

**Title:** BASHH Updated Position Statement on Doxycycline as Prophylaxis for Sexually Transmitted Infections

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In 2017, the British Association for Sexual Health and HIV (BASHH) and Public Health England, now the UK Health Security Agency (UKHSA), published a position statement on the use of doxycycline as prophylaxis for sexually transmitted infections (STIs).<sup>1</sup> It advised ‘extreme caution in the use of doxycycline [as post-exposure prophylaxis (PEP)]...[and] that the use of doxycycline PEP should be restricted to the research setting’. However, increasingly evidence suggests that individuals at higher risk of acquiring bacterial STIs are already using antibiotics to prevent acquisition, accessed through several routes.<sup>2-5</sup> Clinicians are therefore likely to be seeing patients who are self-sourcing antibiotics as STI prophylaxis. For that reason, and to support a person-centred approach to care, the BASHH position statement has been updated. It now includes information about key studies to date and concerns around antimicrobial resistance (AMR) in sexually and non-sexually transmitted infections, as well as providing recommendations for clinicians for how to advise patients about STI prophylaxis. Importantly, it remains the case that doxycycline taken as PEP or pre-exposure prophylaxis (PrEP) for STIs is not endorsed by BASHH or UKHSA. This remains in line with international counterparts.<sup>6</sup> The full position statement is available on the BASHH website: <https://www.bashh.org/guidelines>.

STI prophylaxis is the use of antibiotics as PEP or PrEP to reduce the risk of acquiring certain bacterial STIs. Only the use of doxycycline to prevent syphilis and chlamydia in men-who-have-sex-with-men (MSM) and transgender women has been researched with a single published study powered to show efficacy.<sup>7</sup> This open label, randomised controlled trial (RCT) explored the efficacy of doxycycline PEP taken as a single 200mg dose within the first 24 hours, and no later than 72 hours, after condomless sex among 232 MSM and transgender women using HIV pre-exposure prophylaxis (PrEP). A significant decrease was observed in the occurrence of the first episode of chlamydia and for a first episode of syphilis. No significant difference in the incidence of gonorrhoea was observed. An earlier open-label, pilot RCT of 100mg doxycycline daily as PrEP involving 30 MSM living with HIV did observe reductions in both syphilis diagnosis, and diagnosis of either chlamydia or gonorrhoea, that were not statistically significant.<sup>8</sup> Several further studies of doxycycline PrEP and PEP are ongoing.<sup>2 9</sup>

Despite the lack of a large evidence-base, up to 10% of HIV-PrEP using MSM report taking antibiotic STI prophylaxis in surveys from the UK, Australia and Netherlands<sup>2-6</sup> – with comparable reported use among MSM living with HIV.<sup>10</sup> Notably, interest and acceptability for STI prophylaxis among MSM is much higher, ranging from 53% to 84% in surveys.<sup>2 11</sup> STI prophylaxis use has been found to be associated with higher risk behaviours, for example greater numbers of condomless sex partners and chemsex, and is also associated with STI diagnosis in the past 12 months.<sup>3 4</sup> Although the most

commonly used antibiotic for STI prophylaxis is doxycycline, emerging evidence suggests that up to 40% of MSM who report having ever used STI prophylaxis used an antibiotic other than doxycycline, such as azithromycin or amoxicillin – where there is no evidence of effectiveness in preventing bacterial STIs.<sup>10</sup>

Concerns exist regarding the emergence of AMR in sexually and non-sexually transmitted infections. Tetracycline resistance has not been demonstrated in *Treponema pallidum* (*subsp. pallidum*), the bacterium causing syphilis, or meaningfully confirmed in *Chlamydia trachomatis*. However, high rates of tetracycline resistance in *Neisseria gonorrhoeae* already preclude treatment of gonorrhoea with doxycycline, and its use as prophylaxis is not likely to be effective in preventing gonorrhoea infection. Also of major concern is the potential for selection of resistance amongst potentially pathogenic bacterial flora such as *Staphylococcus aureus* and respiratory tract pathogens. Consideration also needs to be given to the impact on community prevalence of resistance determinants within commensal organisms, with higher prevalence purported among MSM populations.<sup>12</sup>

There remain key gaps in understanding the risk of AMR emergence with prophylactic doxycycline for STIs, as well as some of the facilitators and drivers that lead to individuals' decisions to self-source antibiotics. In addition to addressing the question of efficacy, some current trials examining doxycycline as STI prophylaxis will attempt to address aspects of AMR. In the interim, it is important clinicians ask about antibiotic STI prophylaxis use and discuss the limited benefits and potential risks. This position statement provides an update on the current available evidence and practical guidance for clinicians providing care to individuals reporting antibiotic STI prophylaxis use.

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