showed that DoxyPEP was less effective in preventing gonorrhoea than chlamydia and syphilis. However, a number of observational studies showed that the 4CMenB vaccine was associated with a reduction in gonorrhoea incidence. Confirmation studies were needed, of which this study is one.

The randomised open-label phase three trial – known as DoxyVac – enrolled MSM on PrEP who had a history of a bacterial STI in the last 12 months. They were randomised 2:1 to receive 200mg DoxyPEP within 24 to 72 hours after sex or to receive no DoxyPEP. Participants were then randomised 1:1 to receive two injections of the 4CMenB vaccine or no vaccine.

In September 2022, the study's Data Safety Monitoring Board recommended that the study be stopped early due to the high efficacy of DoxyPEP and the vaccine. They recommended that DoxyPEP and the vaccine be offered to all participants. The results presented at CROI were based on data collected up to July 2022.

According to Molina, there was no interaction between the two prevention strategies and no serious adverse events were reported. 546 MSM on HIV PrEP were randomised in the trial, of which 502 were analysed in these results. They were tested at baseline and then every three months and when symptomatic for gonorrhoea and chlamydia by PCR in throat, anus, and urine.

Taking a widely available antibiotic, doxycycline after condomless sex can reduce the risk of contracting three different sexually transmitted infections (STIs).

In the DoxyPep arm, according to the study abstract, the time to first gonorrhoea episode was 20.5 per 100 person-years, 41.3 per 100 person-years in the no DoxyPEP arm, 9.8 per 100 person-years in the 4CMenB vaccine arm and 19.7 per 100 person-years in the no vaccine arms.

The study abstract concludes that for MSM on HIV PrEP, DoxyPEP significantly reduced the incidence of chlamydia and syphilis and had an impact on the incidence of gonorrhoea. And the vaccine was able to reduce the incidence of gonorrhoea.

“We’ve shown for the first time that the 4CMenB vaccine could reduce the incidence of the first episode of gonorrhoea among MSM,” Molina says. “This vaccine actually reduced the incidence of gonorrhoea by roughly 50% of the participants, who received two doses of the vaccine. What’s interesting also was that these two interventions were independent, meaning that people combined the two intervention benefits from both.”

In response to these results and their implications for South Africa, Kufa-Chakezha explains that vaccine efficacy studies among MSM and other populations at high risk for STIs will be needed in South Africa or a similar setting before it can be rolled out. It also isn’t a silver bullet intervention, as the vaccine works against gonorrhoea and not other STIs, so other interventions will still be needed to reduce STI transmission.

“The DoxyPEP and the 4CMenB vaccine used in the trial were used in the context of an HIV PrEP programme where participants were receiving PrEP, they had screening and treatment for STIs at the start of the study, every three months and when they had symptoms,” she says. “The effect of DoxyPEP or the vaccine is incremental to the effect of these interventions. In our setting where people are not screened often or at all, the results may be different. We also need to provide better services for people at risk of STIs – regular screening for STIs, treatment and partner notification.”

It’s important to get more information about each component-DoxyPEP and the 4CMenB vaccine- individually and then combined, according to Garrett, as neither one of them has been rolled out yet.

STI management in South Africa is mostly syndromic and treatment is provided based on symptoms and signs without testing. PHOTO: Rodrigo Nunes/MS

The problem of resistance?

One concern with using doxycycline as PEP is that widespread use could potentially lead to the development of drug resistance. An analysis of antimicrobial resistance from participants in the original DoxyPEP trial found that overall, there was not a marked increase in antimicrobial resistance associated with DoxyPEP use. This is according to Dr Anne Luetkemeyer, one of the study authors, who presented the findings at CROI.

The aim of the analysis was to find out if intermitted DoxyPEP use affected doxycycline resistance in three bacterial subgroups that could be affected by taking the antibiotic. These were Neisseria Gonorrhoea (N. Gonorrhoea), Commensal Neisseria and Staphylococcus aureus (S. Aureus). STI testing and cultures were done at baseline and then during the study at month 12 in 501 participants.

For gonorrhoea, according to Luetkemeyer, the results suggested that DoxyPEP may be less protective against strains that are resistant to another antibiotic called tetracycline, but this is limited by the small numbers of these strains identified in the study population. Whether DoxyPEP is a potential driver for tetracycline resistance wasn't assessed in the study.

Participants were also tested for S. Aureus present in the nose, of which 40% of participants had what Luetkemeyer refers to as S. Aureus colonisation in their nose. The presence of this bacteria doesn't necessarily cause any problems but can predispose people to clinical infections.

According to Luetkemeyer, overall, there was a low amount of doxycycline-resistant S. Aureus detected in the study. However, it is important to note that there was a small increase in doxycycline resistance in the S. Aureus present in the DoxyPep arm, going from 5% to 13%.

The study also looked at Methicillin-Resistant Staphylococcus aureus (MRSA), which is a drug-resistant strain often treated by doxycycline. Luetkemeyer explains that they detected very little MRSA colonisation, only a 6% prevalence, and this did not change over the course of the study. She adds that doxycycline-resistant MRSA remained unchanged with DoxyPEP use.

Finally, Commensal Neisseria – a bacteria that lives in people's throats and can be a reservoir for drug resistance – was present in 85% of participants. Of those, two-thirds already had doxycycline-resistant strains at the start of the study. Resistance to doxycycline did not increase with the use of DoxyPEP during the study, according to Luetkemeyer.

She said that larger studies with a longer follow-up are needed to understand the "trajectory and the clinical importance of microbial susceptibility patterns associated with doxycycline used as STI PEP".

According to Garrett, it's difficult to determine much about the risk of drug resistance to doxycycline that DoxyPEP use may pose in the short term. But it is a worry because doxycycline is a universally used antibiotic.

What's next

When asked whether the current findings on DoxyPEP in MSM and transgender women are enough to warrant rolling out the intervention in South Africa at this point, Kufa-Chakezha says, "I think operational research is needed to answer questions such as feasibility – who and what is needed to provide this service, acceptability by different groups eligible for DoxyPEP, cost of providing the service and cost-effectiveness, impact on STI burden, and antimicrobial resistance is warranted."

She adds that another question that needs to be answered is "how to provide this service in the face of limited laboratory capacity for STI testing". "This is because STI management in South Africa is mostly syndromic and treatment is provided based on symptoms and signs without testing. Based on the local implementation or pilot studies, a way forward can be mapped out."

For Garrett, the potential of DoxyPEP's use in the future should not distract from diagnostic testing for STIs now, which he stresses needs to be strengthened in the country. "I think there are so many benefits of knowing exactly what your problem is, any of these interventions I would only do in addition to diagnostic testing. That's my approach at the moment."