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### Sex, drugs and mental health among men who have sex with men

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CHAPTER

**1**

**Introduction**

The main topic in this thesis are men who have sex with men (MSM) and, to a lesser extend, transfeminine persons at the sexually transmitted infections (STI) clinic of Amsterdam, the Netherlands. In this introduction, I would like to elaborate on gender, homosexuality and provide some context why MSM have more STI compared to the general population. Since all studies in this thesis are performed at the STI clinic of Amsterdam, I will describe the STI clinic and those STI which are the main outcome of in this thesis, including HIV. Afterwards I'll describe some other noticeable mental health characteristics of men who have sex with men and lastly I'll discuss how these health characteristics intertwine and influence each other according to the syndemic theory.

## **GENDER, HOMOSEXUALITY AND STI**

In sexuology, the genderbread person is often used to describe 4 different aspects of gender<sup>1</sup>. The first aspect is sex, comprised of a persons anatomical, chromosomal and hormonal aspects. Though often used binary (men and women), it is estimated that 0.1-2% of the total population may deviate from this binary definition<sup>2</sup>. Klinefelter syndrome or Turner syndrome are known deviations in the medical world. Second is gender identity, which refers to a psychological sense of self. How one experiences oneself, is based on how much a person aligns with what a person understands are the options for gender. The third aspect is the gender expression, the way a person presents gender through action, clothing, demeanour etc. It is the outward facing self and how others interpret a person based on gender norms. Fourth is sexual attraction. While attraction isn't really a component of gender, we often conflate sexual orientation with gender, or like in this thesis, we categorize it in gendered ways. While homosexuals are categorized by sex and attraction, transfeminine persons are characterized by their born sex and gender identity.

The term homosexual should also be clarified in this context. In healthcare, the term 'men who have sex with men' is often used to describe ones sexual behaviour, usually to assess the risk of a disease such as HIV<sup>3</sup>. A second meaning of being homosexual refers to the sexual preference or attraction of a person. However, homosexual desire or preference does not have to lead to behaviour or activity, and the other way around, homosexual behaviour or activity does not have to reflect a persons sexual or romantic preference. In a British national survey, 28% of the men who reported sex with a man in the past 5 years identified themselves as heterosexual<sup>4</sup>. That leads to a third meaning

of being homosexual, reflecting an identity<sup>4</sup>. A gay life style that is often self-defined by same sex desire and behaviour. The increased risk for STI, derives not so much from one's sexual identity, preference or desire, but someone's behaviour. Direct enquiries into a persons' sexual desires, orientation, or identity can lead to (incorrect) socially acceptable responses and relevant information on risk behaviour is missed. It is, therefore, more appropriate in an STI risk assessment consultation to ask for sex partners: "Do you have sex with men and/or women?"<sup>3</sup>

Though there is no evidence that men are more likely to be 'gay' in any part of the world, a homosexual identity is for the large part a Western construct<sup>5</sup>. Large parts of the adult population do not seek to create a specific identity based on their sexual preference. Outside the industrialized Western world, other sexual identities do exist. The Hijras (transgendered MSM also known as the "third sex") and Kothis on the Indian subcontinent, and Two-spirited used by indigenous North Americans are examples of MSM, some effeminate some masculine in appearance and acting.<sup>6</sup>

Kuypers et al compared the three different meanings of homosexuality: same-sex behaviour, attraction and identity<sup>7</sup>. This survey, conducted in the Netherlands in 2006, indicated that 12.7% of the men had sexual contact with another man during their lifetime and 7.9% in the last 6 months<sup>7</sup>. This was not significantly different from a similar survey in 1989 in the Netherlands, in which 12% reported lifetime sexual contact with another men<sup>8</sup>. When compared to British, French, American or Canadian men, Dutch men scored higher on all three aspects<sup>7</sup>. They argued that the relative favourable social and political environment toward homosexuality in the Netherlands might explain these differences.

In a historical and medical context, homosexuality was removed as a mental health disorder from the DSM by the American Psychiatry Association in 1973. The WHO, however, only removed homosexuality from the ICD10 in 1990<sup>9</sup>. While the Dutch population has a relative positive attitude towards homosexuality, which increases over time, still 27% agreed with the statement 'I find sex between two homosexual men disgusting' according to a representative survey in 2015<sup>10</sup>. Also 35% considered it offensive if two men kiss in public compared to 12% when a man and a woman kiss in public<sup>10</sup>. These differences between same-sex romantic activity among men and male-female romantic activity are examples mentioned in the minority stress model<sup>11</sup>.

It implies that (sexual) minorities experience unique stressors – such as prejudice, victimization and discrimination – which have harmful effect on mental health and explain the elevated levels of depression, suicide and other mental health problems among (sexual) minorities<sup>12-14</sup>. This model will be discussed more extensively later in the discussion.

The Centers for Disease Control and Prevention (CDC) in the US estimates that HIV and early syphilis rates among MSM are more than 40 times higher than those among heterosexuals<sup>15</sup>. This is in line with Dutch numbers, MSM account for 71% of all the HIV infections<sup>16</sup> and 95% of all early syphilis infections<sup>17</sup>. The question arises: Why do MSM have such high risk for STI compared to the rest of the population? Are differences in sexual behaviour and attitudes that vast? Do biological factors make MSM more susceptible for STI? When it comes to sexuality, research has shown differences between men and women in general<sup>18</sup>. Men are usually more focused on arousal and recreational sex while women tend to be more focused on intimacy, partner and relationships<sup>19</sup><sup>20</sup>. Also men have a more positive attitude toward casual sex and score higher on sexual permissiveness than women, while women are more positive towards sexual minorities than men. Though it may seem that men and women are different, it should be stated that the similarities are much greater<sup>18</sup>. Within-gender variation is larger than between-gender variation in reported sexual behaviours and attitudes. Research suggests that the gender differences are a product of societal power differentials, social pressures and biological factors<sup>21</sup>. Nations with greater gender equality have smaller gender differences for many sexual behaviours, including intercourse prevalence and the frequency of oral, anal, casual sex and masturbation<sup>21</sup>.

Two important behavioural aspects for STI and HIV transmission are number of sex partners and condom use. A large population based study in the U.S. showed that MSM reported more lifetime sexual partners (median 45) than heterosexual men (median 8), but also showed that MSM reported higher levels of condom use both during the last sex act (80% vs 57%) and within partnerships lasting >3 months (48% vs 24%) than heterosexual men<sup>22</sup>. The previously mentioned differences (and similarities) between men and women, might explain the higher level of lifetime partners among MSM as women might have a restraining influence on heterosexual men regarding promiscuity<sup>5</sup>. The long-standing lack of encouragement or reinforcement for gay men to establish stable sexual relationships and the casual sex culture which derived from

this, might also have reinforced the number of sexual partners among MSM<sup>5</sup>. Besides these two important and more obvious behavioural aspects there are numerous other behavioural aspects which might influence the risk of STI and HIV acquisition. Two sex-related behaviours described in Part I of this these are anal douching (usually done for hygienic purposes) and drug use for sex (reasons are described as increased sexual arousal, confidence and decreased sexual inhibition).

An important biological factor for sexual transmission - especially for HIV - is the difference related to vaginal and anal sex. Since the anal mucosa is more fragile to lacerations than the vaginal mucosa, transmission is more likely during anal sex. A National British study showed that 60% of MSM engaged in anal sex versus 12% of heterosexual men in the last year<sup>23 24</sup>. A review by Beyrer et al showed that the 5 year cumulative HIV incidence would be reduced by 80-98% if the transmission probability of receptive anal sex was similar to that of unprotected vaginal sex<sup>25</sup>. Furthermore, MSM can engage in both insertive and receptive anal sexual roles (being versatile). The 5 year cumulative HIV incidence would be reduced by 19-55% if MSM would limit to either insertive or receptive roles (50% for each, as in heterosexual networks)<sup>25</sup>. The number of partners is also a substantial driver of the HIV epidemic. If the number of unprotected anal intercourses in casual partnerships would occur within long-term partnerships, HIV prevalence would be reduced by 29-51%<sup>25</sup>.

## THE AMSTERDAM STI OUTPATIENT CLINIC

The STI clinic of Amsterdam, where the studies in this thesis have been performed, is the largest STI clinic in the Netherlands with 50,000 consultations annually<sup>26</sup>. In line with the national guidelines, the clinic focusses at persons at greatest risk of STI<sup>27</sup>. This includes persons: with STI related symptoms, that have been notified of an STI by a sex partner, men who have sex with men (MSM), first or second generation immigrants from STI/HIV endemic area's, those with a sex partner from an STI/HIV endemic area, those aged below 25 years and victims of sexual violence. Testing and care are offered free of charge, and without identification: anonymous care can be provided.

This thesis focusses on the following STI: chlamydia (including lymphogranuloma venereum), gonorrhoea, syphilis, hepatitis C and HIV. Chlamydia is caused by the bacterium *Chlamydia trachomatis*<sup>28</sup>. Around 50% of the urogenital infections are

asymptomatic, but it may cause discharge from the penis, burning sensations with urination, and pain/swelling of the scrotum<sup>28</sup>. Standard treatment includes doxycycline or azithromycin.

Urogenital gonorrhoea (also known as ‘the clap’) is caused by the bacterium *Neisseria gonorrhoeae* and causes a burning sensation with urination or discharge in 95% of the male cases<sup>29</sup>. An anal infection can cause anal itch, proctitis or anal discharge. If left untreated, it can enter the blood stream and cause severe complications. While still treatable with ceftriaxone, the WHO considers gonorrhoea as one of the top 12 antibiotic-resistant priority pathogens that pose the greatest threat to human health<sup>29,30</sup>.

Syphilis is caused by the bacterium *Treponema pallidum subspecies pallidum*<sup>17</sup>. The symptoms of syphilis vary depending in which of the stage it presents (primary, secondary, tertiary and latent stages). While the first three stages cause symptoms, the latent stages can only be diagnosed based on serology. Tertiary syphilis can evolve after many years and cause permanent damage to the heart, nerves system and other organs. Syphilis can effectively be treated with penicillin.

Hepatitis C is a blood-borne viral infection, mostly spread through intravenous drug use, poorly sterilized medical equipment, needle stick injuries, and from mother to child during pregnancy<sup>31</sup>. Since 2009 it is shown that it can also be transmitted via sexual contact among HIV-positive MSM. Hepatitis C virus primarily affects the liver and persists in about 75-85% of individuals who are infected. Over many years it can lead to liver cirrhosis and hepatocellular cancer. While there is no vaccine against hepatitis C, medication registered since 2015 has proven very effective (>95% cure rate), but also very expensive (a 12-week treatment costs ±60.000 €)<sup>31,32</sup>.

HIV is usually mentioned separately from the previously mentioned STI. HIV causes acquired immunodeficiency syndrome (AIDS)<sup>33</sup>. Without treatment, the average survival time after infection with HIV is estimated to be 9 to 11 years. In the Netherlands MSM account for 71% of the new HIV diagnoses and an estimated 14,000 MSM live with HIV<sup>16</sup>. While cure is still not possible, condoms, antiretroviral treatment (since 1996) and post-exposure prophylaxis (PEP) have been known to battle the HIV epidemic. Besides physical damage, STI and HIV can also cause a lot of mental distress and have often been a reason for relationships to break up.

Part of the research described in this thesis, started with encouraging evidence on the effectiveness of a new HIV prevention intervention called pre-exposure prophylaxis (PrEP). PrEP - antiretroviral medication, usually a combination of tenofovir disoproxil fumarate (TDF) and emtricitabine (FTC) - is provided to HIV negative people who are at increased risk for HIV<sup>34</sup>. Evidence shows that PrEP can be taken daily (one tablet) or event driven (two tablets taken between 24 and two hours before sexual intercourse, followed by one tablet every 24 hours up to 48 hours after the last sexual intercourse)<sup>34</sup>. PrEP offers high levels of protection if taken appropriately<sup>34</sup>. Most common side effects reported in studies were gastrointestinal, headache and nausea<sup>35 36</sup>. Use of TDF-FTC as PrEP has been associated with a mild non-progressive decline in creatinine clearance that is reversible on discontinuation of drug. Kidney function and HIV tests to tackle drug resistance are reasons medical monitoring is necessary for PrEP users.

Apart from an increased risk for HIV and STI, MSM have higher prevalence of mental disorders<sup>13 14</sup>. Compared with the heterosexual population, MSM show higher levels of anxiety, depression, suicide and drugs use<sup>13 14</sup>. There are two main frameworks that offer a possible explanation for these sexual preference related differences. The first is the minority stress model that articulates how minority stress processes are related to a range of mental health problems such as substance use, depressive symptoms and suicide ideation<sup>11 12</sup>. As described earlier, a minority stressor is a unique stressor experienced by socially stigmatized people. Daily received stressors (for example prejudice, victimization and discrimination) negatively influence individuals causing internalized psychological disorders such as depression and anxiety disorders<sup>37</sup>. Especially people who deviate the most from traditional masculinity and femininity role models are prone for heterosexist victimization<sup>38</sup>. The minority model describes that individual perceptions and appraisal play a central role in internalized homonegativity and emotional dysregulation<sup>37</sup>.

Another framework that enforces the importance of the minority stress model and gives a possible explanation of the complicated relations between mental health burdens, drug use and sexual risk taking in MSM is the syndemic theory<sup>39 40</sup>. Syndemics are defined as the aggregation of two or more health conditions in a person or population. Subsequently, a harmful biological or behavioral interface exacerbates the negative health effects of any or all of conditions involved. Syndemics involve the adverse interaction of its components (eg, infections, mental health problems, behavioral



conditions, chronic non-communicable diseases, toxic exposure, malnutrition etc). Syndemics are most likely to emerge under health inequality caused by e.g. poverty, stigmatization, stress or structural violence.

Stall found important associations between sexual risk behavior among MSM and conditions such as multiple drug use, intimate partner violence, childhood sexual abuse and depression<sup>40</sup>. In his study involving 3000 MSM, high-risk sex behavior was found in 7.1% among those without any condition to 22.5% for those with all of the aforementioned conditions.<sup>40</sup> The syndemic model conceptualizes the influence of mental health problems and sexual risk behavior on both individual as on population level, in which social environments contribute to disease clustering, interaction, and vulnerability.

The minority model can be considered as an explanation of the increased mental health problems in MSM, which is a problem on itself. The syndemic model conceptualizes the influence of social and mental health problems on sexual risk behavior which adds to the importance of addressing mental health problems in a sexual health setting.

## OUTLINE OF THIS THESIS

In part I we describe sexual activity related behavior - anal douching and drug use - among MSM. **Chapter 2** reports on anal douching, which is practiced by many MSM. We assessed the prevalence of anal douching, sharing douching equipment and the association with STI. In **Chapter 3**, we focus on drug use during sex, which is often linked to higher number of partners and condomless anal sex. We compared drug use among 4 different datasets of MSM at the STI clinic and identified latent classes based on the (combination of) drugs used. Afterwards, sexual behavior and STI prevalence among these subgroups were compared to identify which groups are at highest risk for STI. In **Chapter 4**, we repeated this latent class analysis among MSM of several STI clinics in the Netherlands, comparing Amsterdam versus surrounding urban regions and validated the previous finding.

As described above, HCV can be sexually transmitted among HIV-positive MSM, however evidence for sexual transmission among HIV-negative MSM is sparse. In part II we describe evidence of sexually acquired HCV among HIV-negative MSM. In **chapter 5** we describe a case report of 2 hiv-negative MSM in a long-term relationship

who sequentially acquired a highly similar HCV strain. In **Chapter 6** we provide further evidence of sexual transmission of HCV among HIV-negative MSM who are eligible for PrEP.

In Part III, we describe results of the AMsterdam PrEP (AMPrEP) demonstration project. It is the first demonstration project worldwide to let people choose between daily and event-driven PrEP. In **Chapter 7**, we describe baseline characteristics, preference and motivations for the two PrEP modalities. As described in the syndemic theory, mental health problems are more prevalent among MSM than non-MSM and can be related with sexual behavior. In **Chapter 8**, we present the mental health status, drug use characteristics and other syndemic domains among AMPrEP participants at baseline and during follow-up.

In Part IV, we describe the *syndemic based intervention* (syn.bas.in), an open-label randomized controlled trial, which aims to improve health seeking behavior by screening for mental disorders and personal referral. In **Chapter 9**, we described the design and the protocol of the syn.bas.in study, while in **Chapter 10** we describe the results of this interdisciplinary study.

In **Chapter 11**, the results found in this thesis are discussed and future recommendations on the provision of dedicated health care to MSM at an STI clinic are given.

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