

# POSITION PAPER: SYPHILIS

January 2016

## EXECUTIVE SUMMARY

Since rates of syphilis infection began increasing in the early 2000s, HIV-positive gay, bisexual, and other men who have sex with men (MSM) have been disproportionately affected. Infection data for the first half of 2015 show a significant increase over previous years, with a quarter of all cases being reinfections. HIV-positive MSM experienced the vast majority of reinfections.

Living Positive Victoria recommends the continuation and expansion of public health campaigns to raise awareness of syphilis. A coordinated response should involve:

- I. Continuation and expansion of current public health campaigns, targeting MSM generally and HIV-positive MSM particularly through:
  - a. Online forums: Dating and hook-up sites, mobile apps, social media, LGBTIQ community publications, and community organisation websites;
  - b. Community: LGBTIQ-focused health providers and clinics (e.g. Northside Clinic, Prahran Market Clinic, Centre Clinic, MSHC); and
  - c. Venues: Gay bars, pubs, and clubs, and sex-on-premises venues.
- II. Adoption of standard practice that includes syphilis testing conducted alongside HIV testing for all MSM;
- III. Conduct a multi-centre randomised clinical trial among MSM engaged in high-risk activities to demonstrate the effectiveness of chemoprophylaxis against syphilis, gonorrhoea, and chlamydia;
- IV. Encourage all sexually active HIV-positive MSM to undertake a full sexual health screening at least every four months, particularly those MSM who have a stable viral load and CD4 count who see their s100 provider only one or twice per annum;
- V. An additional campaign informing at-risk MSM that 'syphilaxis' (doxycycline 100 mg daily) is available and could be considered as a potential prophylaxis to reduce syphilis incidence in partnership with VAC; and
- VI. All future versions of key community surveys such as *Gay Community Periodic Survey* and *HIV Futures* should ask all participants questions on syphilis knowledge and testing.

## 1. BACKGROUND

For the first quarter of 2015, notification of syphilis cases increased 75% over the same quarter of the previous year. Men who have sex with men (MSM) with HIV accounted for 43% of total syphilis infections, more than double the 2014 average. Of all cases, 24% were reinfections; HIV-positive MSM represented 77% of all reinfections. Since syphilis rates began to sharply increase in the early 2000s, HIV-positive MSM have been disproportionately affected by syphilis. In spite of this, very few public health campaigns have specifically targeted this group.

## 2. SYPHILIS – OVERVIEW

### 2.1 Symptoms

Syphilis is a sexually transmitted infection (STI) caused by the *Treponema pallidum* bacterium. Syphilis has a number of symptoms, varying depending on the stage of the infection:

- In the **primary stage**, a hard, painless spot, or *chancre* appears at the site of infection. Because it is painless, and sometimes internal, it may go unnoticed. The chancre will appear within three to six weeks, regardless of whether a person is treated.
- If untreated, syphilis enters the **secondary stage**. Some sort of rash, usually rough and red, may show up on various parts of the body. Secondary stage rashes can vary in appearance, and may be accompanied by fever and swollen glands.
- If still untreated, syphilis may then enter the **latent stage**. In the early latent stage, there are no symptoms, but the person is still infectious. In the late latent stage, about two years after infection, there are no symptoms and the person is no longer infectious.
- If left untreated, syphilis may enter the **tertiary stage**, sometimes 10-20 years after infection. In this stage, syphilis causes serious damage to the internal organs, causing organ failure and potentially death.

### 2.2 Transmission, Testing, and Treatment

Syphilis can be contracted through skin-to-skin contact, oral sex, or condomless anal sex. Because it can be passed in so many different ways, it is difficult to prevent syphilis. Condoms can help reduce the risk of passing it on, but do not prevent it completely.<sup>1,2</sup>

Syphilis can be detected through a simple blood test. If detected in the early stages, syphilis can be treated with antibiotics like penicillin. If detected in later stages, syphilis can be treated with intensive intravenous (IV) antibiotics; however, any damage done to the internal organs is irreversible. People who have infectious syphilis should avoid having sex. If treated, a person should wait until seven days after treatment has finished before having sex.

HIV and syphilis have a strong correlation with one another. Syphilis infection makes HIV-negative people more susceptible to HIV infection.<sup>3</sup> In HIV-positive people, infection with syphilis can increase viral load and decrease CD4 counts.<sup>4</sup> Frequent testing and early treatment are important regardless of HIV status given these correlations.

### 2.3 History and Response

In the early 20<sup>th</sup> Century, rates of syphilis were steadily increasing. Since 1928, when penicillin was found to be an effective treatment for syphilis, its spread was easily contained and treated. Up through the 1990s, syphilis infections were all but non-existent in Australia with the exception of amongst Indigenous Australians, particularly those living in remote locations.<sup>5</sup> Over the past 15 years, however, syphilis diagnoses have increased significantly, among gay

and bisexual men, and other MSM.<sup>6,7</sup> More than 50% of these cases were found in HIV-positive men, despite comprising a very small percentage of the population.

In order to address the increase in STI cases, the Commonwealth developed the *National STI Strategy 2005-2008*. This emphasised raising awareness of STIs and their symptoms, promoting safer sex and condom use, and increasing testing and treatment.<sup>8</sup>

Developed alongside the second of these national strategies was the *National Gay Men's Syphilis Action Plan*. This identified three priority areas: increasing the frequency of testing to catch more cases earlier, improving partner notification methods to identify individuals at risk and to limit spread, and starting a trial for chemoprophylaxis.<sup>9</sup> Also known as *syphilaxis*, this involves people at most risk regularly taking an antibiotic in order to prevent them from getting syphilis (discussed in more detail below). Supporting these priorities, was the continued promotion of condom use to reduce rates of syphilis.

It is worth noting is that the syphilaxis component of the plan did not proceed at the time due to a number of reasons, including the lack of evidence supporting a pharmacological intervention, a lack funding to support a trial, and the lack of buy-in from jurisdictions other than New South Wales.

STI prevention and treatment efforts are currently guided by the *Third National STI Strategy 2014-2017*. Each of these strategies has acknowledge a need for specific groups, or *subpopulations*, to have "specifically tailored interventions," including "sexually adventurous gay men, gay men with HIV, and young me reporting same sex attraction."<sup>10</sup>

### 3. ISSUES

#### 3.1 Modes of Infection

Syphilis is contractible through a range of sexual activities other than (and including) anal sex in MSM. According the *Gay Community Period Survey: Melbourne 2015* (GCPS), only those completing the online survey (n=560) were questioned about syphilis knowledge.<sup>11</sup> Of these respondents, 79.5% reported knowledge that some incidences of syphilis are asymptomatic and 72% reported being aware of the transmission of syphilis via oral sex.<sup>12</sup> Therefore, knowledge amongst the online participants is fairly high, however, in order to track knowledge over time, all participants in future surveys should be questioned on their syphilis knowledge.

Given the relative commonplace sexual practice of condomless sex among some HIV-positive MSM,<sup>13</sup> and the fact that condom use does not completely reduce risk of syphilis contraction, Living Positive Victoria recommends emphasising frequent testing, however does not recommend advocating greater condom use amongst HIV-positive MSM as part of the response. This position is supported by the Bolan, et al, study published by the American Sexually Transmitted Diseases Association:

*"From a behavioural standpoint, it is doubtful that further exhortations for HIV-infected MSM to practice safer sex to avoid STDs (sic) will be successful..."<sup>14</sup>*

It should be noted however that the promotion of condom use amongst HIV-negative MSM is important to include in future prevention campaigns. This is evidenced by both the increase of HIV-negative and untested/unknown status MSM engaging in any condomless sex with casual partners, as reported in the *GCPS*.<sup>15</sup> We also know that HIV transmission increases in the presence of syphilis,<sup>16</sup> and that syphilis might play a role in hepatitis C transmission in HIV-positive MSM.<sup>17</sup>

### **3.2 Rates of Infection**

The Victorian Department of Health and Human Services has provided statistics on syphilis notifications for the first quarter of 2015. The number of cases totalled 224, a 75 per cent increase on the same period in 2014. Of the 224 cases, 95 of these were MSM with HIV representing 43 per cent of all cases, more than double the average per quarter for 2014 (mean n=40). Furthermore, that HIV positive MSM comprise 77 per cent of syphilis reinfections for the first quarter of 2015.<sup>18</sup>

### **3.3 Ineffectiveness of Current Campaign**

An analysis of all STI campaigns in the period 2007-2013 provided by the Melbourne Sexual Health Clinic shows that rates of transmission of HIV and other STIs has not decreased despite significant investment in advertisement across multiple channels.<sup>19</sup> The effectiveness of messaging like 'get tested' or 'test often' may have had a positive impact on number of MSM screening for HIV and HIV positive MSM testing for STIs, even though traditional 'safer sex' messages do not seem to have had an effect on sexual behaviour, particularly in HIV negative MSM.<sup>20</sup>

## **4. RESPONSES**

### **4.1 Public Health Campaigns by Living Positive Victoria and Partners**

To promote awareness in Victoria, in late-2014 Living Positive Victoria launched the *Everything Old is New Again* campaign in partnership with the Victorian AIDS Council (VAC) and Melbourne Sexual Health Centre (MSHC). This campaign targeted MSM aged 40-60, using images from U.S. syphilis campaigns in the mid-20<sup>th</sup> century, encouraging these men to get tested.

In mid-2015, Living Positive Victoria launched the *Stamp Out Syphilis* campaign. This campaign encourages people to get tested for syphilis every three months, increases knowledge about syphilis modes of infection and the potential impact of syphilis on HIV viral load.

### **4.2 Prevention Strategies**

#### **4.2.1 Community Awareness of PrEP**

In Melbourne, the self-reported knowledge of PrEP amongst MSM increased from 30.7 per cent in 2014 to 38.3 per cent in 2015.<sup>21</sup> This demonstrates that the concept of taking a daily pill as a HIV prevention strategy is beginning to penetrating the community. In turn, the community is able to not only be informed, but also empowered to self-acknowledge participation in high risk sexual activities and to take steps to protect themselves from HIV.

#### **4.2.2 Syphilaxis: Doxycycline as Prophylaxis for Syphilis**

A recent pilot study in the USA amongst HIV-positive MSM has shown that doxycycline prophylaxis effectively reduced incidences of syphilis, as well as chlamydia and gonorrhoea, in this population.<sup>22</sup> Though the study focused on the feasibility of a large scale syphilaxis trial, the significant reduction in STI diagnoses demonstrated the merit and need for a future study focused on the effectiveness of chemoprophylaxis.

A large-scale clinical trial proposed in 2009 by the Kirby Institute never received the funding necessary to proceed.<sup>23</sup> In light of the findings of the U.S. pilot study, Living Positive Victoria strongly supports reviving this proposal. Such a study is necessary to definitively demonstrate the effectiveness of doxycycline in preventing syphilis transmission, as well as its effect on gonorrhoea and chlamydia.

While the original study proposed limiting participation to certain HIV-positive MSM, biological evidence indicates any MSM engaged in high-risk activities should be included. The presence of syphilis in HIV-negative people correlates with significantly increased rates of HIV transmission. In HIV-positive people, syphilis can cause brief but marked spikes in HIV viral load, even in those who are typically undetectable. These results provide an indication that a localised response should involve identifying high-risk individuals as potential candidates for chemoprophylaxis, in order to prevent both syphilis and HIV transmission. All MSM engaging in high risk sexual activity should be included, not just people with HIV. This position is supported by the Kenyon, et al, study published in Euro Surveillance, which states:

*"...it has been argued that persons with multiple syphilis reinfections are more likely to have high numbers of sexual partners and to be involved in high-risk sexual networks. As a result they may constitute a core-within-the-core and play an especially important role in syphilis spread."<sup>24</sup>*

Current sexual practices should be considered by the client's prescribing doctor. This position is supported by the 2009 report *Phase A of the National Gay Men's Syphilis Action Plan: Modelling evidence and research on acceptability of interventions for controlling syphilis in Australia.*<sup>25</sup>

Any definition of high-risk practices should be determined with input from our members and stakeholders. As evidence suggests HIV-positive MSM are disproportionately affected by syphilis, those who have had two or more syphilis infections since their HIV diagnosis should be a key part of any consultations leading to a clinical trial. Moreover, they should be prioritised as candidates for chemoprophylaxis if and when it becomes available.<sup>26</sup> Living Positive Victoria believes this group should constitute the core and focus of any clinical trials.

Increased community knowledge of PrEP suggests there is a good case that the response to a chemoprophylaxis to prevent syphilis and other STIs will be successful. As already discussed, the modes of infection for syphilis means that in some cases there is very little an individual can do to prevent transmission.

As is the case for antiretroviral medications and PrEP, adherence to a daily routine of a chemoprophylaxis will be vitally important and something that both clinician/doctor and their client need to consider. Due to the limited scope of the US pilot study on the use of doxycycline to reduce syphilis transmission, it is unclear at this stage if strategies such as 'party dosing' would be effective.

### **4.2.3 Syphilaxis: known risks and other issues**

#### **4.2.3.1 Photosensitivity**

There is a known risk of photosensitivity in some people taking doxycycline, however, this relates to risk when exposed to sunlight. A 1993 study showed that there was a 40% and 20% occurrence in patients who were prescribed 200mg and 150mg doxycycline, respectively, for the treatment of acne.<sup>27</sup> This might suggest that occurrence of photosensitivity may be as low as 10% of people taking 100mg dose. People taking syphilaxis, therefore should consider using a high SPF sunscreen when outside in direct and indirect sunlight as a precaution.

#### **4.2.3.2 Prescribing off-script**

Because doxycycline is not approved as a prophylaxis for syphilis, chlamydia and gonorrhoea, it is not available for subsidisation through the Pharmaceutical Benefits Scheme. This means that the consumer will pay between \$18-28 for a 21-day supply.<sup>28 29</sup> The cost may have an impact for low income earners including those on a government pension.

#### **4.2.3.3 Impact of antibiotics on intestinal flora**

Doxycycline is a broad spectrum antibiotic, widely used for both therapeutic and prophylactic application in humans.<sup>30</sup> Two studies show that the oral administration of doxycycline has minor effect on “culturable anaerobic bacteria”.<sup>31,32</sup> However, other studies show that there is a distinct impact on “indigenous bifidobacteria” production in the intestinal tract.<sup>33,34</sup> Furthermore, that one study showed that –tetracycline-resistant bacteria were more prevalent in the antibiotic group compared to the control group, however, that it is was not determined whether the presence of resistant bacteria was temporary or long-term.<sup>35</sup> Any local trial that investigates the effectiveness of syphilaxis should also consider measuring the impact of the antibiotic on intestinal flora, given known gastrointestinal issues for people living with HIV.<sup>36</sup>

## 5. CONCLUSION AND RECOMMENDATIONS

Since rates of syphilis infection began increasing in the early 2000s, HIV-positive gay, bisexual, and other men who have sex with men (MSM) have been disproportionately affected. Infection data for the first half of 2015 show a significant increase over previous years, with a quarter of all cases being reinfections. HIV-positive MSM experienced the vast majority of reinfections.

Living Positive Victoria recommends the continuation and expansion of public health campaigns to raise awareness of syphilis. Though previous campaigns did not produce a corresponding decrease in syphilis rates, new campaigns should be able to leverage the increased awareness of sexual health issues brought about through HIV testing and treatment campaigns. Evidence of increasing health literacy demonstrated in the *Gay Community Periodic Survey* may indicate greater willingness by HIV-positive MSM and MSM generally to consume and act on health messages.

Living Positive Victoria further recommends, in light of the disproportionate presence of syphilis among HIV-positive MSM, that future campaigns specifically target this community. These efforts should include increased research into the benefits and effectiveness of chemoprophylaxis, or *syphilaxis*, for individuals most at risk. An extensive clinical trial should be conducted in order to confirm the preliminary findings of a recent syphilaxis pilot study conducted in the U.S. This study should include all MSM engaged in high-risk activities, but should prioritise people living with HIV.

In light of the fact that such a trial may take time to establish, future campaigns should be expanded to communicate the potential for chemoprophylaxis.

Living Positive Victoria considers the recommended actions to be consistent with the *Third National Sexually Transmitted Infections Strategy 2014-2017*.

## References:

---

<sup>1</sup> Holmes, Levine, Weaver, Effectiveness of condoms in preventing sexually transmitted infections’, *Bulletin of the World Health Organisation*, 2004, 82(6), p. 455-7.

<sup>2</sup> Centers for Disease Control, ‘Transmission of Primary and Secondary Syphilis by Oral Sex – Chicago Illinois 1998 -2002’, *Morbidity and Mortality Weekly Report*, 2002, 51, p. 971-3.

<sup>3</sup> Fleming, Wasserheit. ‘From epidemiological synergy to public health policy and practice: the contribution of other sexually transmitted diseases to sexual transmission of HIV infection.’ *Sexually Transmitted Infections*, 1999, 75, p. 9-10.

<sup>4</sup> Buchacz, Patel, Taylor, Kerndt, Byers, Holmberg, and Klausner. ‘Syphilis increases HIV viral load and decreases CD4 cell counts in HIV-infected patients with new syphilis infections.’ *AIDS: Official Journal of the International AIDS Society*. 2004 18(15), p. 2076-2077.

- 
- <sup>5</sup> National Centre in HIV Epidemiology and Clinical Research, 'Bloodborne viral and sexually transmitted infections in Aboriginal and Torres Strait Islander people', *Surveillance and Evaluation Report 2009*, University of New South Wales, Sydney, 2009, cited in Ward, et al, 'Epidemiology of syphilis in Australia: moving toward elimination of infectious syphilis from remote Aboriginal and Torres Strait Islander communities?', *Medical Journal of Australia*, 2011 194 (10), pp. 525.
- <sup>6</sup> National Centre for HIV Epidemiology and Clinical Research, *Final Technical Report: Phase A of the National Gay Men's Syphilis Action Plan: Modelling evidence and research on effectiveness of interventions for controlling syphilis in Australia*, , University of New South Wales Australia, Sydney, 2009, p. 11.
- <sup>7</sup> McCann, Gray, Hoare, Bradley, Down, Donovan, Wilson, Prestage, 'Would Gay Men Change Their Sexual Behaviour to Reduce Syphilis Rates?', *Sexually Transmitted Diseases*, 2001, 38 (12), p. 1145
- <sup>8</sup> Department of Health and Ageing, *National Sexually Transmissible Infections Strategy 2005-2008*, Commonwealth of Australia, Canberra, 2005.
- <sup>9</sup> National Centre for HIV Epidemiology and Clinical Research, op cit.
- <sup>10</sup> Commonwealth Department of Health, *Second National Sexually Transmissible Infections Strategy 2010-2013*, 2010, p 16; *Third National Sexually Transmissible Infections Strategy 2014-2017*, 2014, p. 35.
- <sup>11</sup> McCann, et al, Op cit, p. 1148.
- <sup>12</sup> Ibid, p. 5, 7
- <sup>13</sup> Crepaz, Marks, Liau, Mullins, Aupont, Marshall, Jacobs, Wolitski, 'Prevalence of unprotected anal intercourse among HIV-diagnosed MSM in the United States: a meta-analysis,' *AIDS: Official Journal of the International AIDS Society*, 2009, 23(13), p. 1620.
- <sup>14</sup> Bolan, Beymer, Weiss, Flynn, Leibowitz and Klausner, 'Doxycycline Prophylaxis to Reduce Incident Syphilis among HIV-Infected Men Who Have Sex With Men Who Continue to Engage in High-Risk Sex: a Randomized, Controlled Pilot Study', *Sexually Transmitted Diseases*, 2015, 42(2), p. 98.
- <sup>15</sup> Crepaz, et al, op. cit., p. 4, 15.
- <sup>16</sup> Solomon, Mayer, Glidden, Liu, McMahan, Guanira, Chariyalertsak, Fernandez, and Grant, 'Syphilis Predicts HIV Incidence Among Men and Transgender Women Who Have Sex With Men in a Preexposure Prophylaxis Trial', *Clinical Infectious Diseases Advance Access*, 59(7), 2014, p. 1020
- <sup>17</sup> Jakopanec, Grjibovski, Nilsen & Aavitsland, 'Syphilis epidemiology in Norway, 1992-2008: resurgence among men who have sex with men', *BMC Infectious Diseases*, 10(1), p. 105. cited in Kenyon , Lynen, Florence, Caluwaerts, Vandenbruaene, Apers, Soentjens, Van Esbroeck & Bottieau, 'Syphilis reinfections pose problems for syphilis diagnosis in Antwerp, Belgium – 1992 to 2012', *Euro Surveillance*, 19(45), 2014, <<http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=20958>>, accessed 18 May 2015.
- <sup>18</sup> Victorian Department of Health and Human Services, surveillance data presented at Syphilis Working Group, 2015.
- <sup>19</sup> Chow, Dutt, Fehler, Denham, Chen, Batrouney, Peel, Read, Bradshaw and Fairley, 'Duration of syphilis symptoms at presentations in men who have sex with men in Australia: are current public health campaign effective?' *unpublished*, 2015, p. 9.
- <sup>20</sup> Lee, et al, op. cit., p. 2, 5, 9, 10, 15
- <sup>21</sup> Lee, et al, op cit., p. 26
- <sup>22</sup> Bolan, et al, op cit
- <sup>23</sup> Drummond, 'Syphilis: A Study of Chemoprophylaxis in HIV Infected MSM', Presentation at AFAO Syphilis Forum, May 2009.
- <sup>24</sup> Fenton and Wasserheit, 'The courage to learn from our failures: syphilis control in men who have sex with men', *Sexually Transmitted Diseases*, 34(3), 2007, p. 162-5, and Kerani, Lukehart, Stenger, Marra, Pedersen and Golden, 'Is early latent syphilis more likely in patients with a prior syphilis reinfection?'

---

Presentation at: 18th International Society for STD Research, London, 28 June - 1 July 2009, cited in Kenyon, et al, op cit., p. 1

<sup>25</sup> 'Final Technical Report,' op cit, p. 5, 43-44.

<sup>26</sup> Bolan, et al, op cit., p. 98

<sup>27</sup> Layton, Cunliffe, 'Phototoxic eruptions due to doxycycline -- a dose-related phenomenon', *Clinical and Experimental Dermatology*, 1993, 18, p. 425-427.

<sup>28</sup> Commonwealth Department of Health, 'Doxycycline', *Pharmaceutical Benefits Scheme*, <<http://www.pbs.gov.au/medicine/item/2715X>>, accessed 10 January 2016.

<sup>29</sup> Commonwealth Department of Health, 'Doxycycline', *Pharmaceutical Benefits Scheme*, <<http://www.pbs.gov.au/medicine/item/10176N-1800R>>, accessed 10 January 2016.

<sup>30</sup> Mättö, Maukonen, Alakomi, Suihko, Saarela, 'Influence of oral doxycycline therapy on the diversity and antibiotic susceptibility of human intestinal bifidobacterial population', *Journal of Applied Microbiology*, 2008, 105, p. 279.

<sup>31</sup> Nord, Heimdahl, 'Impact of different antimicrobial agents on the colonisation resistance in the intestinal tract with special reference to doxycycline', *Scandinavian Journal of Infectious Diseases*, 1988, 53, p. 50-58, cited in Mättö, et al, Ibid, 2008, p. 279, 284.

<sup>32</sup> Saarela, Maukonen, Wright, Salmela, Patterson, Scott, Hämyymen, Mättö, 'Tetracycline susceptibility of the ingested *Lactobacillus acidophilus* LaCH-5 and *bifidobacterium animalis* susp. *Lactis* Bb-12 Strains during antibiotic/probiotic intervention', *International Journal of Antimicrobial Agents*, 2007, 29, p. 271-280, cited in Mättö, et al, Op Cit, 2008, p. 279, 284.

<sup>33</sup> Saarela, et al, Op Cit, 2008, p. 284.

<sup>34</sup> Mättö, et al, Op Cit, 2008, p. 279.

<sup>35</sup> Mättö, et al, Op Cit, 2008, p. 285, 288.

<sup>36</sup> Bahijee, Subramony, Tang, Pepper, 'Human Immunodeficiency Virus- Associated Gastrointestinal Disease: common endoscopic biopsy diagnoses', *Pathology Research International*, 2011.