Literature Review: Extragenital Gonorrhea and Chlamydia in Men Who Have Sex with Men

Andrew Tharp, MSN, APRN, FNP-BC

Southern Illinois University - Edwardsville

Literature Review

Introduction

Gonorrhea and chlamydia are the two most common bacterial sexually transmitted infections (STI) worldwide (World Health Organization, 2015). In the United States alone, gonorrhea and chlamydia infections account for almost $1 billion in direct medical costs annually (Centers for Disease Control and Prevention, 2018). Oftentimes, gonorrhea and chlamydia are thought to infect only the urogenital tract; however, these infections can be harbored at other anatomic sites as well. The term 'extragenital' is used to refer to sites outside of the urogenital tract and commonly includes the rectum and oropharynx.

Extragenital gonorrhea and chlamydia infections are common among men who have sex with men (MSM). Certain sexual behaviors such as condomless receptive anal intercourse can increase the likelihood of infection at extragenital locations (Kumar et al., 2020). Infections at extragenital sites can increase susceptibility to other more serious diseases such as human immunodeficiency virus (HIV) (Barbee et al., 2017; Katz, Dombrowski, Bell, Kerani, & Golden, 2016). Routine extragenital screening recommendations exist for this population, especially in those MSM deemed to be high risk. Screening does not appear to be completed consistently despite evidence in the literature supporting its use. Numerous barriers, including lack of clinician time and knowledge, lack of patient education, and stigma associated with the MSM population all decrease the likelihood of compliance with routine screening recommendations.

Lack of adherence to extragenital screening recommendations is likely to increase the overall disease burden of gonorrhea and chlamydia due to a higher risk of transmission that exists when asymptomatic extragenital infections go undiagnosed (Lutz, 2015). Primary care is

an area of medicine focused on prevention of many diseases and is a suitable place to perform routine extragenital screenings; yet, there is a significant mismatch between current screening rates and screening recommendations. Barriers need to be addressed to allow for better screening rates of extragenital gonorrhea and chlamydia in MSM within the primary care setting.

Aim

The aim of this literature review is multifaceted and seeks to address the following questions regarding gonorrhea and chlamydia within the MSM population:

1. What is known about the incidence of gonorrhea and chlamydia in the MSM population as well as what are the current recommendations for routine screening for these infections within that population?

2. How often are routine screenings currently being offered and taking place, particularly at extragenital (rectum and oropharynx) sites?

3. How are transmission rates of gonorrhea and chlamydia within the MSM population affected by whether routine screening, particularly at extragenital sites, takes place?

4. What other risk factors (aside from transmission of infection) exist if gonorrhea and chlamydia infections, particularly at extragenital sites, are not properly diagnosed and treated?

5. What barriers exist for routine screening for gonorrhea and chlamydia in the MSM population?

Search Strategy

Multiple searches were performed using the EBSCO database through Southern Illinois University - Edwardsville's Lovejoy library website. In the first search, keywords used were

"men who have sex with men" and "gonorrhea and chlamydia." These results were filtered to include items published between 2015 and 2020. The search yielded 88 items. Items were scanned for relevance and those deemed relevant to the literature review aim were included. A second search used the keywords "extragenital" and "gonorrhea and chlamydia." Again, results were filtered to include items published between 2015 and 2020. This search yielded 89 items, some of which were duplicates from the prior search. Items were scanned for relevance and those deemed relevant and not duplicate were included in this review.

Results

A total of 41 items were selected for inclusion based off of perceived relevance to the literature review aim. In review of relevant items from the above searches, numerous articles presented findings and discussed information that required further investigation. In order to obtain more comprehensive information about these topics, reference lists for these articles were accessed. Items on the reference list were selected and reviewed as appropriate. These additional items were selected for inclusion in the literature review if they were deemed relevant. Relevant articles included information pertaining to, but not limited to, statistics on prevalence of infection, risk factors for transmission, complications of infection, recommendations for screening, screening rates, and barriers to screening.

Rise of Sexually Transmitted Infections

There has been a significant rise in the number of reported STIs in the United States and around the world. The Centers for Disease Control and Prevention (CDC) (2017a) estimated a 67% increase in gonorrhea infections and a 22% increase in chlamydia infections since 2013. Many STIs go unreported so these increases could potentially be even higher. Gonorrhea and

chlamydia have increased particularly among MSM and appear to be diagnosed more frequently in MSM with high numbers of sexual partners (Chow et al., 2015). Even more alarming than the rise in STIs is that antimicrobial resistance is becoming a global concern and treatment options for drug-resistant bacterial strains, particularly with gonorrhea, is increasingly limited (Wu et al, 2019). The CDC recently updated treatment guidelines for gonorrhea in order to better address increased antibiotic resistance found in strains of gonorrhea (St. Cyr et al., 2020).

Men Who Have Sex with Men

Men who have sex with men predominately refers to homosexual men but also includes bisexual men and other men who have sex with men. These men represent an underserved population when it comes to healthcare and are disproportionately affected by STIs (Earnest et al., 2020; Johnson-Jones et al., 2019). As is discussed later, there are numerous barriers that prevent MSM from receiving the care that they need, particularly as it relates to sexual health. Men who have sex with men have a disproportionately greater risk than other populations of acquiring chlamydia and gonorrhea (Lutz, 2015). Due to many of the sexual behaviors the MSM population engage in they are also at higher risk for extragenital STI infections, such as those at the rectal and oropharyngeal sites (Kumar et al., 2020; Rietmeijer, 2019). In many instances, STI screening may only include screening for urogenital infections in this population and therefore, MSM may be at higher risk to have undiagnosed, asymptomatic extragenital gonorrhea and chlamydia infection.

Prevalence Rates of Gonorrhea and Chlamydia

Urogenital. Prevalence rates of urogenital gonorrhea and chlamydia are well-documented and appear similar in MSM around the world. In the United States, one study

reported prevalence rates of urogenital gonorrhea and chlamydia are 7.5% and 5.2% respectively

(Abara et al., 2020) and 5.4% and 4.5% respectively (Danby et al., 2016). Slightly lower, but

comparable, prevalence rates were reported by Mustanski et al. (2017) with gonorrhea at 0.9%

and chlamydia at 2.6%. In China, prevalence rates were 5.2% for gonorrhea and 6.7% for

chlamydia (Yang et al., 2018) and in Germany urogenital prevalence was reported to be 1.4% for

gonorrhea and 2.0% for chlamydia (Jansen et al., 2020).

Extragenital. Studies conducted in populations of MSM across the United States found

similar prevalence rates of extragenital gonorrhea and chlamydia. Abara et al. (2020) reported

rectal prevalence of 11.8% for gonorrhea and 12.6% for chlamydia as well as oropharyngeal

prevalence of 9.1% for gonorrhea and 1.8% for chlamydia. Similarly, Danby et al. (2016)

reported prevalence rates of 16.5% and 2.2% for oropharyngeal gonorrhea and chlamydia

respectively and 11.6% and 17.4% for prevalence of rectal gonorrhea and chlamydia. In a study

that analyzed only rectal STIs, Mustanski et al. (2017) found a prevalence of 8.8% for chlamydia

and 5.0% for gonorrhea.

Studies on prevalence rates of extragenital gonorrhea and chlamydia in MSM conducted

internationally have produced similar findings. In Peru, Leon et al. (2016) reported a rectal

chlamydia prevalence of 19.2% and a rectal gonorrhea prevalence of 8.6%. For oropharyngeal

chlamydia and oropharyngeal gonorrhea the authors reported prevalence rates of 4.1% and 5.4%

among MSM respectively. In a study of MSM in China, rectal gonorrhea prevalence was 6.1%

and rectal chlamydia prevalence was 11.2%; whereas oropharyngeal gonorrhea prevalence was

3.9% and oropharyngeal chlamydia prevalence was 1.3% (Yang et al., 2018). Finally, a German

study found prevalence rates of 5.8% and 7.7% for rectal gonorrhea and chlamydia respectively

whereas prevalence rates for oropharyngeal gonorrhea and chlamydia were 4.8% and 1.1% respectively (Jansen et al., 2020).

A large systematic review was conducted by Chan et al. (2016) which summarized existing prevalence rates of extragenital gonorrhea and chlamydia in literature published through 2015. The study included 53 articles pertaining to extragenital prevalence rates of gonorrhea and chlamydia in the MSM population and for comparison included many other studies on women and men who have sex with women. Studies included were conducted with populations of MSM across the world in many different countries. Prevalence ranges for rectal gonorrhea were 0.2-24% (median 5.9%) and for rectal chlamydia were 2.1-23% (median 8.9%). For oropharyngeal gonorrhea prevalence ranges were 0.5-16.5% (median 4.6%) and for oropharyngeal chlamydia were 0-3.6% (median 1.7%).

In studies that analyzed prevalence rates of both extragenital and urogenital gonorrhea and chlamydia infections, a high portion of the total infections were found to be at extragenital locations. For example, 79.6% of all chlamydia infections and 76.5% of all gonorrhea infections in MSM were found at extragenital locations according to Danby et al. (2016). Mena, Crosby, and Chamberlain (2018) reported similar findings in their study which found that in the absence of urogenital positivity, 73% of all chlamydia infections and 77% of all gonorrhea infections identified were found either at a rectal or oropharyngeal location. Although not occurring frequently, the literature does support a smaller prevalence of multisite infections (any combination of gonorrhea or chlamydia infection at urogenital, rectal, or oropharyngeal sites) (Jansen et al., 2020; Mena, Crosby, & Chamberlain, 2018; Leon et al., 2016).

Symptomatic Versus Asymptomatic. The majority of cases of gonorrhea and chlamydia in men are thought to be asymptomatic (Passaro et al., 2018; Yang et al., 2018). This includes

infection at any anatomic site (urogenital, rectal, and oropharyngeal) but particularly at extragenital locations. Chan et al. (2016) report that only 14% of men infected with chlamydia infection are symptomatic; while 40% of men infected with gonorrhea infection are symptomatic. When symptomatic, gonorrhea and chlamydia infection in the rectum can cause rectal pain, bleeding, discharge and proctitis. In the oropharynx, these infections can cause pharyngitis and lymphadenopathy/lymphadenitis when symptomatic.

Missed Infections

Numerous studies also comment on the percentage of possible missed gonorrhea and chlamydia infections should extragenital screening not to take place. There are varying percentages depending on how the authors quantified their findings; however, all of the reviewed studies draw similar conclusions regarding missed infections. In one study, Abara et al. (2020) comment on the number of missed extragenital gonorrhea cases that would have been missed without screening in a population of MSM with urogenital chlamydia. Of the participants with urogenital chlamydia, extragenital gonorrhea would have been missed or even undertreated in 13% of participants. Danby et al. (2016) reported that in MSM 80% who tested positive for chlamydia and 77% who tested positive for gonorrhea were only positive at extragenital sites.

In a more robust study done over the course of a year, Anschuetz and colleagues (2016) reported findings which showed the high likelihood of missed extragenital infections if routine screening were not to occur. The authors analyzed data from two different clinics in Pennsylvania with a large number of MSM participants. Results showed that without extragenital testing of gonorrhea, 80.7% of patients with infection would have been missed at one clinic, and 83.3% would have been missed the other clinic. Similarly, without extragenital testing of chlamydia, 72.4% of patients with infection would have been missed at the first clinic, and

73.0% would have been missed at the second clinic. Though their study mostly focused on

prevalence rates, Chan et al. (2016) also analyzed existing literature for missed infection rates

and reported a wide range of possible missed extragenital infections. After review of numerous

articles, Chan and colleagues reported that if only urogenital screening had taken place, 14-85%

of rectal and pharyngeal gonorrhea and chlamydia would have been missed.

Duration of Extragenital Infection

Much remains unknown about the duration of extragenital chlamydia and gonorrhea

infections should they go untreated. Largely, this is due to ethical considerations which prevent

this data from being collected. Once a diagnosis of extragenital infection (or any infection) is

made, it is wrong to delay proper treatment. Given this, it is hard to know how long an

extragenital infection may last and whether or not it might clear on its own if left untreated. Few

studies have investigated this phenomenon of self-clearing infections and have reported

clearance rates between time of diagnosis (positive test result) and consultation for treatment

which could be up to a couple of weeks later.

In a comprehensive study conducted by van Liere et al. (2019), spontaneous clearance of

urogenital, anorectal, and oropharyngeal chlamydia and gonorrhea was studied in MSM,

heterosexual men, and women. Unfortunately, a rather small number of MSM participants were

involved in this study. Between screening and treatment consultation, no MSM participants

(0/11) had spontaneously cleared chlamydia from the urogenital tract, and 66% (2/3) had

spontaneously cleared gonorrhea from the urogenital tract. Eighty percent (4/5) of MSM

spontaneously cleared chlamydia from the oropharynx, and 30% (4/13) spontaneously cleared

gonorrhea from the same location. Finally, only 4% (1/25) of MSM spontaneously cleared

anorectal chlamydia, and 22% (2/9) MSM spontaneously cleared anorectal gonorrhea between

the time of screening and treatment consultation. The median time between screening and treatment consultation for the study, including MSM, heterosexual male, and female participants was 10 days.

In order to circumvent the ethical concerns of researching the true duration of extragenital infections, Chow et al. (2016) reviewed numerous longitudinal cohort studies in order to estimate the duration of infection. The authors used prevalence and incidence rates from these studies, and although the data was indirect and somewhat limited, the authors were able to suggest length of duration at various sites. The estimated duration of pharyngeal gonorrhea was 114-137 days whereas the estimated duration of pharyngeal chlamydia was 667 days. Rectal gonorrhea was estimated to be present for up to 346 days and rectal chlamydia for 578 days.

Risk Factors for Transmission and Infection

Condomless anal sexual intercourse and condomless oral sex remain two of the most common ways for transmission of extragenital gonorrhea and chlamydia in MSM. Numerous studies report increased risk of rectal gonorrhea or rectal chlamydia after condomless receptive anal intercourse (Chamberlain, Crosby, Mena, Chan, & Mayer, 2017; Mustanski et al., 2017). Chow & Fairley (2019) reported evidence which suggested oropharyngeal gonorrhea can be transmitted by kissing in addition to the established route of condomless oral sex. Furthermore, anorectal gonorrhea can be acquired when saliva is used as a lubricant for anal sex in addition to the established route of condomless anal sex in MSM. The authors state that condomless anal sex remains the major route for chlamydia transmission.

In addition to the more common ways that extragenital infections can be transmitted, there are numerous studies that comment on independent risk factors associated with infection.

Independent factors associated with rectal only chlamydia are being a sex worker and exclusively having sex with men while factors associated with rectal only gonorrhea are having been warned for STIs by a partner or ex-partner and oropharyngeal gonorrhea infection (van Liere et al., 2015). Hassan et al. (2017) report on rectal hygiene as an independent risk factor for gonorrhea or chlamydia at the rectal site. Using enemas or douching is a common practice among MSM. The authors present findings which support the conclusion that use of enemas/douching increases the odds of acquiring rectal gonorrhea or chlamydia.

Another risk factor reported by Priest et al. (2018) is the number of partners and timing of sexual encounters with those partners. The authors reported that oropharyngeal gonorrhea positivity was associated with the number of partners in the past 3 months but not the number of partners 4-12 months ago. Furthermore, men who had six or more partners in the past 3 months had significantly higher odds of acquiring oropharyngeal gonorrhea, but this was not the case for men who had a similar number of partners 4-12 months ago. Finally, Priest et al. (2018) reported that anorectal gonorrhea and chlamydia and urogenital chlamydia were associated with the number of partners in both time periods.

Risk of HIV Infection after Gonorrhea or Chlamydia Infection

An association between recent rectal gonorrhea or chlamydia infection and increased risk for HIV has been well established in the literature. Studies have shown varying degrees of association but have been limited in their ability to show a causal relationship. However, multiple studies have shown an increased incidence of new HIV infection after infection with gonorrhea or chlamydia (Barbee et al., 2017; Katz et al., 2016). Barbee et al. (2017) found that diagnosis of rectal STI within the past 12 months was associated with higher risk of HIV

diagnosis. The authors concluded that one in seven HIV diagnoses could be attributed to rectal STI.

In a study conducted by Katz et al. (2016), similar conclusions were reached with the authors finding that men who have sex with men recently diagnosed with rectal gonorrhea were at the greatest risk for being diagnosed with HIV infection after STI diagnosis. Specifically, the authors reported that HIV infection incidence was 4.1 per 100 person-years after rectal gonorrhea infection compared to just an estimated incidence of 0.4 per 100 person-years for all other MSM in that population.

Another study relied on a modeling analysis to address the challenges in estimating the causal impact of rectal gonorrhea and chlamydia in regards HIV risk. Jones et al. (2019) used "a stochastic, agent-based model of a sexual network of MSM with co-circulating HIV, gonorrhea, and chlamydia infections" (p. 357). They estimated the effect of gonorrhea and chlamydia infection on overall HIV incidence as well as HIV acquisition and transmission. It was concluded that 10.2% of HIV infections studied were attributable to gonorrhea or chlamydia infections.

Recommendations for Screening

According to the CDC (2015), guidelines for STI screening in sexually active MSM include at least annual screening at all exposed anatomic sites (Johnson Jones et al., 2019). More frequent screening (every 3-6 months) is recommended for MSM at elevated risk for STIs. Factors that put MSM at higher risk for chlamydia, gonorrhea and other STIs including syphilis and HIV are: multiple or anonymous partners, intravenous drug use, sex in conjunction with illicit drug use (including methamphetamines), and sex partners who engage in those activities

(California Department of Public Health, 2015). Additionally, MSM who take pre-exposure prophylaxis medication (PrEP) should have screening for HIV and syphilis as well as rectal, oropharyngeal, and urogenital gonorrhea and chlamydia every 3 months (Centers for Disease Control and Prevention, 2017b).

Types of Screening

Nucleic Acid Amplification Tests. Nucleic acid amplification tests (NAAT) are the gold standard when testing for urogenital gonorrhea or chlamydia but are not approved by the U.S. Food and Drug Administration (FDA) for use in detecting rectal or oropharyngeal gonorrhea or chlamydia (Rawre, Agrawal, & Dhawan, 2018). However, the CDC recommends NAAT be utilized for this purpose due to their sensitivity in detecting gonorrhea and chlamydia (Centers for Disease Control and Prevention, 2015). The NAAT test has shown both higher specificity and sensitivity for detecting extragenital infections when compared to culture (Rawre, Agrawal, & Dhawan, 2018).

One major disadvantage of using NAAT over culture is the inability to determine bacterial viability and antimicrobial susceptibility (Rawre, Agrawal, & Dhawan, 2018). For example, potentially lower sensitivity in the pharynx and rectum could be linked to colonization of other organisms at these locations, such as those in the *Neisseria* species. This could lead to difficulty in isolation of gonorrhea. If treatment failure occurs, it is recommended a culture be obtained so that antimicrobial susceptibility can be performed (Rawre, Agrawal, & Dhawan, 2018).

Self-Collected Tests. Most often, screening swabs are collected by the clinician. However, self-collected swabs have emerged as an effective alternative to clinician collected

swabs. The use of self-collected NAAT swabs for extragenital gonorrhea and chlamydia has been found to be reliable in accurately detecting similar rates, if not better, as clinician collected swabs (Sexton et al., 2013). Use of self-collected tests have been shown to have high acceptance among patients and also increases likelihood of returning for additional screenings in the future among MSM (Soni & White, 2011).

Screening Rates

Most screening rates for STIs are self-reported and, for the MSM population, remain lower than recommended screening rates. Only 42% of American MSM reported any STI screening test within the past 12 months (de Voux, Bernstein, Kirkcaldy, Zlotorzynska, & Sanchez, 2019). In the same study, an even lower percentage of participants reported extragenital screenings at any site (16%). Of those who did report extragenital screening within the past 12 months, 19% reported only an oropharyngeal swab, 14% reported only a rectal swab, and 68% reported receiving both (de Voux et al., 2019).

Other studies using different time periods found similarly low screening rates. In a study of HIV infected MSM, screening rates of gonorrhea (29%) and chlamydia (32%) over an 18-month period were low (Barbee, Dhanireddy, Tat, & Marrazzo, 2015). Especially alarming were that many participants had higher risk factors such as drug use (16.4%) and recent bacterial STI (25.5%), which would suggest they should be screened at more frequent rate than someone at average risk. Self-reported lifetime testing history in Chinese MSM was 28.5% for chlamydia and 30.6% for gonorrhea (Wu et al., 2019).

Despite current low levels of screening rates, there is some evidence that rates are improving. Self-reported testing within the past 12 months in MSM for chlamydia was 37% in

2011, and 47% in 2014 and for gonorrhea was 38% and 47% respectively (Hoots, Torrone, Bernstein, & Paz-Bailey, 2018). A more recent study showed that of interviewed MSM only 1 in 3 reported that they had not been screened within the past 3 months irrespective of anatomic site (Johnson Jones et al., 2019).

Barriers to Screening

There is somewhat limited research that has been devoted to understanding the barriers that the MSM population may face in routine screenings for STIs, particularly chlamydia and gonorrhea. Even less is known about the barriers pertaining to extragenital screenings and whether those barriers may differ from those of the more common urogenital and serum screening tests. The studies that have identified various barriers to routine screening for STIs have found fairly consistent contributing factors to poor screening rates. Many of the barriers to screening can be attributed to either the clinician or the patient (Barbee et al., 2015; Heijman et al., 2017; Lutz, 2015).

Clinician. In a study of HIV infected MSM, Barbee et al. (2015) discussed several clinician related barriers to screening for STIs. After interviewing 28 clinicians (nurse practitioners, medical students, residents, fellows, and attending physicians), the most common barrier identified was lack of time (68%). Lutz (2015) outlined similar concerns by clinicians who stated that full schedules prevented them from being able to perform a comprehensive sexual history and make adequate screening recommendations. Another commonly reported barrier by clinicians is that they do not feel comfortable taking a sexual history (Barbee et al., 2015; Lutz, 2015). Lutz (2015) further reported clinician discomfort is attributed to either lack of education or personal bias. Additional barriers identified on behalf of the clinician were: patient

seemed reluctant to testing, clinician was afraid of appearing judgmental, and the clinician

lacked staff support or an interpreter (Barbee et al., 2015).

The study conducted by Barbee et al. (2015) further discussed perceptions of the clinician

as to why patients refused STI screening. Clinicians reported the most likely barriers for patients

being: patient not being "prepared" (55%), seeking testing elsewhere (82%), patient not

believing they were at risk (64%), patient not having time (23%), or preferring a same sex

clinician (27%). It is important to be clear that these percentages represent the number of

clinicians reporting that this was their perception of patient barriers, rather than these being

actual patient reported barriers.

Patient. The same study by Barbee et al. (2015) presented results from 31 surveys

completed by HIV infected men who do not routinely screen for STIs at their primary care

location. These respondents identified reasons why they chose to seek screening elsewhere

including: easier testing (42%), preferring anonymity (21%), wanting more frequent testing

(13%), cost or convenience (5%), and forgetting (5%). However, these responses are limited in

their ability to apply to screening for STIs in general as they pertain to reasons the individual

might have sought testing elsewhere from their primary care clinic.

In another study of HIV infected (newly) MSM, Heijman and colleagues (2017)

discussed barriers to STI screening in more depth. The authors completed 30 interviews in total

and identified the most common barriers to testing. Participant answers were categorized into

perceptions of safety, misperceptions about testing procedures, situational barriers, and

burdensome testing procedures. Some men felt that using condoms protected them from STIs,

and therefore did not get routine testing. Another false belief was that they were being checked

for STIs with their other routine care (Heijman, Zuure, Stolte, & Davidovich, 2017). Similarly,

Lutz (2015) reported that patients thought that urogenital screening for gonorrhea and chlamydia would test for all gonorrhea or chlamydia throughout the body.

Lutz (2015) comments on additional patient related barriers highlighting similar feelings to those of the clinician. Patients reported a lack of comfort in discussing sexual practices. Additionally, many MSM reported non-disclosure of sexual preference, sexual practices, or HIV status to their clinician out of fear of judgement and bias. Finally, lack of knowledge served as a barrier for many MSM as they reported not understanding their risk for extragenital infections. Within the realm of situational barriers, Heijman et al. (2017) reported some respondents had aversion to certain testing locations; particularly those where they had a bad previous experience such as receiving an HIV diagnosis. Patients also spoke on the burdensome testing procedures, both in regards to time waiting to test and time to complete testing.

In addition to barriers to routine STI screening, Heijman et al. (2017) reported results from respondents pertaining to motives for regular testing. Most respondents identified health consciousness as a motive, whereby getting tested would prevent STI related problems and prevent infection from going unnoticed. Similarly, respondents were concerned about protecting a partner from STI. They reported beliefs that getting tested regularly would prevent their partner from becoming infected. Finally, some participants reported feeling vulnerable to infection as a reason to be tested regularly. This feeling of vulnerability revolved more around developing possible symptoms than it did on being conscious of engaging in high risk sexual behavior.

Discussion

Multiple studies have suggested that prevalence rates of extragenital gonorrhea and chlamydia are significant in the MSM population. Extensive systematic analyses found that

prevalence rates of extragenital gonorrhea and chlamydia are higher in MSM compared to women and men who have sex with women (Chan et al., 2016). Many of the studies that reported prevalence rates were conducted with data from STI clinics; so, it is possible that the prevalence rates do not accurately reflect those in a broader population of MSM (Johnson Jones et al., 2019). However, Yang et al. (2018) found similar or even higher rates in a population of community clinic MSM compared to STI clinic MSM. This highlights the similarity in prevalence of extragenital infection among all MSM and reinforces the likelihood of transmission to sexual partners if screening is not routinely conducted.

The studies reporting prevalence rates presented in this review also included populations of MSM in various parts of the world. The consistency found between these prevalence rates suggests that no specific ethnicity or socioeconomic class of MSM is unaffected by extragenital infection. Many of these same studies suggest that a large portion of extragenital infections would be missed if screening were only to be conducted at urogenital sites. Though the literature does show some variability in regards to missed infection rates, collectively these results indicate that missed infections do occur, oftentimes quite frequently within the MSM population.

The degree to which missed infections occur may be, in part, due to the asymptomatic nature of extragenital gonorrhea and chlamydia infections. Symptomatic infections are rare in the MSM population. This increases the risk in which individuals might unknowingly pass an infection to a sexual partner; especially if safety measures such as condom use are not in place or if those individuals are engaged in other high risk behaviors. The burden of disease is much higher when transmission occurs unknowingly, and those with infection continue to be asymptomatic.

Though studies are limited in their ability to determine how long extragenital infections can persist without treatment, they suggest that the time frame can be significant. In one particular study, despite a relatively low number of MSM participants, a low percentage of infections were spontaneously cleared between time of diagnosis and time of treatment (van Liere, 2019). Modeling analysis suggests that untreated infection may persist for as long as 1-2 years in affected individuals (Chow et al., 2016). The combination of a lengthy infectious period and high asymptomatic rates of disease increases the likelihood of transmission to multiple individuals and raises the burden of disease in this population.

Given that many STIs, especially those at extragenital locations, are asymptomatic in the MSM population, screening is an integral step in minimizing the transmission of those infections. If sexually active MSM, especially high risk men, are not routinely screened for these infections, there is likely to be increased risk of transmission among partners and between anatomic sites. Transmission of the asymptomatic infection can occur exponentially in this population, particularly in those men with multiple sex partners. To underscore this, Earnest et al. (2020) presented findings that suggest improved extragenital screenings substantially reduced site-specific gonorrhea in MSM, particularly when interventions aimed at increasing rectal screenings were implemented.

The population level benefits of screening for extragenital infections goes beyond reducing prevalence and transmission of those diseases. Studies have shown that rectal gonorrhea and chlamydia infections are associated with high risk of HIV infection. Biello et al. (2018) discuss that there is likely a biological basis for this association; but, there also may be overlapping of risk factors that increase the likelihood of new HIV infection. For example, in the MSM population, condomless receptive anal intercourse is a risk factor for either rectal

gonorrhea or chlamydia as well as HIV infection. From a biological standpoint, it is thought that a previous rectal gonorrhea or chlamydia infection causes an inflammatory cascade of leukocytes to the target area which subsequently disrupts the rectal mucosa and increases the risk for HIV infection (Barbee et al., 2017; Jones et al., 2019).

Screening for extragenital gonorrhea and chlamydia in MSM is supported by numerous governing health organizations including the CDC and WHO. The CDC recommends at least annual screening for extragenital gonorrhea and chlamydia in any MSM and more frequently (up to every 3 months) for those MSM who engage in high risk behaviors and those who take PrEP. The World Health Organization guidelines suggest that if prevalence of asymptomatic urethral and rectal gonorrhea and chlamydia infection is greater than 1-2% then the benefits of periodic testing for these infections among MSM outweighs the harms and costs (Wu et al., 2019). This is consistent with recommendations from the CDC for routine screening of gonorrhea and chlamydia at all anatomic sites in MSM. However, in their conclusion that more frequent screening may be necessary, van Liere et al. (2019) conclude that annual screening for gonorrhea and chlamydia may be insufficient to reduce extragenital infection prevalence, particularly at the oropharyngeal site.

Although a majority of the studies reviewed support these screening recommendations in reducing prevalence rates and overall burden of disease, one study presented findings that suggest the opposite. Tsoumanis et al. (2018) conducted a review of 12 studies and concluded there is little evidence that screening for gonorrhea and chlamydia in MSM has an effect on the prevalence of these infections. The authors stated no evidence was found that more frequent screening reduces prevalence more effectively than annual screening. The authors suggested

randomized controlled trials are required to better assess the risks and benefits of gonorrhea/chlamydia screening in high and low risk MSM.

In a direct rebuttal of the review conducted by Tsoumanis et al. (2018), Ridpath et al. (2018) concluded the majority of studies that had been reviewed did not measure the population prevalence of disease, nor did the researchers evaluate a change in STI screening practices. The authors also commented on the inclusion of predominately small cohort studies within the review which were not representative of the population. Finally, Ridpath et al. (2018) concluded that there were errors in interpretation of data from these reviewed studies which, consequently makes it difficult to interpret the findings. Ridpath et al. (2018) discussed their conclusions regarding the impact of STI screening suggesting that lack of evidence does not mean that routine screening of MSM does not have individual level benefits, but that there have been no studies to evaluate the individual level benefits of screening among MSM.

There are clear recommendations from the CDC regarding routine extragenital screening for gonorrhea and chlamydia, and these recommendations should be followed by clinicians who care for MSM. Yet, as presented in this review, it is apparent that current screening rates among this population are not consistent with the screening recommendations. This mismatch provides an opportunity for clinicians to close the gap in order to reduce the burden of infection in the MSM population. A commentary from Rietmeijer (2019) supported this notion, suggesting that in primary care the focus should be on improving STI screening rates. Additionally, Rietmeijer (2019) suggested extragenital testing for gonorrhea and chlamydia should be available in settings serving populations more vulnerable to STI acquisition at those anatomical sites, including MSM. In order to increase the screening rates of extragenital gonorrhea and chlamydia, it is imperative the existing barriers are thoroughly addressed.

The barriers to screening that have been presented are likely to be significant in their contribution to higher prevalence rates and missed infections, largely due to their prohibitive effect on routine screening in MSM. The literature is clear that barriers involve many parties including clinicians, patients, and the healthcare system. To start, clinicians have opportunities to do a better job taking a detailed sexual history particularly with the MSM population. This would include key pieces of information such as number of partners, types of sexual acts engaged in, and any high risk behaviors the individual may partake in. This information is crucial to risk stratifying patients and offering screenings when appropriate. However, time has been a limiting factor for many clinicians when it comes to taking a detailed history. This is something that may need to be addressed operationally within the clinic setting or reviewed by healthcare administration. If clinicians don't have the time to provide quality care to their patients, this needs to be satisfactorily addressed.

The limited time that many clinicians feel they have during an office visit is largely due to the multiple tasks needed in order to allow for extragenital screenings to occur. Clinicians must take a detailed sexual history, educate the patient on STIs and recommendations for screening, offer screening when appropriate, and collect the specimens if the patient is agreeable. One way to reduce the amount of time clinicians need would be through use of patient self-collected swabs. The literature is clear that these swabs are no less accurate in detecting extragenital infection. Not only would this decrease the amount of time a clinician needs to spend with a patient, but it might also increase the likelihood that patients agree to screening recommendations, as they may feel more comfortable collecting these somewhat invasive swabs on their own. With this in mind, MSM patients may be more likely to comply with screening

recommendations, not just on one occasion, but for as long as they continue to be indicated in the future.

Another common barrier among clinicians is lack of knowledge or comfort level with having these discussions. Addressing these barriers may include educating primary care clinicians on the MSM population and common sexual practices MSM might engage in which put them at higher risk for extragenital infection. It may also include ensuring that clinicians feel comfortable collecting swabs from extragenital locations. However, improved knowledge base will only go so far in improving screening rates. In order to address overall comfort level, clinicians simply need to start taking an active part, understanding that having these conversations and offering appropriate screenings are essential to high quality care. To be cliché, practice makes perfect - the more often these conversations take place, the more comfortable clinicians will be.

Similar barriers to screening exist with MSM individuals. Lack of knowledge regarding the importance of screening or the risk factors which put them at higher risk for infection should be addressed. For example, a common false belief in MSM patients is that they are being checked for STIs with their other routine care (Heijman et al., 2017). Similarly, Lutz (2015) reported that many MSM patients thought that urogenital screening for gonorrhea and chlamydia would test for all gonorrhea or chlamydia throughout the body. Though these barriers are due to knowledge level of patients, the key to addressing them involves the clinician. Clinicians have the responsibility to educate patients regarding importance of testing, risk factors for infection, and consequences for undiagnosed infections. It is important that MSM have a fundamental understanding of extragenital infections in order to improve compliance with screening recommendations. The MSM community tends to be a rather close knit community; so, having

these conversations with even just a few patients may have broad positive effects on the greater population.

Another important educational initiative is conveying HIV risk to individuals within the MSM population. Clinicians as well as the public health community can, and should, do a better job explaining the increased risk of HIV associated with rectal gonorrhea and chlamydia infection. Biello et al. (2018) found that MSM participants in their study did not perceive their risk of HIV infection as any higher after having been diagnosed with rectal gonorrhea or chlamydia. This suggests that MSM are not well-educated on this association, which subsequently presents a potential barrier to routine use of HIV prevention strategies such as wearing a condom during anal intercourse or taking daily PrEP.

Finally, MSM patients may be hesitant to disclose information regarding their sexual history, oftentimes due to fear of judgement. It is imperative that clinicians minimize the chance that patients will feel this way. One way this can be achieved is through building a trusting relationship with the patient whereby the patient may feel more comfortable disclosing personal information in order to benefit their overall health. This can be difficult since many MSM patients may not frequently come in for preventative care. Clinicians can show support of MSM patients by providing a safe and comfortable environment that allows an easy way for patients to provide important sexual history information.

Development of a sexual history information form that also serves as a risk stratification tool for STI screening is one way that this information could more easily be attained. This tool could be given to patients at their preventative visit and be filled out while they wait for the clinician to see them. It would include questions pertaining to their sexual history such as who they engage in sexual activity with (men, women, or both), what types of sexual behaviors they

engage in (oral sex, receptive anal intercourse, etc.), and how many different partners they have recently had. Additional risk factors such as whether they use any illicit drugs could also be included to more comprehensively assess their overall risk.

Patients who are hesitant to provide such personal information may be more likely to disclose such information if doing so through non-confrontational means such as circling choices on a piece of paper. Having preset choices available on a risk stratification tool that pertain directly to the MSM patient shows that the clinician has knowledge about their population and is comfortable in discussing this information. This provides a level of trust and minimizes the chance that the patient worries about feeling judged for answering a question a certain way. It also allows for patients to spend more time reflecting on their sexual history to ensure information is accurate and minimizes some of the time the clinician may need to spend with the patient collecting information. If a detailed sexual history is available immediately when the clinician goes in to see the patient, he or she can have a discussion with the patient if needed, and then make recommendations for any necessary screening tests. This may also provide an opportunity to discuss HIV risk prevention strategies such as regularly using a condom and taking daily PrEP. A tool can address many of the current barriers discussed, allowing for increased screening rates of extragenital gonorrhea and chlamydia and potentially reducing the risk of HIV in the MSM population.

Conclusion

Extragenital gonorrhea and chlamydia infections are common in the MSM population and often occur asymptomatically. Self-reported screening rates for gonorrhea and chlamydia, particularly at extragenital sites, do not meet current recommendations for the MSM population, especially those deemed to be higher risk. The importance of extragenital screening goes beyond

reducing transmission of gonorrhea and chlamydia as there is an association with increased HIV risk/susceptibility after rectal gonorrhea or chlamydia infection. Many barriers (including those pertaining to clinicians, patients, and the healthcare system) prevent screenings from taking place as regularly as they should. Primary care clinicians have an opportunity to help address some of these barriers in order to improve overall extragenital screening rates and reduce transmission of gonorrhea and chlamydia in the MSM population.

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