NZSHS doxy-PEP statement for Aotearoa New Zealand

Sexually transmissible infections (STIs) are on the rise worldwide and in Aotearoa/New Zealand. Specifically, the rates of three major STIs (syphilis, gonorrhoea, chlamydia) are all increasing again in Aotearoa after an apparent decline during the COVID-19 pandemic. (ESR, 2023) Three subpopulations bear the heaviest burden of STIs in Aotearoa:

- Gay, Bisexual, and other Men who have sex with men (GBMSM): rate of syphilis in 2023 760/100,000 compared to 6/100,000 among the heterosexual population; rate of gonorrhoea in 2023 5,587/100,000 compared to 129/100,000 among heterosexual men and 142/100,000 among heterosexual women (ESR, 2023).
- Māori and Pacific people: in 2023, rates among Māori and Pacific people of syphilis were twice and of gonorrhoea 3-4 times that of people of other ethnicities. Among 35 cases of congenital syphilis between 2017 and 2023, 26 were Māori and 6 Pacific babies (ESR, 2023)
- Young people: in 2023, the age group 20-24 had the highest rate for gonorrhoea and chlamydia (ESR, 2023).

NZSHS believes that the epidemics of STIs in Aotearoa/New Zealand can be controlled, similar to the most recent trends of the HIV epidemic, by implementing a comprehensive STI prevention approach. Drawing on the Consensus Statement on Comprehensive HIV Prevention in Aotearoa/New Zealand (hivconsensus.org.nz) and Aotearoa New Zealand Sexually Transmitted and Blood Borne Infection Strategy 2023-2030 (Ministry of Health, 2023), we define comprehensive STI prevention as using a range of evidence-informed behavioural, biomedical and structural STI prevention approaches strategically, simultaneously and at scale, tailored to specific needs of individuals and communities. and responsive to developments and innovations in epidemiology, pharmaceutical and non-pharmaceutical interventions. This statement addresses one aspect of comprehensive STI prevention; post-exposure doxycycline prophylaxis (doxy-PEP)

Following the example of HIV post-exposure (PEP) and pre-exposure (PrEP) prophylaxis, the use of doxy-PEP against STIs has been investigated in randomised controlled trials, and several organisations have issued guidance regarding its use (ASHM, 2023; NYSDOHAI, 2023; CDPH, 2023; BCCfE, 2023) The United States

Centers for Disease Control and Prevention (US-CDC) has developed draft guidelines for doxy-PEP and these were published for public consultation in September 2023 (US-CDC, 2023; Federal Register, 2023). The most recent published statement in 2022 from the British Association for Sexual Health and HIV and the UK Health Security Agency did not endorse the use of doxy-PEP due to limited long-term data and concerns about antimicrobial resistance (Kohli et al, 2022).

Three randomised controlled trials among cisgender men who have sex with men and transgender women who have sex with men at risk of bacterial STIs have shown a relative risk reduction of 70 to 80% for syphilis and 70 to 90% for chlamydia in those randomised to take a single dose of 200mg doxycycline within 72 hours after a possible exposure.(Molina et al, 2018; Luetkemeyer et al, 2023; Molina et al, 2023) These studies showed variable efficacy of doxy-PEP against gonorrhoea, from 0 to 50%, which is likely to be due to geographical differences in levels of tetracycline resistant gonorrhoea. One randomised controlled trial in cisgender women in Kenya on PrEP found doxy-PEP was not effective for bacterial STI prevention in this population (Stewart et al, 2023).

Concerns have been raised about doxy-PEP, which could be summarised as: (1) the risk of doxycycline-specific side-effects (photosensitivity, oesophagitis); (2) the possible impact on the microbiome; (3) possible selection of antibiotic-resistant non-STI bacteria; and (4) possible selection of antibiotic-resistant gonorrhoea and *Mycoplasma genitalium*. For example, an analysis of over 2,000 gonococcal isolates in Europe found that the presence of 2 common tetracycline-associated mutations was strongly associated with mutations conferring cross-resistance to other antibiotics, including beta-lactams and macrolides (Vanbaelen, 2023).

While acknowledging these concerns and the need for careful monitoring, we believe that the targeted use of doxy-PEP has the potential to contribute at both individual and population levels to the prevention of STIs, particularly syphilis, in Aotearoa. Its use must be prudent and balanced to maximise its benefits while minimising its risk, while further studies are being conducted and their results accumulate. The long-term benefits and risks including impacts on AMR are unknown, and therefore implementation will be monitored through sexual health clinics and surveillance systems.

We advise:

- Considering doxy-PEP, primarily as an intervention to prevent syphilis, to people assigned male at birth who have sex with men who are at risk of syphilis with the following suitability criteria:
    - Proactively discussing doxy-PEP with GBMSM with a diagnosis of syphilis or two other bacterial STIs (i.e. gonorrhoea, chlamydia) during the previous 12 months;
    - Considering doxy-PEP for GBMSM who identify an upcoming period of heightened STI risk, for example, attendance at a sex event, or holiday plans that likely involve sexual activity with multiple casual sexual partners;

    - Considering doxy-PEP for GBMSM with concurrent male and cisgender female sexual partners or other sexual partners with a uterus, recognising the additional health risks posed by chlamydia, gonorrhoea and syphilis for people with a uterus;
    - Considering doxy-PEP for all GBMSM who are Māori or Pasifika, given inequities in syphilis for these populations.
- Prescription of doxy-PEP should be undertaken in the context of comprehensive sexual health care and with counselling on the benefits and harms including side effects and antimicrobial resistance (AMR).
- Doxy-PEP users should be assisted to maximise the benefits of Doxy-PEP while minimising overall antibiotic use. For example, if a Doxy-PEP user tends to have multiple sexual partners during weekends, a single Monday morning dose of 200mg Doxy-PEP should adequately cover their STI risk, rather than multiple doses over the weekend. The recommended maximum amount of doxycycline prescribed for each 3-month period should not exceed 72 x 100mg tabs, which equates to 3 doses per week for 12 weeks.
- People who use doxy-PEP should have or continue to have frequent STI checks (every 3 months) including multisite chlamydia and gonorrhoea and HIV/syphilis testing.
- The need for ongoing doxy-PEP should be reviewed at each follow up visit.
- Every time gonorrhoea is diagnosed in a doxy-PEP user, an additional swab for culture and antibiotic susceptibilities should be requested for surveillance purposes.
- If a doxy-PEP user presents as a contact of syphilis or gonorrhoea they should be treated as a contact if within the window period for infection. If they present as a contact of chlamydia, re-testing outside the window period rather than presumptively treating is recommended.
- Doxy-PEP may result in an attenuated syphilis serological response, therefore any reactive syphilis serology (including EIA only) in a doxy-PEP user should be discussed with a sexual health physician.

- Monitoring the amount of antibiotic used by individuals taking doxy-PEP at an individual level.
- Surveillance of AMR in organisms of concern, including gonorrhoea, *Mycoplasma genitalium*, *Staphylococcus aureus*.
- Considering how to assess the impact of doxy-PEP on STI incidence including considerations of equity of access and impact (ethnicity, geography).

The draft of this statement was written by Dr Massimo Giola (Infectious Disease & Sexual Health Physician, NZSHS Executive member representing the AChSHM) & Dr Julia Scott (Public Health & Sexual Health Physician). It was then shared and discussed with relevant stakeholders during an online meeting on 16th February 2024 (see list of the participants below). Amendments were introduced and this final

version was approved by the NZSHS Executive Committee during the meeting of Wednesday 27th March 2024.

Participants in doxy-PEP stakeholder discussion

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