

COMPARISON OF BEHAVIORAL AND SEXUAL NETWORKING RISKS AMONG
PATIENTS WITH SYPHILIS OR GONORRHEA: THE SOCIAL AND SEXUAL
NETWORK (SSN) STUDY, BALTIMORE

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DEDICATION

I dedicate this dissertation to my awesome family: my amazing parents; father Krishnan and mother Sundrambal, my precious gem of a son Haarshan, my ever supportive brother Vignapraavin, husband Kunasegaran, sister in law Vitiashini and also to my future children. They have been my pillars of strength through out my journey in achieving my doctorate. I am who I am because of their unconditional love.

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Last but not least, I dedicate this achievement to God for always being there, especially during tough times and for granting me serenity and strength to keep moving forward without giving up.

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ABSTRACT

Syphilis is caused by the bacterium *Treponema pallidum* and is associated with significant complications if left untreated besides also facilitating the transmission and acquisition of 'Human Immunodeficiency Virus' (HIV) infection. Gonorrhea (infection due to *Neisseria gonorrhoeae*) is the second most commonly reported sexually transmitted disease (STD) in the United States. The purpose of this dissertation is to develop an epidemiologic profile among patients with syphilis and gonorrhea from STD clinics in Baltimore. Networking risks and behavioral factors associated with sexual risk taking were investigated.

The first of three studies sought to determine the associations between the presence of syphilis vs. gonorrhea with sexual characteristics and associations between the presence of syphilis vs. gonorrhea with peer influences on condom use before any sexual intercourse. The second study attempted to determine the associations between the network characteristics of the social contacts with the presence of syphilis vs. gonorrhea, describe differences in associations between sexual behaviors with presence of syphilis vs. gonorrhea by different types of networks (more sexual networks than non-sexual networks and vice versa) and determine the associations between some sexual behaviors with presence of syphilis vs. gonorrhea among men having sex with men (MSM) from this study. Finally, study three aimed to determine if depression and drug abuse are co-morbid with the presence of syphilis vs. gonorrhea among patients with syphilis or gonorrhea, describe differences in the associations of drug abuse with syphilis vs. gonorrhea between people with different types of networks and to determine if sexual abuse is associated with depression among these patients.

Findings from all three studies covered in this dissertation confirm that there are behavioral factors with sexual risk and networking risks among patients with syphilis or gonorrhea. They also provided thorough information on their network characteristics and associated risk factors in different types of social networks (individuals named as part of sexual

or non-sexual network). All three studies provided suggestions for future research in order to increase understanding of sexual and networking risks among patients with STDs.

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LIST OF ABBREVIATIONS

ACASI	Audio Computer-Assisted Self-Interview
aOR	Adjusted Odds Ratio
BCHD	Baltimore City Health Department
CBT	Cognitive Behavioral Therapy
CDC	The Centers for Disease Control and Prevention
CES-D	Center for Epidemiologic Studies Depression
CI	Confidence Interval
CSA	Child sexual abuse
DIS	Disease Intervention Specialists
FTA-ABS	Fluorescent Treponemal Antibody-Absorbed
GLM	Generalized Linear Model
HIV	Human Immunodeficiency Virus
IDU	Injecting Drug User
IPT	Interpersonal Therapy
IPV	Intimate Partner Violence
IVs	Independent Variables
MSM	Men Having Sex with Men
MSWO	Men Having Sex with Women Only
NAAT	Nucleic Acid Amplification Tests
NSFG	National Survey of Family Growth
PID	Pelvic Inflammatory Disease
P&S	Primary and Secondary

RFLP	Restriction Fragment Length Polymorphism
RPR	Rapid Plasma Reagin
SSN	Social and Sexual Network
STD	Sexually Transmitted Diseases
STI	Sexually Transmitted Infections
US	United States
USAF	United States Air Force
VIF	Variation Inflation Factor
WSW	Women Having Sex with Women

CHAPTER 1.
INTRODUCTION

Behavioral, networking, mental health and substance abuse risks of syphilis and gonorrhea as public health issues.

Sexual behaviors and sexually transmitted diseases

Syphilis is a genital ulcerative disease and most times, facilitates the transmission of human immunodeficiency virus (HIV). The rate of primary and secondary (P&S) syphilis reported in the United States (US) decreased during the 1990s and in 2000 was the lowest since 1941. Nonetheless, the number of cases of P&S syphilis increased during 2000-2002 and continued to increase from 2002 (6,862 cases) to 2003 (7,177 cases).¹ During 2000-2014, the rise in the P&S syphilis rate was mainly attributable to increased cases among men, precisely among gay, bisexual, and other men who have sex with men (MSM). However, during 2013-2014, the rate increased both among men (14.4%) and among women (22.7%). This increase among women is of particular concern because congenital syphilis cases tend to increase as the rate of P&S syphilis among women increases.²

Gonorrhea has been one of the most reported sexually transmitted diseases (STDs) in the US since 1940's. Even though the rates declined during the late 40's and early 50's after penicillin therapy, the rates increased rapidly from 1966 to 1975 as the sexual behavior patterns changed drastically.³ *Neisseria gonorrhoeae* is also a main causative organism that causes pelvic inflammatory disease (PID) among women which could cause infertility if not treated earlier.⁴ The national rate of reported gonorrhea cases reached as low as 98.1 cases per 100,000 population in 2009 but during the period from 2009 to 2012, the rate increased slightly each year, to 106.7 cases per 100,000 population in 2012. Again in 2013, the rate decreased to 105.3 cases per 100,000 population. Then, in 2014, a total of 350,062 gonorrhea cases were reported, and the national gonorrhea rate increased to 110.7 cases per 100,000 population.² The increase in gonorrhea rate during 2013–2014 was observed primarily among men. In 2014, the rate of reported gonorrhea cases remained highest among blacks (405.4 cases per 100,000 population) and the rate among blacks was 10.6 times the rate among whites (38.3 cases per 100,000 population).²

A study examining the effect of patient defining non-regular sexual relationships and other risk behaviors on the incidence of sexually transmitted infections (STIs) among heterosexual men, found patients who had many sexual partners and who were more likely to practice anal sex with increasing condom use, were associated with decreasing incidence of

gonorrhoea.⁵ A study among sexually experienced women from US found that rates of syphilis, gonorrhoea and PIDs were highest in adolescents and decreased exponentially with increasing age due to sexual behaviors and reproductive physiology.⁶ Risk factors for gonorrhoea, syphilis and trichomonas among women attending family planning clinics in Nairobi were, being unmarried and having more than one sex partner in the previous year.⁷

An interesting spatial analysis examining the association between county-level socio-demographic characteristics with syphilis and gonorrhoea reported a greater number of reported cases of syphilis in counties with higher fraction of employed men, divorced men and higher standard living among the adult population in Guangdong Province, China.⁸ Another study among unmarried male migrants investigating sexual risk behaviors in Shanghai, found that younger age at first sexual intercourse, more cities of migration, poor perception of acquiring HIV, frequent exposure to pornography and having peers who engaged in sex with non-regular sex partner were several indicators of sexual risk behavior associated with increased risk of HIV.⁹ A study conducted in Baltimore, found that even though gonorrhoea rates were similar in men and women, both genders differed in sexual behaviors predictive of infection.¹⁰ Men with a new or casual partner were more likely to have gonorrhoea than men with no such partners but this finding did not hold true for women. Condom use in the previous month reduced the chances of gonorrhoea acquisition for both men and women, more than 33% continued to engage in sexual activity after onset of symptoms or knowledge of sexually transmitted disease exposure and individuals with repeated episodes of gonorrhoea exhibited an array of risk-taking behaviors, such as casual sex partners.¹⁰

A cross-sectional study investigating the association of violent behavior with coercive condom practices, sexual infidelity, forms of sexual risk behavior and self-reported STDs and HIV diagnosis found that men's intimate partner violence (IPV) perpetration was associated with STD/HIV risk behaviors and diagnosis.¹¹ Another similar study among adolescent and young adult women attending family planning clinics found that recent physical or sexual IPV was associated with HIV risk, unprotected vaginal and anal sex, involuntary condom non-use and fears of requesting condoms and refusing sex.¹² Men who reported both physical and sexual violence against a partner, perpetration both before and within the past 12 months, or more than one episode of perpetration reported significantly higher levels of HIV risk behavior than men who reported less severe or less frequent perpetration of violence.¹³ Women who reported IPV also reported greater difficulties in negotiating safer sex behaviors with their abusers. Thus, fear of violent consequences appeared to hinder their ability to protect themselves against HIV infection.¹⁴

The terms MSM and WSW (women who have sex with women) have been intensely studied in the public health literature to examine sexual orientation disparities in sexual health. STD risk was found to be increased among self-identified heterosexual-WSW and bisexual women, whether they report same-sex partners or not, and gay identified WSW were less likely to report a STI compared to heterosexual women with opposite sex relationships only.¹⁵ Among males, heterosexual-identified MSM did not have a greater likelihood of reporting an STI diagnosis; rather, STI risk was concentrated among gay and bisexual identified men who reported both male and female sexual partners.¹⁵ MSM with early syphilis are at high risk of reinfection in San Francisco. A study found that at least one third of MSM diagnosed with syphilis did not test during the one to six months post-diagnosis.¹⁶ Key features of the current syphilis outbreaks among MSM include meeting partners in anonymous venues, thus making traditional partner notification interventions more challenging.¹⁷

During the period of 2000 and 2001, the number of cases of P&S syphilis increased among men, which ended the decade-long pattern, characterized by annual declines in syphilis cases among both men and women.¹⁸ This increase in syphilis cases among men is associated with reports in several cities of syphilis among MSM.¹⁹ In 2014, men accounted for 91% of all cases of P&S syphilis and, of those male cases for whom gender of sex partner was known, 83% were MSM.² Reported cases of P&S syphilis continued to be characterized by a high rate of HIV co-infection, particularly among MSM.^{19,20} In 2014, 26 states reported both sex of sex partner and HIV status (HIV-positive or HIV-negative) for at least 70% of P&S syphilis cases and among P&S syphilis cases in these states, 51.2% of cases among MSM, 10.7% of cases among MSW and 5.9% of cases among women, were HIV-positive.²

Research in Catalonia among MSM found that unprotected anal intercourse was higher in men, who were HIV positive, men who had more than 20 sexual partners in the past 12 months prior to the study and men who met casual sex partners on the internet.²¹ An Internet based study among MSM in Norway found that gonorrhea was associated with unrevealed ethnic background, having more than 50 lifetime male partners and being HIV infected was associated with unrevealed income, number of lifetime male partners besides being under the influence of drugs.²²

Disease intervention efforts may be more effective if risky sexual behaviors or characteristics among all STD patients and their sexual networks in the US are identified and examined thoroughly.

Networking risks and sexually transmitted diseases

Identifying and treating syphilis cases rapidly, and interviewing syphilis cases to identifying their sex partners from their sexual networks, and bringing those partners to evaluation and treatment are the basis for syphilis control in the US.^{23,24} A network is defined as a set of nodes which can be either individuals or organizations, which are closely tied either with one type of relationship or more specific types of relations between them.²⁵ Thus, a person's sex network is usually comprised of individuals with whom he or she has sex. A personal network includes a focal individual and his or her ties and a social network will be a group of linked personal networks.²⁵

Among the main strategies in the prevention and control of STDs after the identification of asymptotically infected persons and persons with symptoms associated with STDs as stated in the current guidelines by the CDC include: effective diagnosis, treatment, counseling, and follow up of infected persons; and evaluation, treatment, and counseling of sex partners of persons who are infected with an STD.²³ The fundamental principle of disease control using the source and spread precept is to decrease the probability of transmission through therapy and to reduce acquisition by directed personal counseling to decrease risk behavior.

The national epidemiology of syphilis and gonorrhea has been different.²⁶ Syphilis is described as an STD that occurs in older individuals (25-35 years of age) who tend to engage in injection drug use and exchange of sex or money for drugs and in contrast, gonorrhea is described as an STD that occurs in relatively younger individuals (15-21 years of age) who have not established sustained high-risk behaviors, who may engage in drug use, but do have multiple sexual partners.²⁶ The sexual network or core group for each of these STDs has been considered different and no assessments of similarities, differences, or overlap of these subgroups have been reported. A network analysis allows examination of such population variation and by using statistical models that are developed for social network analysis; one is able to make inferences about the probable route of spread of different STDs. Changes in social and behavioral patterns may contribute to the increase in syphilis among older individuals as they are increasingly likely to be single or possibly undergoing some kind of relationship changes (e.g., divorce or bad break-ups) and less likely to use condoms when having sexual intercourse with random partners.²⁷ Studies have also shown that the greater the difference in age between sexual partners the more likely it is that risky sexual behavior will occur as protections are not taken into account during sexual encounters.²⁸

Contact tracing for early syphilis cases was reported as less effective in control of disease spread compared to that for gonorrhea in a study conducted in Oregon.²⁹ Syphilis patients were

more likely to report drug use, to have exchanged sex for drugs, or money and to have reported larger numbers of partner compared to those with gonorrhea. Since the incubation period for syphilis is 9 to 90 days, partner notification and therapeutic intervention strategies should work in preventing disease spread. Similar interviewing techniques, however, produced far fewer locatable sex partners with syphilis than for those with gonorrhea.²⁹ In another similar study among male syphilis patients in Georgia, MSM case patients resulted in higher mean numbers of contacts named and located per case than men having sex with women only (MSWO).³⁰ A retrospective audit of contact tracing activities in a regional sexual health clinic found that past partners were treated less often than current regular partners and were rarely seen at the clinic.³¹

In a study on sexual mixing patterns (selections of sex partners) in the spread of gonorrhea and chlamydia, partnerships discordant in terms of race, age, education and number of partners were associated with risk for gonorrhea and chlamydia.³² Another similar study on social and sexual network mixing among MSM, network mixing on risk behaviors was more assortative (preference in sex partners with similar characteristics like oneself) in the sexual network compared to the social network and black MSM reporting a social network enabler (set of software modules to create a social network) were more likely to practice unprotected anal intercourse and this finding was not observed in the sexual network.³³

In general, syphilis cases in Baltimore meet their sex partners outside their immediate neighborhoods. The most common location type was a street or corner but differed according to risk behaviors.³⁴ Another similar study among HIV infected young black MSM in Mississippi, found that all but one participant was connected through a network of venues where they had met partners during the 12 months prior to diagnosis of HIV. They reported having partners from all regions of Mississippi and 5 other states.³⁵

A study among urban African-American women that focused on 2 primary outcomes: having 2 or more sex partners and having a risky sexual partner found that women having 2 or more sex partners within the past 90 days, were associated with having a larger personal network, and more network members who pitched in to help.³⁶ The same study also showed that women having a risky sexual partner were associated with having a larger personal network and having more social networks who used heroin and cocaine.³⁶

Ever since the advancement of online social networking tools such as 'Facebook', 'Whatsapp' and many more, online social networking have been growing rapidly among at-risk populations such as MSM, young men and women and STD infected people. A study involving 'Facebook' registered MSM, found that number of sexual partners met from online social

networking technologies is associated with increased likelihood of having exchanged sex for food, drugs or place to stay, number of new partners, number of male partners and frequency of engaging in oral sex; all in the past three months from the study period.³⁷

Although sexual networks may differ between syphilis and gonorrhea in terms of risky behaviors, (e.g., anonymous sexual contacts, number of partners, age of self and partners and few others)²⁹, the personal and social network characteristics of both these STDs may be similar and overlap. Thus, intervention and control efforts may not have to apply to each separate STD but could be simultaneously developed and then implemented.

Depression, substance abuse and sexually transmitted diseases

Depression often occurs after stressful events in one's life and this can include STD. Both STD and depression are subjected to stigma. Medically depressed patients are more vulnerable to diseases. Depression is one important factor that is associated with high-risk sexual behaviors and STD among youth in the US.³⁸ While sexual risk behaviors and STD are risk factors for depression, depression could also increase susceptibility to risk behaviors and infection. Depression may impair cognitive function and memory, decrease impulse control and contribute to psychosocial impairment including emotional reactivity in peer relationships.³⁹ These depression-related effects may hinder clear perception of STD risk and the ability to prevent risk behavior. Depression is also associated with substance use⁴⁰, a consistent correlate of STD and related behaviors. Adolescents affected by one or both of these disorders (depression and substance abuse), may be more likely to have high-risk peers and sexual networks characterized by high levels of STD, hence increase the risk of sex with an infected partner and STD acquisition.^{41,42}

A study on depression, STDs and sexual risk behavior among young adults in the US found that among all adult groups, adult depression was associated with multiple partnerships but not with condom use and among black men, depression was found to be strongly associated with STD.⁴³ STD history was associated with depression in men younger than 35 years in a study that was conducted in Canada.⁴⁴ In another similar study among African-American female adolescents in Birmingham, the STD positive adolescents had higher depressive symptom levels at 6 months compared to the negative group.⁴⁵ Another study, also among African-American female adolescents, found that those with a history of depressive symptoms were more likely to have STD and also had prior pregnancies along with current STD infections.⁴⁶ Female adolescents with a high level of depressive symptoms had higher odds of having had intercourse, and high levels of depressive symptoms were also independently associated with increased

numbers of lifetime sexual partners and an external locus of control.⁴⁷ Substance use problems were reported to be associated with increased risk behavior and increased likelihood of acquiring STDs in a study among African-American female adolescents with a history of seeking mental health services.⁴⁸

An interesting 3 year prospective study among male to female transgender persons found that gender abuse predicted depressive symptoms and gender abuse combined with depressive symptoms predicted high risk sexual behavior (unprotected anal intercourse) and the incidence of HIV and STDs.⁴⁹ High rates of depression have been reported among MSM. Having anal sex with casual male partner and being diagnosed with an STD 12 months before the study were associated with depressive symptoms.⁵⁰

A study on psychiatric and substance dependence co-morbidities, lifetime STIs, and reported high-risk sexual behaviors for methamphetamine-dependent, gay and bisexual men at entry to outpatient drug abuse treatment in Los Angeles, found significant differences in lifetime prevalence of STIs among those who have generalized anxiety disorder (higher rates of genital gonorrhea), specific phobia and major depressive disorder (higher rates of oral gonorrhea), social phobia (higher rates of syphilis) and bipolar disorder type I (higher rates of HIV), compared to those without psychiatric diagnoses.⁵¹ Prevalence of HIV, Hepatitis B, syphilis and chlamydia among adults with psychiatric illness in India was found to be associated with behavioral characteristics such as having multiple partners, exchanging sex for money and unprotected anal sex.⁵²

Substance use has been associated with high rates of sexual risk behavior in adolescents.^{53,54} Risk appears to be highest among youth who use substances frequently, who use substances before or during sex, and who use more serious substances like cocaine.^{53,55} Substance use could impair decision-making ability, reduces risk perception and judgment, and may heighten arousal which then reduces the likelihood of using condoms and negotiating safer sex practices.^{56,57} Crack cocaine use and HIV have resulted in a large number of people living with HIV, many of whom continue to engage in unprotected sex.⁵⁸

Large increase in syphilis among a minority group of heterosexuals began in 1986 in Philadelphia.⁵⁹ A case-control study that was conducted to investigate this sudden increase discovered that cocaine use among men and women and exchanging of drugs for sex were the risk factors for syphilis.⁵⁹ A study examining the prospective association between baseline self-reported drug and alcohol use of the network members of injection drug users, and self-reported sexual behaviors and alcohol use at 5-month follow-up, found that sexual risk behaviors were associated with their drug network members' level of crack cocaine use.⁶⁰ During follow-up,

higher levels of alcohol and crack use among drug network members were observed to be associated with indexes' (initial participants of the study) reports of multiple sex partners and increased alcohol consumption while higher levels of crack use among the drug network members were associated with the indexes' reporting casual sex partners at follow-up.⁶⁰ Male African-American crack users reported more sexual partners in the last 12 months, more STDs in their lifetime, and greater frequencies of paying for sex, exchanging sex for drugs, and having sex with injection drug users. Users also reported greater current depression, anxiety, and social isolation and earlier initiation into alcohol use and less positive parenting experiences during their adolescence.⁶¹ A prospective study involving Latino migrant men found that for both binge drinking and drug use, having sex with a female sex worker was associated with increased risk of STDs and symptoms of depression was reported to be associated with increased drug use.⁶² Early and current marijuana use predicted a higher number of lifetime sexual partners among young women who were pregnant teenagers which were significant risk factors for STDs.⁶³

Condoms were less likely to be used with non-primary partners when alcohol is consumed among patients attending an STD clinic.⁶⁴ A similar study among the same type of study population among men showed that drinking in sexual contexts as well as their partner's drinking were related to higher rates of unprotected intercourse and similarly, women's partners drinking before sex was related to higher frequencies of unprotected intercourse.⁶⁵ A study that examined the association between baseline drinking frequency and STDs among Kenyan women reporting transactional sex found that STD was associated with consumption of 1 to 7 drinks weekly among HIV-positive women.⁶⁶

A study on social network characteristics that are risk factors for and protective factors against heavy episodic drinking among a sample of women at risk for HIV or STIs, found that women who engaged in heavy episodic drinking had fewer social network members who were in drug treatment, employed and with whom the participant socialized and higher number of social network members with whom they drank alcohol with.⁶⁷

As of today, STDs and HIV still remain as serious public health issues for youth and adults in the US. Psychological distress has been consistently associated with sexual risk behavior, along with substance abuse in youth and adults. Among sexually active high school youth, approximately 40% reported unprotected sex at their last sexual encounter; close to 25% used drugs or alcohol at last sexual encounter, and 15% reported sexual intercourse with 4 or more partners in their lifetime.³⁸ Thus, it is definitely important to understand these factors that contribute to the incidences of STDs like syphilis and gonorrhea.

All 3 studies focused on patients with syphilis compared to patients with gonorrhea (the control group for patients with syphilis). As stated earlier, gonorrhea has been one of the most reported STDs compared to syphilis. Compared to syphilis, gonorrhea is also much more common. Many people with syphilis are still undiagnosed and untreated in the US.⁶⁸ The clinical manifestations of syphilis besides primary, secondary and latent syphilis are: tertiary syphilis (cardiovascular syphilis with incubation period: 10-30 years), neurosyphilis (when syphilis invades the nervous system) and congenital syphilis (can result in premature delivery or perinatal death). Studies have shown 15-40% of untreated patients with syphilis develop recognizable late complications.⁶⁸ Higher mortality rate was noted in populations with syphilis, where men were twice as likely to develop late complications, and it was suggested that African-Americans were more likely to develop cardiovascular syphilis whereas whites were more vulnerable to develop neurosyphilis.⁶⁹ Recent congenital syphilis rates were 8 times higher among infants born to black mothers compared to white mothers.² Also, over the past several years, increases in syphilis among MSM have been reported in various cities besides Baltimore like Chicago, Seattle, San Francisco, Miami and New York City, and the recent outbreaks showed high rates of HIV co-infection ranging from 20-70%.² Untreated syphilis leads to devastating outcomes including deaths regardless of age and gender. Late stages of syphilis can occur in people who have not been treated at all for syphilis and can appear 10-20 years after the first infection, hence damaging internal organs including the brain, nerves, blood vessels, liver and most important body parts which gradually lead to death. Thus, all 3 studies focus on patients with syphilis compared to patients with gonorrhea.

Purpose of my dissertation

The objectives of my dissertation are to:

- A. Investigate the association between the presence of syphilis (vs. gonorrhea) and sexual characteristics among people with syphilis or gonorrhea.

- B. Investigate the association between the presence of syphilis (vs. gonorrhea) and network characteristics of social networks (individuals named as part of sexual or non-sexual network) among people with syphilis or gonorrhea.

- C. Investigate the co-morbidity of depression/drug abuse with the presence of syphilis (vs. gonorrhea) among people with syphilis or gonorrhea.

Research Questions

This dissertation includes several research questions that are addressed in three distinct but related studies.

Study 1: Are there associations between the presence of syphilis (vs. gonorrhea) and sexual characteristics*, among people with syphilis or gonorrhea?

Study 2: Are the network characteristics# of individuals named as part of sexual or non-sexual network of the patients associated with the presence of syphilis (vs. gonorrhea) among people with syphilis or gonorrhea?

Study 3: Are depression and drug abuse co-morbid with the presence of syphilis (vs. gonorrhea) among people with syphilis or gonorrhea?

**Sexual characteristics-numbers of different sexual partners in the past 90 days, sex practices (anal sex, vaginal sex and oral sex) in the past 90 days, have a main sexual partner, sexual identity and age when having sex for the first time*

#Network characteristics of social networks-types of each sexual contact in the past 90 days, age of the contacts, gender of contacts, employment status of the contacts, distance from the contacts, education level of the contacts and drug abuse by the contacts.

Innovation

The Baltimore Program has been in the lead of defining the HIV and STD relationship in the US. Baltimore is in the midst of the Nation's largest urban syphilis epidemic.⁷⁰ One of the first studies conducted by Dr. Rompalo upon arrival in Baltimore was to define the association of syphilis with risk of HIV infection.⁷¹ In 1988, 731 patients with newly diagnosed (primary, secondary, or early latent stage) syphilis were treated in Baltimore City Health Department (BCHD) STD Clinics. Patients with syphilis were more likely to be homosexually active, to use drugs, or to have had syphilis in the past compared to the entire STD clinic population. 24.3% of

patients with a reactive syphilis serologic test result were HIV infected. A multivariate analysis found that a reactive serologic test for syphilis was significantly associated with HIV infection in all major risk categories. Among heterosexuals who denied parenteral drug abuse, HIV infection rates were 6.8 and 8.7 times greater for women and men who had a reactive serologic test for syphilis. These data were among the first to establish the strong association between syphilis and HIV infection and also, the importance of heterosexual HIV transmission among patients attending STD clinics.⁷¹

Dr. Rompalo and colleagues continued their teamwork with the BCHD and reviewed the clinical data on 309 patients with early syphilis attending the STD clinics.⁷² These data found that the clinical presentation of syphilis in patients with HIV infection presented more often in the secondary stage, were more likely to have chancres (ulcers in the genitals). In 1993, a prospective study to determine the etiology of genital ulcer disease, Dr. Rompalo and colleagues found that syphilis was the leading cause of genital ulcers among 155 men attending the BCHD STD clinics.⁷³ Primary syphilis caused more genital ulcer disease among HIV infected men as compared to HIV uninfected men [9/23 (39%) versus 23/123 (19%)].

In 1996, Dr. Rompalo and colleagues carried out an investigation on the outbreak of syphilis. From the period of 1993 until 1995, the number of primary and secondary syphilis cases that were reported in Baltimore City increased 97%, from 170 to 352 cases per year. This outbreak resulted in a 'Centers for Disease Control and Prevention (CDC) Epidemic-Aid (Epi-Aid)' investigation. With the collaboration of BCHD, the Maryland Department of Health and Mental Hygiene, and Drs. Rompalo and Zenilman from the Johns Hopkins University School of Medicine, a CDC task force was enforced to investigate potential reasons for this increase.⁷⁴ The investigators analyzed data from the 'Disease Intervention Specialists (DIS)' case interview records used for sexual contact tracing, as well as information collected in clinic patient medical records in order to describe the epidemiology of early syphilis.

In every year from 1992-1995, males and females with P&S syphilis reported a median of 2 infectious period sex partners (3 months plus the duration of primary symptoms or 6 months plus the duration of secondary symptoms). The proportion of men reporting ≥ 4 infectious period sex partners increased from 10.2% in 1994 to 20.9% in 1995, whereas proportion of females reporting ≥ 4 infectious period partners decreased from 19.4% in 1994 to 10.2% in 1995.⁷⁴ Most men and women reported that they were heterosexual. Increasing sexual activity as measured by traditional contact tracing methods was not clearly associated with increasing infectious syphilis rates.

Further analyses of the 1992-1995 syphilis data including information on patients diagnosed with early latent syphilis (asymptomatic disease acquired within the previous year.⁷⁵) showed that over these 4 years, the percentage of African-American patients decreased, the median age and the percent of patients with secondary disease increased, and more males and females denied sex with injecting drug user (IDU) (Table 1.1).

Table 1.1: Epidemiologic Characteristics of Early Syphilis Patients in Baltimore: 1992-1995

	1992: N=498	1993: N=353	1994: N=489	1995: N=719
African-American	96.2%	90.4%	87.1%	91.0% *
Median Age (years)	29.0	29.0	30.6	33.9 *
Male	56.6%	59.9%	55.2%	58.0%
Primary syphilis	18.1%	27.1%	14.9%	19.5%
Secondary syphilis	20.9%	20.1%	20.9%	28.8% *
Early latent	61.0%	52.8%	64.2%	51.7%
Same sex contact	46.0%	42.4%	48.3%	37.6% *
Self-reported IDU	17.7%	15.0%	15.7%	12.9%
Sex with IDU	17.3%	8.5%	11.5%	8.1%
Sex for Drugs/Money	22.3%	18.1%	23.7%	20.9%

(* P<0.001, Trend Test-carried out by Dr. Rompalo)

Prior to all these previous studies, this research is unique as it not only focuses on sexual behaviors of the attendees of the STD clinics but also on characteristics of all their reported social networks. Social network members include sex or drug partners, friends or family, neighbors, or co-workers and are believed to mediate the behavior of network members through social influence, engagement, and social support, thus projecting a strong influence on numerous health behaviors. STDs are transmitted in ignorance rather than knowingly between regular partners with whom there is most frequent contact and least apparent risk, and this makes the networking data for this study valuable.

The concept of sexual networks was founded as early as 1930s when local public health departments traced the partners of patients with syphilis.⁷⁶ People at the center of a network are more susceptible to both the benefits and risks of social connections (e.g., for infectious diseases like STIs). It is not just how connected a person is but also who a person is connected to and what those people are doing, that has an effect. Social networks consist of 2 elements that are: individuals (nodes) and the social ties between them. Networks are usually represented as graphs (sociograms) in which “nodes” denote people and links indicate a sexual tie between two people. Social ties can be described as “edges” (undirected relationships between nodes) or “arcs” (directed relationships from one node to another). Generally, network analysis focuses on connections between homogenous nodes. Characteristics distinguishing nodes from one another may be based on examination of the network itself. Nodes can obviously vary in their degree. Nodes having higher degree are usually interpreted as being more prominent and influential within the network.⁷⁷ Network density provides an assessment of the overall connectedness and is defined as the proportion of actual ties among people, from all possible links (if every node is tied to every other node).⁷⁶ Thus, denser sexual networks are an indication of higher contact rates among people, creating more chances for any possible STD transmission. Node degree can be easily assessed by asking index persons to report total number of sex partners, or extracted from the graph produced in a sociometric study by counting the number of links per node.⁷⁶ Measures of centrality in networks capture the extent to which a node connects on lies between other nodes, hence its tendency to be positioned near the center of his or local network. People with more friends will tend to be more central. But this measure does not account for differences in the centrality of one’s friends. Individuals who are connected to many well-connected peers are more central than those who are connected to an identical number of poorly connected peers. In Colorado Springs, network analysts found that HIV+ persons had high levels of risk behavior but were located in outlying areas of risk networks, explaining the relatively low HIV transmission levels.⁷⁸ In contrast, HIV+ persons in New York City occupied central positions

within their needle sharing and sexual risk networks, which helped explain the high-observed levels of infection.⁷⁹

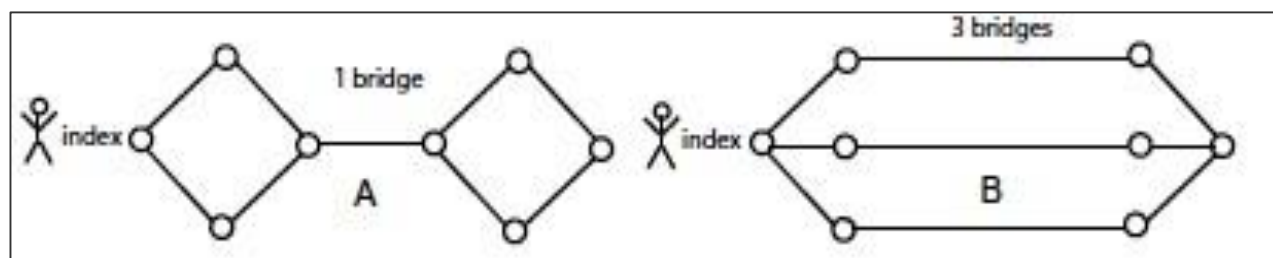
The various ways persons select partners affect how quickly STDs can spread. The different types of sexual partnerships are:

1. True monogamous partnership: people mutually reporting to one partner
2. Indirect multiple partnerships: people who report one partner, although his/her partner has many sexual partners
3. Simple multiple partnership: people reporting many sexual partners but later report only one sexual partner
4. Indirect concurrent partnerships: people who reported one partner whereas his/her partner had sex between two coitus or sexual intercourse occurred between two coitus with another partner
5. Direct concurrent relationships: people who reported overlapping sexual partnerships in which sexual intercourse with one partner occurs between two coitus with another partner
6. Complex multiple partnerships: people who reported many sexual partners who are themselves involved in many sexual relationships with others

Concurrent relationships have the potential to increase the probability for transmission, because later partners could infect the earlier partners. Furthermore, they could serve as “nodes” which means, connecting all persons in a dense cluster, creating highly connected networks that facilitate transmission. Concurrent partners can connect each of their respective clusters and networks as well. Concurrency alone can fuel an epidemic even if the average number of partners is relatively low.

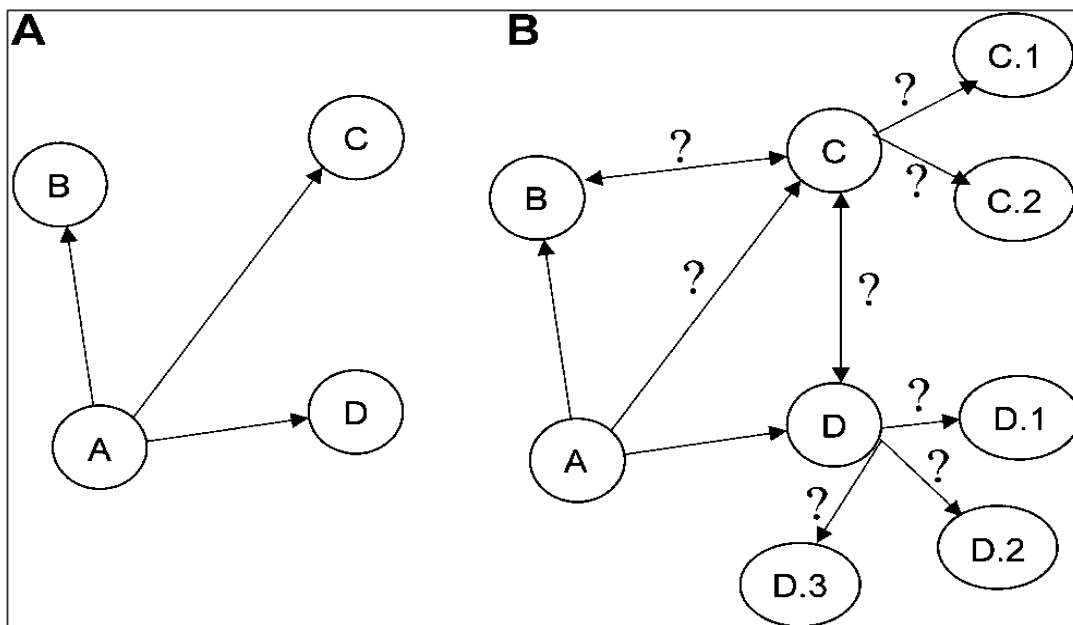
As Figure 1.1 portrays, each index has 8 persons (represented by the tiny circles) connected into 9 relationships (represented by the lines that connect one circle to another). Two persons each have 3 partners and the other 6 each have 2 partners. In A, within 2 steps from the index, half the network could be infected and half spared but in B, everyone could be infected except for the person at the far right. Transmission in A could be less efficient by just cutting down that one bridge but prevention would be more difficult in B as it requires in cutting three bridges. Hence, for STI/HIV epidemics, network structure is like destiny.⁸⁰

Figure 1.1: Two different types of networks



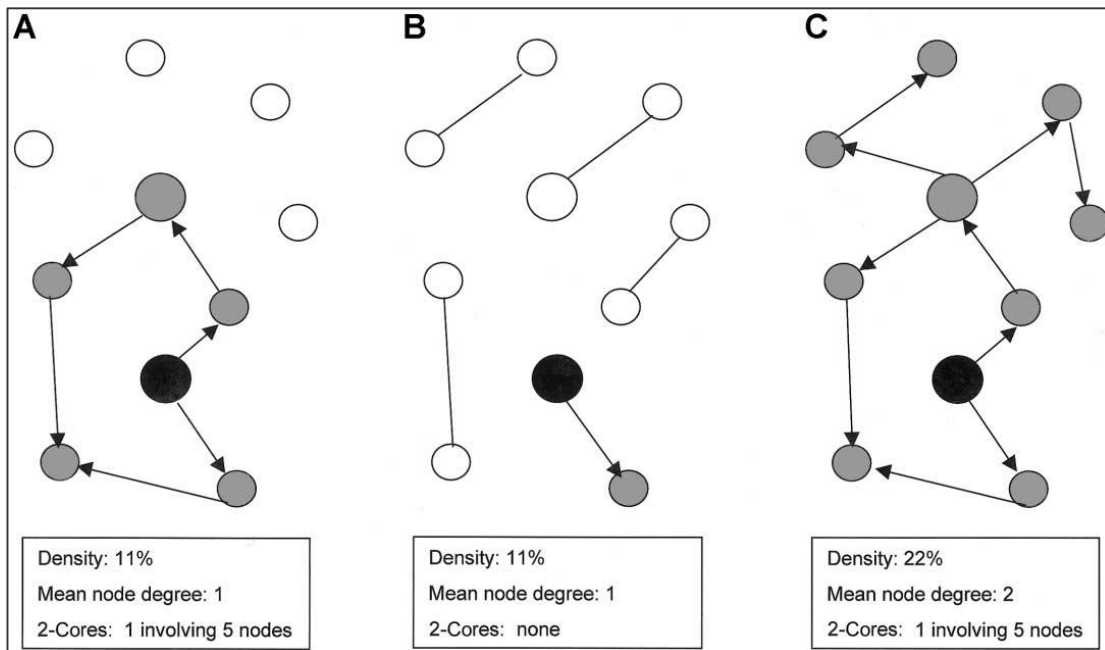
Two basic approaches to conducting network-based research have evolved: egocentric and sociometric. In an egocentric study design, the index subject (person A) names his or her sex partners (persons B, C, and D) and describes them⁷⁶ (Figure 1.2A). The index subject (A) provides information about his or her sex partners, thus characterizing subject A's personal network. Information learned from the index subject about each partnership includes the duration of the relationship, the type of partner (e.g., steady, casual, or anonymous), the frequency and types of sexual activity, and the frequency of condom use, as well as other risk and demographic data about each partner (e.g., race/ethnicity, age, and drug-using habits). In contrast, the sociometric study design requires theoretical specification and compilation of all ties among people and recruitment of as many of the identified partners as possible.⁷⁶ In figure 1.2B, person A represents the index subject, who names persons B, C, and D. The sociometric approach entails an iterative process in which persons B, C, and D are traced, recruited, and then asked to name their contacts, to assess if they are linked to each other and to identify other contacts in the network. These data are used to create graphs, called "sociograms," of the topology of relationships among people (Figure 2B). Sociograms that were created by Dr. Rompalo on the patients with syphilis or gonorrhea and their networks after the completion of this study are added in the Appendix.

Figure 1.2: Differences between egocentric and sociometric study designs



Generally, sociometric assessments characterize the structure of the network. These measures describe overall network connectedness within the population, microstructural details of network configuration, and individual position and prominence within the network and, when considered together, can provide insights into the potential of STD transmission, as illustrated in figure 1.3.⁷⁶ The density and average node degree of the networks in panels A and B are equal; however, greater disease transmission could occur in the network in panel A, owing to the existence of a 2-core involving 5 nodes. Furthermore, both networks in panels A and C contain a single 2-core of 5 nodes; yet, the density and average node degree are higher in the network in panel C, which accelerates transmission. Nevertheless, egocentric approach signifies an important intangible advancement beyond traditional, precisely individual based epidemiological methods addressing partnership linkages.

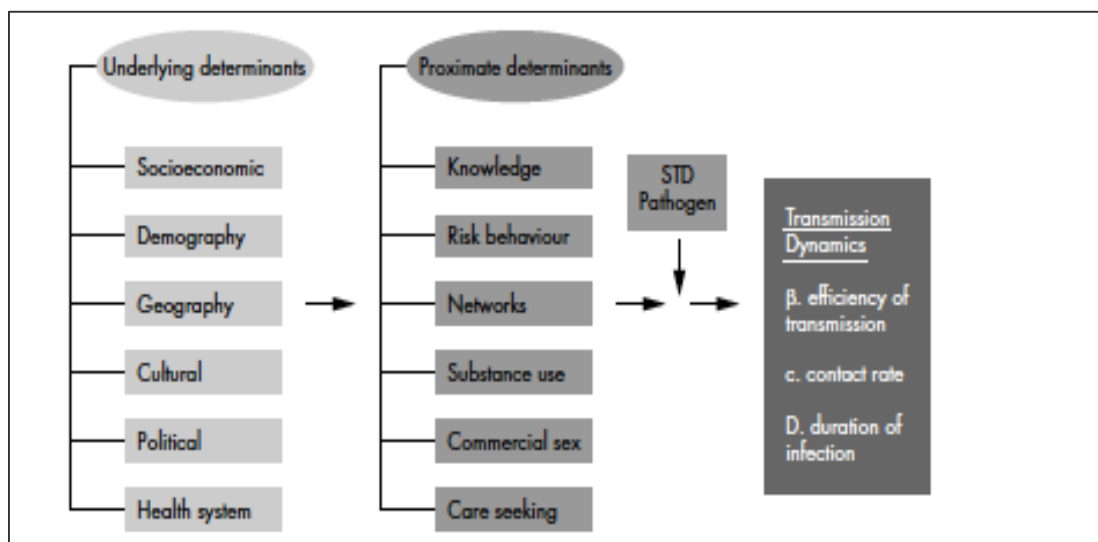
Figure 1.3: The relevance of network assessments. Black circle, infected individual; gray circle, partner with potential for infection



Determinants of sexual networks

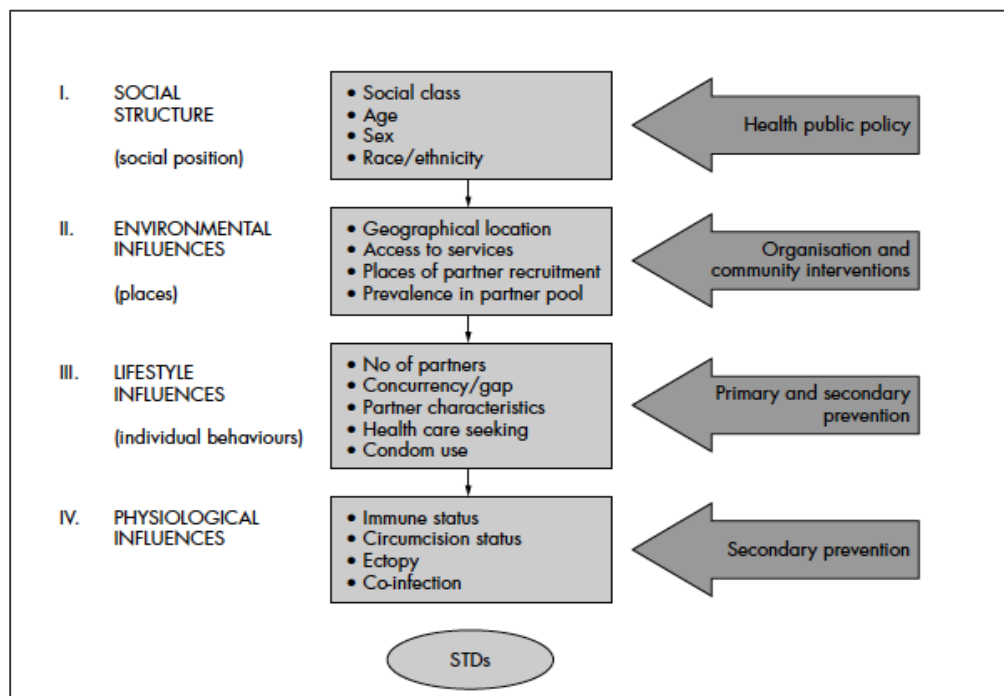
Social factors of all kinds including those related to education, occupation, neighborhoods, migration, urbanization, mobility, wealth, media, religion, substance use, incarceration and technological change can influence sexual behaviors, partnership formation and sexual networks, resulting on effects on STD dissemination. The key determinants of the level of spread of an STD (R_0) from an infected person to another are: likelihood of transmission during sexual contact (β), sexual contact rate/sexual network patterns (C) and duration of infectiousness of an infected person (D). This crude framework⁸¹ is shown below (Figure 1.4). Theoretical work on the levels of causation of health conditions and corresponding types of health intervention provides helpful suggestions for describing determinants of morbidity (Figure 1.5). This conceptualization distinguishes between social structural, environmental, lifestyle, and physiological influences on morbidity and suggests types of intervention, including those related to public health policy, organization and community interventions and to primary and secondary prevention that are appropriate for each level of causation thus, helping to prevent the spread of sexually transmitted pathogens.⁸¹

Figure 1.4: Determinants of STD epidemics: a crude framework



From: Aral, S. O. (2002). Determinants of STD epidemics: implications for phase appropriate intervention strategies. *Sexually Transmitted Infections*, 78(Suppl 1):i3–i13.

Figure 1.5: Levels of causation of STD and corresponding types of health intervention



From: Aral, S. O. (2002). Determinants of STD epidemics: implications for phase appropriate intervention strategies. *Sexually Transmitted Infections*, 78(Suppl 1):i3–i13.

Two important determinants of sexual networks are social norms and the physical spaces in which networks form. Social norms are molded by cultural factors at the communal level and continue to develop within the networks themselves, hence manipulating individual and partnership behaviors that affect network structure, density, and propagation over time. The places where the networks are formed are important determinants of sexual networks. Persons living in close functional proximity are more likely to form social relationships than those further apart.⁸² The CDC recommends that DIS working in public health departments collect information about where people meet their partners and where they live as a way to trace and treat partners and prevent additional infections.⁸³ The majority of gonorrhea cases in Colorado Springs were diagnosed among people living within four census tracts of a large military institution, who met their partners at a limited number of bars, clubs, and social gathering places.⁸⁴ One study in Baltimore found the mean distance between sex partners in geographically defined main areas was lower than in other areas; meaning that people with gonorrhea (past or present) were literally closer to each other than were uninfected people.⁸⁵

A study on STD co-infections in the Netherlands indicated that attendees belonging to specific sexual networks such as MSM, ethnic groups and young heterosexuals were at increased risk for STD co-infections.⁸⁶ The different pattern with age in MSM versus heterosexuals suggests that both these high-risk networks have determinants of higher risk such as age related sexual risk-taking, biologic susceptibility and insufficient knowledge or acquiescence with prevention measures.

Evidence suggests that patterns of sexual networks may differ between black versus white populations. One difference is that, among black persons, more frequent sexual contact occurs between those with many partners (the “core”) and those with few partners.⁸⁷ In addition, data from the 1995 National Survey of Family Growth (NSFG) sponsored by the National Center for Health Statistics, Hyattsville⁸⁸ indicated that the prevalence of concurrent sexual partnerships is greater among black women than among white women. This difference in concurrency appears to be regularly due to lower marriage rates and younger age at first sexual intercourse among black women. Major events such as war, famine and migration result in the increased sexual mixing of different groups of people and in social turmoil that increases the exchange of sex for goods, services and personal security.⁸⁹

One of the most important social determinants of sexual health is socioeconomic status. At the macro level, poverty and unemployment are associated with residential instability, segregation, and migration⁹⁰ resulting in racism. Populations of minority groups have suffered uneven poverty and have had fewer employment and educational opportunities. Residential

instability, which can result from poverty, was identified as a key contributor to rising HIV rates in blacks.⁹¹ Lack of resources and inequality of resource distribution has been found to be associated to risky sexual behavior, lack of health care, and rising STD rates.⁹² Lack of employment can stimulate migration and sexual networks. The migration of skilled black men to the southeastern US for better employment opportunities has been associated with rising STD rates in one county in North Carolina.⁹³

The increase of the drug culture within poor black communities has worsened the uncountable problems caused by segregation and concentrated poverty with direct effects on sexual networks and transmission of STDs.⁹⁴ Crack cocaine has directly altered sexual networks through increased sexual exploitation of women and high-risk sexual behavior, including augmented numbers of sex partners and the exchange of sex for drugs, and has been found to promote heterosexual transmission of HIV infection.⁹⁵ In a Philadelphia study involving heterosexual adults and adolescents (most of whom were black), using crack cocaine, having sex at a crack house, and exchanging sex for money or drugs were found to be related to syphilis.⁵⁹

Incarceration directly affects sexual networks through the disruption of existing partnerships. The partner entering prison is now at risk of forming new (sometimes forced) sexual connections with a group of individuals among whom the prevalence of high-risk sexual behaviors, HIV infection, and other STDs are high.⁹⁶ The prevalence of HIV infection among prison inmates is estimated to be 8-10 times that of the general US population.⁹⁷ Incarceration also contributes to the maintenance of poverty rates and places individuals at a further economic disadvantage.⁹⁸ High incarceration rates in North Carolina counties were found to be significantly correlated with high rates of STD infection, including chlamydial infection, gonorrhea, syphilis, and HIV.⁹⁹

Selective mixing patterns also can influence the spread of STIs and HIV. Assortative mixing, which is when individuals choose socio-demographically similar sexual partners leads to segregated networks that can contain infection. A combination of assortative mixing with differential levels of concurrency across groups makes it possible to sustain long-term prevalence differences across populations. This kind of network pattern could help to explain the persistent racial differentials in HIV and other STD that was observed in the US.^{100,101} Disassortative mixing in contrary, could lead to bridging across groups. This may facilitate the spread of HIV when sexual partnerships occur between high-risk groups and low-risk groups. A study among American Indians/Alaskan Natives MSM and WSW, disassortative mixing based on partner racial characteristics or gender characteristics may be a proxy measure of “bridging” between two sexual networks.¹⁰² In another study on sexual mixing patterns in the spread of

gonorrhea and chlamydia, partnerships discordant in terms of ethnicity, age, education and number of partners were associated with significant risk for gonorrhea and chlamydia infections.³²

This study was designed to investigate STD clinic patients with syphilis or gonorrhea along with their sexual or non-sexual networks. This study aimed to study this comparison in order to better understand how these 2 STDs may differ and how that would inform disease interventions and control. Through this study, the interconnectedness with their networking contacts could be identified, studied and understood. In cities with limited resources to treat STDs and to track sexual contacts, a network approach to contact tracing may allow health departments to utilize their funds more efficiently. By identifying the sexual network members or types of networks that are at highest risk for syphilis and gonorrhea transmission, resources could be focused on these individuals or networks. If networks with high levels of syphilis vs high levels of gonorrhea are found to be associated with certain types of behaviors, such as specific types of sex practices, type of sexual partners and number of sexual partners, then it may be cost effective to engage in health education in geographic areas where these behaviors are highly prevalent. Such data will be applied to develop targeted and specific screening and possible treatment interventions in core locations of Baltimore City where syphilis may have the greatest potential to spread.

Prevention and control of many STDs usually focuses on the promotion of safer sex practices as well as minimizing the number of sexual partners. These alone are not sufficient for effective interventions. A more effective intervention to reduce STD morbidity often requires messages targeted to specific communities (e.g., those diagnosed with STDs, MSM, persons who abuse drugs or alcohol). These are the types of populations that are considered to be at high risk. Patients who are already diagnosed with syphilis and gonorrhea could be re-infected again even after treatment, due to their ignorance on risky sexual behaviors and having multiple sexual networks. Reliable methods for preventions would be sexual abstinence (which is impossible to hold on to for a long time), monogamous relationships and using protections at all times during intercourse. This is why I feel it is still important to estimate the associations between the independent variables (IVs) and presence of syphilis (vs. gonorrhea) in this target population with people with either syphilis or gonorrhea and understand the differences among syphilis patients versus gonorrhea patients. This attempt could substantially improve the likelihood of successful public health interventions in the future.

Hence, my research project is aimed to significantly add more useful findings to the previous investigations by Dr. Rompalo and her team, contributing to the control of prevalent

STDs like syphilis and gonorrhea in Baltimore. This research could be a pilot study for more longitudinal studies that would have higher internal and external validity, thus contributing to control strategies of STDs in the US.

Human subjects protections

Participants in this study were recruited from the BCHD STD Clinics. For this study, any male or female patients, regardless of age, who were present at the STD clinics for evaluation or treatment of primary and/or secondary syphilis were recruited. Based on 1997 statistics,^{70,71} 97% of primary and secondary syphilis patients are African-American; 56% are male; all were over 15 years old and approximately 50% were 30 years of age or older. At the same time period, patients who attended these clinics for evaluation or treatment of gonorrhea were recruited for this study.

Consenting study participants had swab-specimens collected from the base of any primary or secondary syphilis lesions and/or a skin scrape specimen collected from any secondary syphilis rash. These specimens were used for restriction fragment length polymorphism (RFLP) analysis for *Treponema pallidum*. An additional 5 milliliters of blood were collected during the patient's routine phlebotomy, which will also be stored for RFLP analysis. Consenting gonorrhea patients provided their urine to be tested for the presence *Neisseria gonorrhoeae* using the 'Nucleic Acid Amplification Tests (NAAT)'. All data collected during interviews at the STD clinics or at the 'Lighthouse', as well as all specimens collected, were used for research purposes only.

Any patients who were present to the BCHD STD clinics for evaluation and treatment of primary or secondary syphilis infections were referred to the study clinician. The study clinician escorts the patient to a confidential interview/examination room and will explain the purposes and procedures of study participation in a non-coercive manner. At the 'Lighthouse', the participant reviewed and consent obtained by trained study personnel in a private room. These procedures included full disclosure and documentation of consent in writing.

Potential risks for this study included a physical risk specimen collection and of the needle stick for venipuncture to collect blood. Legal and social risks were possible if study participants were drug users who engaged in illegal activities. However, with assurances of confidentiality, the researchers have encountered few challenges and no problem in regards with this issue.

Procedures to minimize risk included careful training of personnel to be competent in venipuncture and to maintain confidentiality. The BCHD has established a standard policy and procedure to maintain the confidentiality of all patients attending its STD clinics. All clinic personnel and research personnel were required to sign a confidentiality agreement. To further promote confidentiality, only unique study numbers were used on data collection forms and specimens, and identifiers (for follow-up reminders) were maintained in locked files in a separate building with access restricted only to trusted study personnel.

All the procedures for this study have been reviewed and approved by the Institutional Review Boards of the Johns Hopkins Medical Institution, the Baltimore City Health Department and University of Hawai'i, Mānoa. The documentations of these approvals are included in the Appendix.

CHAPTER 2.

STUDY 1 : SEXUAL BEHAVIORS AND PRESENCE OF SYPHILIS VS. GONORRHEA: THE SOCIAL AND SEXUAL NETWORK (SSN) STUDY, BALTIMORE

ABSTRACT

Background: Sexually transmitted diseases (STDs) have always been threats to the human population globally, regardless of age, ethnicity and gender. The aims of this study were to (1) estimate associations between the presence of syphilis vs. gonorrhea and sexual characteristics, (2) estimate associations between the presence of syphilis vs. gonorrhea and peer influences on condom use before sexual intercourse and, (3) estimate associations between the presence of syphilis vs. gonorrhea and sexual characteristics among sexual partners of the index patients who were traced back to this study through ‘partner notification’.

Methods: The Social and Sexual Network (SSN) data from 526 respondents who were patients with syphilis or gonorrhea were used to address the research questions of this study. Parameter estimates (adjusted odds ratios [aORs]), 95% confidence intervals (CIs), and p-values were generated using SPSS 18.0. aORs were used to estimate associations adjusted for the effects of confounders. Three separate multivariable logistic regression analyses were performed to examine all research questions while controlling for selected confounders.

Results: Results indicated that those who were gay (aOR=1.79, 95%CI: 0.25, 12.71) and patients with close friends/people who are important who do not think that using condom prevent HIV (aOR=2.48, 95%CI: 0.89, 6.91) were more likely to have syphilis (vs. gonorrhea) compared to those who are straight and with friends who thought otherwise. Among sexual partners of index patients who were traced back to the study (n=172), those who were under 14 years old when having sex the first time (aOR=1.17, 95%CI: 0.47, 2.90)] and those who did not have a main sexual partner (aOR=1.16, 95%CI: 0.28, 4.78)] were more likely to have syphilis (vs. gonorrhea) compared to 14 years and above and having a main sexual partner.

Public Health Implications: Health promotion programs by public health organizations should be focused on syphilis patients attending STD clinics. Incorporating assessment on the sexual characteristics of the sexual networks may also aid clinicians in identifying risky sexual behaviors not only in syphilis patients but also in their identified sexual partners and help create awareness in the spread of syphilis from the infected to other sexual partners who could be syphilis free before sexual intercourse with the patients.

Key words: Syphilis, Gonorrhea, Sexual characteristics, STDs, SSN study

BACKGROUND

Sexually transmitted diseases (STDs), formerly referred to as “venereal diseases,” are among the most common infectious diseases in the world. CDC’s new estimates show that the total (curable and “incurable”) new STDs in the United States (US) is approximately 20 million and US has the highest rate of STDs in the industrialized world, exceeding other nations by almost 50 to 100 times.¹⁰³ The burden of diseases like syphilis and gonorrhea has been closely linked to society’s sexual practices, the availability of sensitive and specific diagnostic testing and access to appropriate antibiotics.¹⁰³

A large syphilis epidemic occurred in Baltimore in the mid-1990s where the number of primary and secondary (P&S) syphilis cases reported in Baltimore City increased 97% and resulted in the Centers for Disease Control and Prevention (CDC) Epidemic-Aid investigation.⁷⁴ Those who were heterosexual, African-Americans and attributed to increases in crack-cocaine use, transactional sex and prostitution were more likely to have syphilis in this large epidemic. Even though the incidence of syphilis decreased during the course of 1990s until 2000, it increased again in the US and the overall increase in syphilis incidence since 2000 had been attributed to increases among men having sex with men (MSM).⁷⁵

A study among patients attending Baltimore City Health Department (BCHD) STD clinic found that those who had 3 sexual partners and 1 or more new sexual partners in the past month were more likely to have gonorrhea.¹⁰ A study conducted in Baltimore among pregnant women found a high prevalence of gonorrhea, early syphilis and other STDs like chlamydia and lower likelihood of reporting high risk sexual behaviors such as new or multiple sex partners.¹⁰⁴ Another study using surveillance data from 2005 through 2008 to investigate syphilis testing behavior following diagnosis with early syphilis among MSM in San Francisco found that those who had 5 or more sexual partners and resided outside of gay-identified neighborhood were more likely to have early syphilis.¹⁶

A study among US young adults found that sexual-minority (people who are gay or bisexual) women had higher prevalence of sexual risk behavior which includes having multiple sexual partners while black men and sexual-minority men appeared to be at heightened risk for STDs.¹⁰⁵ During 2005-2013, number of P&S syphilis cases reported each year in the US doubled and the annual rate increased almost 2 times. These increased rates were greatest among men and especially from 2005-2009, rate increases were greatest among black men (14.6 in 2005 to 29.8 in 2009).¹⁰⁶

Another cross-sectional study involving men in the northeastern US was analyzed to estimate the prevalence of intimate partner violence perpetration and associations with sexual measures, coercive condom practices, sexual infidelity and few others. The findings showed that men's intimate partner violence perpetration was associated with sexual measures like practicing anal sex, coercive condom practices, sexual infidelity and transactional sex with female partner.¹¹

STDs like syphilis have always been threats to the human population globally and it is vital to understand the transmission patterns and the associations of these diseases with some socio-demographic measures, sexual behaviors, peer influences and coercive condom practices, which are critical for developing successful intervention and control measures. This study aims to determine associations between syphilis (vs. gonorrhea) and all these possible predictors.

This study is designed to address the research question: Are there associations between the presence of syphilis (vs. gonorrhea) with sexual characteristics* among people with syphilis or gonorrhea?

**Sexual characteristics-numbers of different sex partners in the past 90 days, sex practices (anal sex, vaginal sex and oral sex) in the past 90 days, have a main sexual partner, sexual identity and age when having sex for the first time*

Sub-question 1: Are there associations between the presence of syphilis (vs. gonorrhea) with peer influences on condom use before sexual intercourse?

Sub-question 2: Are there associations between the presence of syphilis (vs. gonorrhea) with sexual characteristics* among individuals named as part of a sexual network of patients with syphilis or gonorrhea who were traced back to this study through 'partner notification'?

- *I wanted to examine the associations between the presence of syphilis (vs. gonorrhea) and sexual behaviors/characteristics among sexual partners of the index patients who were traced back to this study, because individual and factors like types of sexual practices and numbers of sexual partners do have associations with the number, structure and dynamics of sexual partnership over time, thus creating the networks that enable STIs to proliferate.*

METHODS

Data Sources

The Baltimore syphilis epidemic facilitated this study. In 1997, over 25,000 clients attended the BCHD STD clinics for evaluation and treatment of STDs.^{70,71} During this year, the BCHD STD Program reported 941 early latent syphilis cases; 441 secondary syphilis cases; and 226 primary syphilis cases. This represented a case rate of P&S syphilis of 98/100,000 population.^{70,71} During 1998, BCHD clinical services improved and over 28,000 clients were seen. In Baltimore, 303 cases of secondary syphilis and 155 cases of primary syphilis were diagnosed. As expected, case rates for 1998 declined slightly with improved services, but remained high at 70/100,000.⁷¹ This study is a secondary data analysis of the Social and Sexual Network (SSN) study data. It focuses on the demographic measures and sexual behaviors; and their impact on the two main STDs: syphilis and gonorrhea. The SSN survey data are cross-sectional, as the information collected is from a single point in time.

Study sites

Patients were recruited from BCHD's two STD clinics: Eastern STD clinic and Druid STD clinic. Interviews were conducted at the Social Network Research Clinic (The Lighthouse), which is a row house located 5 blocks from the BCHD Eastern STD clinic, and 2 miles from the BCHD Druid STD Clinic. The off-site social network interviews were found to have provided a more controlled and confidential setting with more flexible hours than do STD clinic-based interviews. Interviews were conducted in private rooms by trained interviewers who have completed the interviewer-training course developed by the University of Michigan.

Standard STD Clinic Procedures

All patients diagnosed with primary/secondary/early latent syphilis and patients diagnosed with gonorrhea in the STD clinics were considered syphilis and gonorrhea index cases, and were treated on site. They received STD/'Human Immunodeficiency Virus' (HIV) counseling. They were interviewed by trained 'Disease Intervention Specialists' (DIS) to obtain information regarding STD/HIV risk. All information on index patients are kept in a locked, confidential file in the BCHD Disease Registry according to standard procedures approved by the CDC.

Recruitment

Volunteers for this protocol were recruited from the BCHD STD Clinics. Potential participants were patients diagnosed as having primary/secondary stage syphilis and gonorrhea at their STD clinic visit. All study participants were asked to provide a urine specimen for gonorrhea testing using nucleic acid amplification tests (NAAT) and to have blood drawn for syphilis testing using Rapid Plasma Reagin (RPR) nontreponemal screening test, with the Fluorescent *Treponemal* antibody-absorbed (FTA-ABS) test confirmation. Criteria for diagnosis of P&S syphilis were according to the following standard clinic protocol below:

Primary syphilis: Patient presents with a genital lesion and secretions collected from the lesion are found to contain spirochetes consistent with *Treponema pallidum* by dark-field microscopic examination.

Secondary syphilis: Patient presents any constitutional symptoms consistent with secondary syphilis (fever, chills, myalgias, arthralgias, patchy alopecia, mucous patches) and/or rash (including condylomata lata) with reactive serologic-tests for syphilis [positive Rapid Plasma Reagin test (RPR) with confirmatory Fluorescent Treponemal Antibody-Absorbed test (FTA-ABS)].

Criteria for enrollment

Patients having primary/secondary/early latent syphilis and gonorrhea were eligible for study enrollment as syphilis and gonorrhea index cases. Any patient diagnosed with gonorrhea during the same time frame was eligible for study enrollment as gonorrhea index cases. All eligible patients were fully notified about the study protocol. Informed consent was obtained from all willing participants, and a certificate ensuring the patient's confidentiality was signed by the clinician and the patient. The clinician recorded all the patient's clinical signs and symptoms on standardized data collection forms, collected additional specimens from lesions or rashes and ordered an additional 5 milliliters of blood to be collected during routine phlebotomy. Unique study numbers on data collection forms and specimens were used to ensure the patient's confidentiality. If the patient had confirmed primary/secondary syphilis or gonorrhea according to the above routine criteria, she/he was treated and escorted to a DIS. The DIS interviewed each patient and recorded the names and addresses of all known, identified sex partners according to standard confidential operating procedures for partner notification purposes. Participants were escorted back to the study clinician. The study clinician then asked the participants if they were (1) willing to present to the 'Lighthouse' for a network interview and (2) willing to bring, or refer, at least 3 of their friends and all of their sex partners who they have

identified as members of their personal networks for interview. At the 'Lighthouse', consenting index participants were interviewed using standard forms about their opinions, knowledge, attitudes and lifestyle including drug use and sexual behavior and about friends and other people that constituted their social/sexual network. Both syphilis and gonorrhea index patients were interviewed using standardized instruments. All procedures were repeated for all the individuals named as part of a sexual or non-sexual network of the index patients who were traced back and participated in this study.

Participation rates

The response rate for this study is 43.7%. The numerator is 'Numbers of patients that completed the interview' and the denominator is 'Total numbers of patients that completed the interviews, refusals and those who could not be contacted'. Cooperation rates are outcome rates among those eligible and usually slightly higher than the response rates.¹⁰⁷ The cooperation rate for this study is 48.1%. The numerator is 'Numbers of patients that completed the interview' and the denominator is 'Total numbers of patients that completed the interviews and refusals'. The refusal rate for this study is 47.2%. The numerator is 'Numbers of patients that refused to participate' and the denominator is 'Total numbers of patients that completed the interviews and the refusals'

Compensation for participants

The index patients were remunerated \$10 for enrollment in the specimen collection protocol and \$35 for enrollment and social interview completion.

Measures/Variables of Interest

The SSN survey data from 2001-2005 were used to address the research question and the sub-questions of this study. The survey design, sampling scheme, and all the survey questions were consistent for all 5 years.

Demographic measures

Age of the patients was determined based on their reported birth dates in their survey, and later grouped into 13 categories as used by the CDC for the STD surveillances: "0-4 years", "5-9 years", "10-14 years", "15-19 years", "20-24 years", "25-29 years", "30-34 years", "35-39 years", "40-44 years", "45-54 years", "55-64 years" and "65 years and above". For the purpose of all regression analyses, age was used as a continuous variable due to small cell counts in each

category. Ethnicity is grouped into two main groups: African-American and others, as patients were predominantly from the African-American descent.

The other desired measures for the final analysis are: gender, current employment status, history of ever having syphilis before and history of ever having gonorrhea.

Peer influence on the patients' lifestyle

Variables on peer influence on patients' lifestyle are initially from the questionnaire. They are: Friends think it's OK to have sex with someone more like a stranger without a condom, friends think it's OK to have sex with someone who refuses to use condom, close friends/people who are important think that using condoms implies no trust on partner, close friends/people who are important think that using condoms prevent HIV and peers encouraging the use of condom. For variables named "Friends", both friends and relatives who consider being friends were included and for variable named "Peers", both friends and people who are important were included. These variables were captured on 6-point scales: "1=None", "2=A few", "3=Some", "4= Most", "5=All" and "6=Other". Responses with 2, 3, 4 and 5 were collapsed together into "Yes". Responses with '6' were collapsed with missing values as 'other' represented either don't know or unsure. The final response for these variables was dichotomous: none and yes.

Behaviors of partners when condom use is discussed or suggested by patients each time before having sex

The variables on partners' behaviors on the use of condom before having a sexual encounter are initially from the questionnaire. They are: suspecting infidelity if condom is suggested and gets mad if condom is used.

Sexual characteristics

Sexual characteristics were measured by asking participants on their sexual behaviors in the last 90 days prior to the study. The desired measures for the analyses are: types of sex practices (anal/vaginal/oral), sexual identity, numbers of different sexual partners in the past 90 days and having a main sexual partner. 'Age when having sex for the first time' was categorized into: "Less than 14 years" and "14 years and above". These two categories were chosen for this study after obtaining the overall mean response for analysis (the mean age in years when having sex the first time for patients who have syphilis is 15.3 and 14.5 for patients who have gonorrhea), and also because of smaller cell counts that would occur if there were

more categories. A study investigating the impact of a history of sexual abuse on high risk behaviors among female school attendees had a similar variable, 'Sexual initiation before age 14'.¹⁰⁸ Numbers of different sexual partners in the past 90 days' was categorized into: "No more than 1 sexual partner" and "2 or more sexual partners".

Analyses

SPSS 18.0 was used for the analyses of these data. Frequencies of baseline demographics, sexual characteristics, peer influences on condom use were summarized and tabulated accordingly. Logistic regression was used to estimate associations between the presence of syphilis vs. gonorrhea and participants' sexual characteristics.

Primary independent variables (IVs) were selected based on my research questions and literature^{10,70,75}; potential confounders of the associations between the primary IVs and syphilis vs. gonorrhea were selected through literature and prior knowledge on some potential confounders suggesting that they could be predictive of syphilis/gonorrhea (gathered while discussing with primary investigator, Dr. Anne Rompalo at the time I was given the raw data set). The primary IVs and the potential confounders that are chosen for this study are shown in Table 2.1 below.

**Table 2.1: The primary IVs and potential confounders chosen for study 1
[Dependent variable: Syphilis (vs. gonorrhea)]**

Research question/sub-questions	Primary IVs	Potential confounders
Main Research Question	<ul style="list-style-type: none"> • Having anal sex in the past 90 days • Having vaginal sex in the past 90 days • Having oral sex in the past 90 days • Age having sex the first time • Sexual identity • Have a main sexual partner • Number of different sexual partners in the past 90 days 	<ul style="list-style-type: none"> • Ever having syphilis before • Ever having gonorrhea before • Age • Current employment status • Gender
Sub-question 1	<ul style="list-style-type: none"> • Friends think it's OK to have sex with someone more like a stranger without a condom • Close friends/people who are important think that using condoms prevent HIV • Friends think it's OK to have sex with someone who refuses condom • Close friends/people who are important think that using condom implies no trust on partner • Peers encouraging the use of condom 	<ul style="list-style-type: none"> • Partners suspect infidelity if condom is suggested • Partner gets mad if condom is suggested
Sub-question 2	<ul style="list-style-type: none"> • Having anal sex in the past 90 days • Having vaginal sex in the past 90 days • Having oral sex in the past 90 days • Age having sex the first time • Have a main sexual partner • Number of different sexual partners in the past 90 days 	<ul style="list-style-type: none"> • Ever having syphilis before • Ever having gonorrhea before • Age • Current employment status • Gender

Variables were then assessed for collinearity. I performed collinearity tests for all the selected IVs before beginning the univariate analysis. If the value of correlation was close to +1 or -1, then that indicated that the selected variables were highly correlated, implying the presence of collinearity. I also carried out multicollinearity tests once all the variables were fit into the respective models. If the variance inflation factor (VIF) was between 1- 10, then there was no serious multicollinearity problem. A VIF between 5 and 10 indicates high correlation that may be problematic but the values of VIF obtained from all the variables chosen for this study were below 5. All analyses were complete case analysis using list wise deletion in SPSS as missing cases for all variables in the multivariable models had less than 15% of missing data.

My goal was to obtain the least biased and confounded estimates of association. Hence, I decided to carry out analyses for multiple models as I was not sure on which set of covariates would result in the least confounded effects of the IVs, especially with data from patients with either syphilis or gonorrhoea. I had 1 model to obtain crude estimates and 3 other models for my final multivariable logistic regression analyses. The models are:

1. **Model 1:** Crude (unadjusted)
2. **Model 2:** Each primary IV adjusted for the effects of all other primary IVs
 - This model assumes that all primary IVs are confounders of each other and that there are no other confounders.
 - For each primary IV-outcome association, none of the other primary IVs are in the causal path between the primary IV and the outcome.
3. **Model 3:** Each primary IV adjusted for the effects of confounders (excluding the other primary IVs)
 - This model assumes that for each primary IV-outcome association, none of the other primary IVs are confounders and all of the covariates in the model meet the definition of confounding which means that they are associated with the primary IV, predictive of the outcome, and not in the causal path between the primary IV and the outcome.
4. **Model 4:** Each primary IV adjusted for the effects of all other primary IVs plus the potential confounders
 - This model assumes that for each primary IV-outcome association, all other primary IVs and “potential confounders” meet the criteria for confounding of that primary IV-outcome association.

Adjusted odds ratios (aORs) with 95% confidence intervals (CIs) were used to estimate associations.

RESULTS

A total of 526 patients with syphilis or gonorrhea were analyzed for this study. From a total of 526 patients, 78 index patients reported details on all their contacts (n=172) who were then successfully traced back and participated in the study. Demographic characteristics among patients with syphilis or gonorrhea are shown in Table 2.2. Sexual behaviors/characteristics are shown in Table 2.3. Peer influences on patients, behaviors of patients when condom use is suggested by their partners and behaviors of their partners when the patients suggest on using condom are shown in Table 2.4, 2.5 and 2.6, respectively. The sexual behaviors and characteristics of individuals named as part of a sexual network of patients with syphilis or gonorrhea who were traced back to this study through 'partner notification' are shown in Table 2.7.

For patients with syphilis: 'Numbers of different sexual partners in the last 90 days', mean (standard deviation [SD]) = 2.17 (6.04), median = 1.00. For 'Age having sex the first time', mean = 15.30 (6.85), median = 15.00. For 'Age', mean = 36.30 (10.98), median = 38.00. For patients with gonorrhea: 'Numbers of different sexual partners in the last 90 days', mean = 2.18 (1.57), median = 2.00. For 'Age having sex the first time', mean = 14.50 (2.82), median = 15.00. For 'Age', mean = 29.9 (10.18), median = 26.00. Furthermore, 63.3% of them had syphilis prior to this study (as shown in Table 2.2).

(a) Results for main research question

When controlling for 'Ever having syphilis before', 'Ever having gonorrhea before', 'Age', 'Current employment status' and 'Gender', results from both Model 3 and Model 4 showed that patients who were gay were more likely to have syphilis (vs. gonorrhea) compared to those who were straight but the estimates were attenuated toward the null in relative to the crude estimates. Table 2.8 presents the resulting aORs and 95% CIs showing the associations between their sexual behaviors or characteristics and presence of syphilis or gonorrhea, respectively.

(b) Results for sub-question 1

When controlling for 'Partner gets mad if condom is suggested' and 'Partners suspect infidelity if condom is suggested', results from both Model 3 and Model 4 showed that patients with close friends/people who are important who do not think that using condom prevent HIV were more likely to have syphilis (vs. gonorrhea) compared to those with friends who thought otherwise but the estimates were attenuated toward the null in relative to the crude estimates.

Table 2.9 presents the resulting aORs and 95% CIs showing the associations between peer/partner's influences on condom use before sexual intercourse and presence of syphilis and gonorrhea, respectively.

(c) Results for sub-question 2

For individuals named as part of a sexual network of index patients with syphilis and gonorrhea who were traced back to the study (n=172), when controlling for 'Ever having syphilis before', 'Ever having gonorrhea before', 'Age', 'Current employment status' and 'Gender' results from Model 3 and Model 4 showed that those who were under 14 years old when having sex the first time and those who did not have a main sexual partner were more likely to have syphilis (vs. gonorrhea), but the estimates were attenuated toward the null in relative to the crude estimate. Table 2.10 presents the resulting aORs and 95% CIs showing the associations between sexual behaviors/characteristics and individuals named as part of a sexual network of patients having syphilis or gonorrhea who were traced back to the study through 'partner notification'.

Table 2.2: Number (percent) of patients with syphilis or gonorrhea, by disease status and demographic factors

Demographic factors	Patients with Syphilis Total, N=330	Patients with Gonorrhea Total, N=196
	n*(%)	n*(%)
Age-groups		
15-19 years	19 (5.8)	24 (12.2)
20-24 years	46 (13.9)	53 (27.0)
25-29 years	32 (9.7)	37 (18.9)
30-34 years	31 (9.4)	22 (11.2)
35-39 years	59 (17.9)	21 (10.7)
40-44 years	67 (20.3)	20 (10.2)
45-54 years	60 (18.2)	13 (6.6)
55-64 years	14 (4.2)	4 (2.0)
65 years and above	1 (0.3)	1 (0.5)
Ethnicity		
African-American	300 (90.9)	190 (96.9)
White, Non-Hispanic	23 (7.0)	4 (2.0)
Others	7 (2.1)	2 (1.0)
Gender		
Male	187 (56.7)	154 (78.6)
Female	142 (43.0)	42 (21.4)
Education Level		
Grade 1-11	128 (38.8)	74 (37.8)
High School Dip.	106 (32.1)	75 (38.3)
GED	24 (7.3)	10 (5.1)
College	66 (20.0)	35 (17.9)
Grad School	6 (1.8)	2 (1.0)
Marital Status		
Married	22 (6.7)	13 (6.6)
Separated/Divorced/ Widowed	71 (21.5)	23 (11.8)
Single	237 (71.8)	160 (81.6)

Table 2.2 (continued):

Demographic factors	Patients with Syphilis Total, N=330	Patients with Gonorrhoea Total, N=196
	n*(%)	n*(%)
Current employment Status		
Full Time	94 (28.5)	86 (43.9)
Part Time	38 (11.5)	23 (11.7)
Seeking job	106 (32.1)	55 (28.1)
Jobless	88 (26.7)	31 (15.8)
Living with partner		
Yes	113 (46.3)	53 (32.5)
No	131 (53.7)	110 (67.5)
Living Conditions		
Own place	147 (44.5)	82 (41.8)
Someone else's place	151 (45.8)	106 (54.1)
Hotels/Boarding home	7 (2.1)	3 (1.5)
Halfway house/shelter	23 (7.0)	3 (1.5)
Homeless	-	2 (1.0)
Receiving any sources of income		
Yes	6 (1.8)	2 (1.0)
No	321 (97.3)	193 (98.5)
Receiving any kinds of healthcare services		
Yes	9 (2.7)	4 (2.0)
No	319 (96.7)	191 (97.4)
Ever having syphilis before		
Yes	209 (63.3)	19 (9.7)
No	120 (36.4)	177 (90.3)
Ever having gonorrhoea before		
Yes	108 (32.7)	172 (87.8)
No	222 (67.3)	24 (12.2)

Table 2.2 (continued):

Demographic factors	Patients with Syphilis Total, N=330	Patients with Gonorrhea Total, N=196
	n*(%)	n*(%)
Self-conditions 10 years before study		
Unemployed		
Yes	272 (82.4)	139 (70.9)
No	57 (17.3)	57 (29.1)
Receiving public assistance		
Yes	156 (47.3)	42 (21.4)
No	172 (52.1)	154 (78.6)
Being homeless		
Yes	257 (77.9)	21 (10.7)
No	172 (21.8)	175 (89.3)
Being in prison		
Yes	119 (36.1)	69 (35.2)
No	210 (63.6)	127 (64.8)
Drug addiction		
Yes	68 (20.6)	9 (4.6)
No	261 (79.1)	187 (95.4)

*Percentages are rounded to the first decimal place, category-specific estimates may not equal overall total due to differences in missing values.

Table 2.3: Number (percent) of patients with syphilis or gonorrhea, by disease status and sexual behaviors/characteristics

Sexual behaviors and characteristics	Patients with Syphilis Total, N=330	Patients with Gonorrhea Total, N=196
	n*(%)	n*(%)
Types of sexual acts in the past 90 days^a		
Anal Sex		
Yes	51 (15.5)	33 (16.8)
No	269 (81.5)	156 (79.6)
Vaginal Sex		
Yes	267 (80.9)	187 (95.4)
No	59 (17.9)	7 (3.6)
Oral Sex		
Yes	176 (53.3)	137 (69.9)
No	142 (43.0)	52 (26.5)
Have a main sexual partner		
Yes	225 (68.2)	154 (78.6)
No	102 (30.9)	42 (21.4)
Sexual identity		
Straight	275 (83.3)	176 (89.8)
Bisexual	15 (4.5)	5 (2.6)
Gay	27 (8.2)	3 (1.5)
Numbers of different sexual partners		
None	28 (8.5)	1 (0.5)
1 partner	168 (51.9)	76 (38.8)
2-10 partners	111 (33.6)	114 (58.2)
> 10 partners	3 (0.9)	1 (0.5)
Having oral sex with main partner		
Yes	153 (46.4)	118 (60.2)
No	114 (34.5)	56 (28.6)
Age when having sex for the first time		
< 14 years	104 (31.7)	62 (32.0)
≥ 14 years	224 (68.3)	132 (68.0)

*Percentages are rounded to the first decimal place, category-specific estimates may not equal overall total due to differences in missing values.

^aHaving vaginal, anal and oral sex with partner or others.

Table 2.4: Number (percent) of patients with syphilis or gonorrhea, by disease status and peer influences

Peer influences	Patients with Syphilis Total, N=330	Patients with Gonorrhea Total, N=196
	n*(%)	n*(%)
Friends think it's OK to have sex with someone more like a stranger without condom		
Yes	205 (62.1)	48 (24.6)
No	118 (35.8)	144 (73.8)
Friends^a think it's OK to have sex with someone who refuses to use condom		
Yes	188 (57.0)	126 (64.6)
No	132 (40.0)	67 (34.4)
Close friends/people who are important think that using condom implies no trust on partner		
Yes	222 (67.3)	135 (69.2)
No	103 (31.2)	57 (29.2)
Close friends/people who are important think that using condoms prevent HIV		
Yes	305 (92.4)	188 (96.4)
No	19 (5.8)	6 (3.1)
Peers^b encouraging the use of condom		
Yes	253 (76.9)	145 (74.4)
No	76 (23.1)	50 (25.6)

*Percentages are rounded to the first decimal place rounded to nearest whole number, category-specific estimates may not equal overall total due to differences in missing values; ^aFriends include friends and relatives who consider to be friends and ^bPeers are combination of friends and people who are important.

Table 2.5: Number (percent) of patients with syphilis or gonorrhea, by disease status and behaviors when their respective partners suggest condom use

Behaviors of patients when condom use is suggested by their partners	Patients with Syphilis Total, N=330 n*(%)	Patients with Gonorrhea Total, N=196 n*(%)
Refuse sex because partner refuses condom Yes No	149 (45.2) 181 (54.8)	95 (48.5) 98 (50.0)
Fear of what partner might do/say when condom use is suggested Yes No	41 (12.4) 289 (87.6)	21 (10.7) 172 (87.8)
Gotten mad if partner asks to use condom Yes No	26 (7.8) 304 (92.1)	20 (10.2) 173 (88.3)
Threatened to hit the partner thinking they cheated on them when condom use is discussed Yes No	98 (30.0) 232 (70.3)	45 (23.0) 148 (75.5)

*Percentages are rounded to the first decimal place, category-specific estimates may not equal overall total due to differences in missing values.

Table 2.6: Number (percent) of patients with syphilis or gonorrhea, by disease status and behaviors of partners when condom use is suggested to them

Behaviors of partners when condom use is suggested by the patients	Patients with Syphilis Total, N=330 n*(%)	Patients with Gonorrhea Total, N=196 n*(%)
Partners suspect infidelity if condom is suggested Yes No	178 (54.0) 127 (38.5)	121 (61.7) 67 (34.2)
Partner gets mad if use condom Yes No	121 (36.7) 170 (51.5)	86 (43.9) 93 (47.4)
Sex partner breaks up if condom is used Yes No	22 (6.7) 265 (80.3)	13 (6.6) 160 (81.6)
Partner threatens to hit or get violent if condom use is suggested Yes No	8 (2.4) 311 (94.3)	7 (3.6) 186 (94.8)
Partners refuse sex if condom is used Yes No	54 (16.4) 276 (83.6)	33 (16.8) 160 (81.6)
Acceptance of partner if condom is used Yes No	4 (1.2) 307 (93)	2 (1.0) 185 (94.4)

*Percentages are rounded to the first decimal place, category-specific estimates may not equal overall total due to differences in missing values.

Table 2.7: Number (percent) of patients with syphilis or gonorrhea, by disease status and sexual behaviors/characteristics of individuals named as part of a sexual network who were traced back to the study through ‘partner notification’

Sexual behaviors and characteristics	Patients with Syphilis Total, N=132	Patients with Gonorrhea Total, N=40
	n*(%)	n*(%)
Types of sexual acts in the past 90 days^a		
Anal Sex		
Yes	9 (6.8)	8 (20.0)
No	121 (91.7)	32 (80.0)
Vaginal Sex		
Yes	112 (84.8)	37 (92.5)
No	19 (14.4)	3 (7.5)
Oral Sex		
Yes	56 (42.4)	137 (69.9)
No	73 (55.3)	52 (26.5)
Have a main sexual partner		
Yes	97 (73.5)	35 (87.5)
No	35 (26.5)	5 (12.5)
Sexual identity		
Straight	123 (93.2)	36 (90.0)
Bisexual	4 (3.0)	2 (5.0)
Gay	1 (0.8)	1 (2.5)
Numbers of different sexual partners		
≤1 partner	94 (71.2)	25 (62.5)
≥2 partners	28 (21.2)	15 (37.5)
Age when having sex for the first time		
< 14 years	47 (35.6)	15 (37.5)
≥ 14 years	84 (63.6)	25 (62.5)

*Percentages are rounded to the first decimal place, category-specific estimates may not equal overall total due to differences in missing values; ^aHaving vaginal, anal and oral sex with partner or others.

Table 2.8: Estimated associations (crude and adjusted odds ratios [aORs] and 95% confidence intervals [CIs]) of sexual behaviors/characteristics (primary independent variables [IVs]) with having syphilis (vs. gonorrhoea): Results from simple and multivariable logistic regression analyses

Measures (Primary IVs)	Syphilis (vs. Gonorrhoea)			
	Crude OR (95% CI) {Model 1}	aOR (95% CI) {Model 2}	aOR (95% CI) {Model 3}	aOR (95% CI) {Model 4}
Sexual identity				
Straight	Ref	Ref	Ref	Ref
Bisexual	1.92 (0.69-5.38)	2.43 (0.78-7.57)	0.99 (0.25-3.90)	1.35 (0.31-5.80)
Gay	5.76 (1.72-19.27)	3.47 (0.74-16.23)	2.73 (0.61-12.20)	1.79 (0.25-12.71)

Model 1: Unadjusted

Model 2: Adjusted for the effects of all other primary IVs

Model 3: Adjusted for potential confounders[#] (excluding the other primary IVs)

Model 4: Adjusted for the effects of all other primary IVs plus all the potential confounders[#]

^aHaving sex anally, vaginally or orally with main partner or others

[#]Potential confounders for all the primary IVs are: Ever having syphilis before, Ever having gonorrhoea before, Age, Current employment status and Gender

Table 2.9: Estimated associations (crude and adjusted odds ratios [aORs] and 95% confidence intervals [CIs]) of peer influences on condom use before sexual intercourse (primary independent variables [IVs]) with having syphilis (vs. gonorrhea): Results from simple and multivariable logistic regression analyses

Measures (Primary IVs)	Syphilis (vs. Gonorrhea)			
	Crude OR (95% CI) {Model 1}	aOR (95% CI) {Model 2}	aOR (95% CI) {Model 3}	aOR (95% CI) {Model 4}
Close friends/people who are important think that using condoms prevent HIV				
No	2.58 (0.94-7.08)	2.58 (0.94-7.08)	1.99 (0.78-5.12)	2.48 (0.89-6.91)
Yes	Ref	Ref	Ref	Ref

Model 1: Unadjusted

Model 2: Adjusted for the effects of all other primary IVs

Model 3: Adjusted for potential confounders[#] (excluding the other primary IVs)

Model 4: Adjusted for the effects of all other primary IVs plus all the potential confounders[#]

^aFriends include friends and relatives who consider to be friends

^bPeers are combination of friends and close friends/people who are important

[#]Potential confounders for all the primary IVs are: Partners suspect infidelity if condom is suggested and Partner gets mad if condom is suggested

Table 2.10: Estimated associations (crude and adjusted odds ratios [aORs] and 95% confidence intervals [CIs]) of sexual behaviors/characteristics (primary independent variables [IVs]) with having syphilis (vs. gonorrhea) among individuals named as part of a sexual network of index patients with syphilis and gonorrhea who were traced back to the study: Results from simple and multivariable logistic regression analyses

Measures (Primary IVs)	Syphilis (vs. Gonorrhea)			
	Crude OR (95% CI) {Model 1}	aOR (95% CI) {Model 2}	aOR (95% CI) {Model 3}	aOR (95% CI) {Model 4}
Age having sex the first time < 14 years ≥ 14 years	1.07 (0.52-2.23) Ref	0.99 (0.45-2.20) Ref	1.23 (0.53-2.88) Ref	1.17 (0.47-2.90) Ref
Have a main sexual partner No Yes	2.53 (0.92-6.96) Ref	1.72 (0.51-5.83) Ref	2.01 (0.69-5.84) Ref	1.16 (0.28-4.78) Ref

Model 1: Unadjusted

Model 2: Adjusted for the effects of all other primary IVs

Model 3: Adjusted for potential confounders[#] (excluding the other primary IVs)

Model 4: Adjusted for the effects of all other primary IVs plus all the potential confounders[#]

^aHaving sex anally, vaginally or orally with main partner or others

[#]Potential confounders for all the primary IVs are: Ever having syphilis before, Ever having gonorrhea before, Age, Current employment status and Gender

DISCUSSION

This study is rather unique as it examined associations of behavioral factors with sexual risk and peer influences among patients from STD clinics who either had syphilis or gonorrhea, predominantly African-Americans and single, relevant to a study that investigated behavioral contributions to acquisition of gonorrhea in patients attending an STD clinic.¹⁰ This study attempted to better define behaviors predictive of current syphilis or gonorrheal infection and describe dimensions of sexual behavior that may contribute to the prevalence of syphilis vs. gonorrhea. Previous studies have focused on demographic descriptors, geographic clustering, socioeconomic status, and repeated episodes of infection,^{109,110} but relatively little is known regarding sexual behaviors/characteristics of individuals who already have syphilis, how it is possible for them to be infected again with much higher risk for HIV and how they could be the beginning of an infected sexual network.

This study found that patients who were gay were more likely to have syphilis (versus gonorrhea) compared to those who were straight, but there is uncertainty in the exact magnitude of effect as reflected in the wide CI. This was similar to a study that found among persons with early syphilis diagnosis, 94% of them were gay and 6% were bisexual.¹¹¹ Another finding in this study showed that about 64% of the patients with syphilis in this study had syphilis prior to this study as a syphilis infection does not confer immunity.⁶⁸ However, this study lacked detailed information on condom use during each sexual intercourse with different type of sexual practices. Information on condom use would have been valuable in this study.

During late adolescence, individuals forge their identities and their behavior patterns through a process of socialization and acceptance by peers.¹¹² The perception of their peers on the subject of sexual behaviors is an important normative predictor of intention with regard to the beginning of sexual relations and engaging in sexuality.¹¹³ This study showed patients with close friends/people who are important who do not think that using condom prevent HIV were more likely to have syphilis (versus gonorrhea) compared to those with friends who thought otherwise, but even with uncertainty in the exact magnitude of the effect, this finding is explained by a study on peer influence on risk taking which found that participants of the study made riskier decisions when in peer groups than being alone.¹¹⁴

Individuals named as part of a sexual network who were traced back to this study who were under 14 years old when having sex the first time were found to be more likely to have syphilis (versus gonorrhea) but even with the uncertainty in the exact magnitude of effect as reflected in the wide CI, this finding could provide some important information on how having sex the first time at very young age could have led to risky sexual behaviors among adolescents

and lead to acquisition of syphilis in comparison to gonorrhea and increase the risk for HIV as well. A study among young females with STI that found those who had sex first time before age 16 were more likely to have any kinds of STD compared to those who had sex the first time after 16 years.¹¹⁵ Another finding was that those who did not have a main sexual partner were more likely to have syphilis (versus gonorrhea) in this study but there was uncertainty in the exact magnitude of effect as reflected in the wide CI, yet similar to a study that found female adolescents who had a main sexual partner were less likely to be infected with HIV compared to those who did not have a main sexual partner.¹¹⁶ Unfortunately, this study lacked information on incarceration and gang membership.

My findings for this study could not be directly compared to previous studies due to the sample of patients with syphilis being compared to patients with gonorrhea who attended STD clinics in Baltimore, but in general my findings are consistent with those which are more population based.

Limitations

There are inherent limitations in this study. This study is based on secondary analysis from a cross-sectional study. The study had already been designed and data collection completed. This is a common limitation in any secondary analysis. At times, data may not be able to facilitate a particular research question. For example, 93% of the subjects were African-American and the rest were other races. Even though there was interest in examining possible effect modification by race/ethnicity it could not be achieved as this study had already been completed. A study investigating the significance of black-white differences in risky sexual behavior found that there was tremendous variability between the ethnic groups in the factors that predict risky sexual behaviors.¹¹⁷ Therefore, research questions could only be designed based on available data and resources of the study. African-Americans have noticeably higher rates of STDs compared to other ethnic and racial groups in the US.^{118,119} A report published by CDC in 1996 emphasized that there are no known biological reasons to explain why ethnic factors alone should alter the risk for STDs and that ethnicity is an indicator associated with other more essential determinants of health status such as poverty, illicit drug use and living in communities with high prevalence of STDs.¹¹⁹ However, this does not preclude ethnicity from modifying the effect sexual behaviors on risk of syphilis vs. gonorrhea as reported by the study that concluded differences between African-Americans and whites exist and clearly distinguish those that characterize risk between these 2 ethnicities.¹¹⁷

Certain categories of the independent variables had low cell counts, hence the large width in the confidence intervals thus, indicating the uncertainty in the exact magnitude of effect. The sample sizes for patients with syphilis and gonorrhoea were fairly small in this study.

Another limitation is that the data are from 2001-2005. At times, data collected far back will be outdated, hence affects the interpretation of the results and discussion for the current time. As the SSN project is related to STDs, sexual characteristics and networking risks, the data will not be affected by the fact of being collected 10-15 years ago.

As stated earlier, the SSN study was cross-sectional (all the measurements on each person were made at one point in time), thus temporal ambiguity between exposure and outcome variables limits causal inferences. Cross-sectional studies are the best way to determine prevalence and are useful at identifying associations that can then be more rigorously studied using a cohort study or randomized controlled study.

The participation rate for this study is not too high and could account for a type of selection (volunteer) bias. Volunteer bias occurs when those who volunteer to participate in a study differ systematically with regard to either exposure or disease status from those who did not volunteer. A study with a low response rate could result in bias due to differences in the exposure effect between participants and non-participants. A review of the published social research literature suggests for interview surveys, a response rate of at least 50 percent is considered adequate for analysis and reporting.¹²⁰ For the past 30 years, participation rates in epidemiologic studies have been declining with potential participants increasingly refusing to take part and harder to find subjects who will be eligible to participate.¹⁰⁷ One possible reason for 47.2% refusals in this study would be because of some questions on sexual behaviors that question them on their sexual lifestyles and behaviors. Some people consider sexual topics taboo and prefer to opt out from participating. The aORs in my study might not be affected much by the low participation rates. Participation rate alone does not determine the extent of bias present in any study and low participation rates do not always indicate a high level of bias essential in a study.^{121,122} What matters most are the differences in factors that affect exposure effect that determine the amount of bias present. Most studies have found little evidence for substantial bias as a result of non-participation that decreases the participation rates.¹²³ Even so, participation should be optimized as much as possible as epidemiologic studies with really low levels of participation may be more vulnerable to self-selection bias (individuals selecting themselves for the study) than those with higher participation.¹²⁴ Based on this information, participation rates can be improved for future studies by probably targeting a larger population with more variations in the races; increasing monetary incentives; using web-based modes of

data collection allowing respondents to complete surveys at a time and place convenient for them; and having experts explain to those who refuse due to the sexual sections on the benefits of their participation that could be used as a tool to identify potential predictors on STDs and how they could contribute to mitigate these diseases in the future.

Another type of selection bias (admission bias) could have occurred because study participants were drawn from STD clinics. Admission bias occurs when cross-sectional or case-control studies are done exclusively in hospital or clinic settings where the population studied does not reflect other general populations. It is definitely impossible to eliminate this type of bias as this research was conducted in STD clinics but if studies similar to this study have target populations comprised of people in the community with syphilis or gonorrhea, then estimates derived from community-based samples are less prone to selection bias and would likely be more valid and generalizable to the community to which the STD clinics serve.

This study had surveys and they were all self-reported, thus the veracity of study participants' responses may be questioned and lead to some information bias. There is a tendency for respondents to provide what they believe to be socially acceptable answers rather than the truth. This is especially possible with regards to behavioral aspects and health conditions associated with taboos.¹²⁵ This research was mainly on sexual characteristics and there would definitely be possibilities on some subjects to provide answers that hide the real truth as these kinds of questions are sensitive to many. One example would be 'age having sex for the first time'. Patients could have forgotten the exact age when they had sex the first time or were embarrassed to list down the exact age they had sex the first time and this could have caused possible non-differential misclassification because all study participants have an STD. Variables like employment status could have the same misclassification as some patients would have selected their part time jobs as their full time jobs. Thus, the aORs from this study involving these variables could have been biased towards the null. Applying standardized and validated methods and using objective measures can help reduce information inaccuracies. In this study, patients' clinical signs and symptoms were recorded on standardized data collection forms, and the standard confidential operating procedures were followed throughout the research.

Another limitation in this study would be that the data lacking in detail on the partner notification process. Thus, this design suffers from incomplete-network bias that occurs when all the sexual partners of the index cases could not be traced or recruited for a variety reasons. Therefore, the estimates of the findings on the sexual characteristics of the individuals who were traced back, had CIs that are wider than they would be if more index patients had reported their

sexual contacts and were traced back to participate in this study, and could also be possibly underestimated or overestimated than the true value as only 14.8% of the index patients reported on their sexual networks who could be traced back to the study. One way to minimize the misreporting of sexual behaviors and information on their sexual networks would be to use the audio computer-assisted self-interview (ACASI).¹²⁶ This program allows participants to privately answer sensitive personal questions on a computer with headphones, eliminates data entry time and errors, provides consistent questionnaire delivery (all questions will always be asked in the exact same way) and works well for patients with literacy issues.

Confounding is another type of bias that could occur in this study. There were a few variables that could be potential confounders that I could not control for from the questionnaire on risky sexual behaviors such as injection behavior, having sex with drug users, exchanging sex for other purposes and condom use that could not be used in the analyses due to missing data and scarcity in the frequencies. This is something unavoidable when it comes to secondary data analyses. Nonetheless, this will be something to look at for future research. This study focuses on sexual behaviors of participants and their associations to the presence of syphilis vs. gonorrhea among persons with either syphilis or gonorrhea. There were 3 multivariable models for the analyses in this study because of not being sure about a single model specification that would give the least confounded estimates. The possible differences in point estimates between models were probably due to random variability that is shown in the width of most CIs because of low sample sizes and low cell counts for certain categories or due to the differences in the covariates between models. Model misspecification could have occurred possibly due to covariates that aren't confounders and also because of the differences in assumptions about associations between covariates and associations of covariates with syphilis vs. gonorrhea between models. For this study, Model 4 would be the best model to provide results closest to the truth compared to Model 3 because some of the primary IVs were potential confounders as well and Model 4 controls for all the chosen primary IVs and potential confounders that were selected for this study based on relevant studies^{10,70,75} and also on some prior knowledge gathered from discussions with the primary investigator of this study. But, the estimates from Model 4 would be still a little biased due to residual confounding because I was not able to control for some variables that might be predictive of syphilis/gonorrhea as described earlier because I did not have the data and, over-adjustment as not all the primary IVs were potential confounders, only some of them were, thus precision is generally reduced. An example for a possible over-adjustment would be that 'Age having sex the first time' and 'sexual identity' (the other primary IVs) could predict numbers of different sexual partners in the past 90 days (main

primary IV) and also the presence of syphilis vs. gonorrhea but the other primary IVs (main sexual partner and having anal/vaginal/oral sex in the past 90 days) do not associate with numbers of different sexual partner in the past 90 days. However, even though some potential confounders could not be accessed due to absence of data on them, I made full effort to identify all the potential confounders which had sufficient data in this study based on literature or prior knowledge and had them controlled for in all analyses.

Another possible limitation of this study is that the sampled population limits the generalizability. The target population in this study is people with syphilis or gonorrhea identified from BCHD STD clinics. The associations between the IVs and syphilis vs. gonorrhea in this target population are likely very different from the associations between IVs and syphilis that would be observed in populations that include people without gonorrhea and vice versa for the associations between the IVs and gonorrhea. Thus, the results would not be generalizable to lower risk populations, people in established couple relationships or general population samples not seeking STD care or persons with gonorrhea or syphilis outside of BCHD STD clinic settings. Generalizability typically relates only to the external validity of a study, but the main determinants include elements of internal validity, which is determined by the degree to which a study minimizes systematic error or bias. Nonetheless, even though the results from this study do not necessarily mean the results are generalizable it does show that the results are consistent with other studies which are more population based.

Strengths

One strength of this study would be that the STDs among all participants of this study were diagnosed clinically as opposed to be depending on self-report that may underestimate STDs because of social desirability bias (tendency of survey respondents to answer in a manner that will be viewed favorably by others: e.g., over-reporting a good behavior or under-reporting a bad behavior) in reporting and undiagnosed infections.¹²⁷ Next, would be that all the sexual partners who were traced back to the study were interviewed personally by the DIS and not by gathering information based on the index patients' knowledge of their partners. This would have minimized some information bias in this study. Another strength would be the meticulous approach in the analyses in this study. I performed analyses with 3 multivariable models with different sets of covariates to estimate adjusted effects under different assumptions of the potential confounding effects of covariates for addressing each research question and sub-question of this study.

Conclusions and Public Health Implications

Even though, my findings for this study had uncertainty in the exact magnitude of the effect due to a complex data set with small sample size/low cell counts for some independent variables, these findings are still important for baseline implications targeted for patients with STDs like syphilis or HIV who attend STD clinics in the US. This study is rather unique and investigates the differences between patients with syphilis and patients with gonorrhea. ‘Non-significant’ results do not mean ‘no-effect’, hence if my study could be replicated in larger populations and in studies with less potential selection bias and confounding in the near future, besides obtaining estimates with confidence intervals that are narrow in width showing precision, we could also determine if the estimates from these new studies are consistent with the estimates obtained from my study.

This research would still be beneficial for future research among populations made of attendees from STD clinics in the US, who are tested and diagnosed with STDs including HIV. It is essential to study patients and learn their lifestyle and risky sexual behaviors that increase the risk of contracting STDs. A study examining three ethnicities (White, Black and Hispanic) and HIV prevalence found racial/ethnic disparities in HIV prevalence¹²⁸ and unfortunately, this study lacked this information and should be given importance for future studies among patients with STDs to investigate ethnic disparities. Partner notification has been an important component of public health efforts to reduce the spread of STDs. Therefore, more studies are necessary to determine how public health and provider services towards betterment in expediting patient-initiated partner notification as well as to educate patients regarding the significant role of partner notification in decreasing all types of STD transmission.

The observations from this cross-sectional study based on a population of STD clinic patients from Baltimore with gonorrhea or syphilis and in combination with data from prior studies suggest that being diagnosed with syphilis vs. gonorrhea may be influenced by the interplay of behavioral factors that help to define groups of patients who could be at risk for reinfection or be potential ones to transmit syphilis/gonorrhea to their sexual networks and be the beginning of an infected egocentric sexual network.

The findings of this study suggest that among patients with either syphilis or gonorrhea, those who are gay, aged under 14 years old when having sex the first time and who do not have a main sexual partner increase the odds of syphilis (compared with gonorrhea). Syphilis enhances HIV transmission and acquisition, and HIV infection affects the natural history and clinical progression of syphilis.¹²⁹ The rising incidence of syphilis in MSM is in part attributable to recent increases in high-risk sexual behavior. High rates of new sex partner acquisition and partner

change rates with rises in unprotected penetrative sex have been documented across the US.¹³⁰ Among MSM, an extensive proportion of men with incident syphilis infection are also HIV positive, reflecting both high risk sexual behaviors within this group, as well as participation in sexual networks which enable disease transmission.¹³¹ Having syphilis once does not protect a person from getting it again because even with successful treatment, people can be susceptible to re-infection. Thus, public health should focus in enhancing clinical services for syphilis cases which include early access to care, STIs screening, accurate diagnosis, appropriate treatment, patient counseling, partner management, and follow-up. Prompt quality clinical management of individuals diagnosed with or exposed to infectious syphilis is a fundamental component for the prevention and control of syphilis and is a joint responsibility between health departments and providers. Syphilis sores can be hidden in the vagina, rectum or mouth and may not be obvious if a sex partner has syphilis, therefore patients with syphilis should be educated by their clinicians on how it is important to know if each of their sexual partner is diagnosed with syphilis and whether they have been treated completely or not, before having any sexual intercourse. Also, syphilis patients should be strongly encouraged to notify their sexual partners of their syphilis diagnosis and abstain from any sexual relationships until they get full treatment. Screening at least once a year for syphilis and HIV should be encouraged by public health and also health studies in high schools and educational institutes especially for all sexually active gay men and other MSM who are at the highest risk.

Public health should have health programs among STD patients to create awareness on the possibilities of getting infected with syphilis again and also increase the susceptibility in contracting HIV due to histories of having sex the first time at very early age that could have led them to risky sexual behaviors throughout their adolescence and also for not having a main sexual partner but having more casual or new sexual partners who had syphilis without them knowing prior to their sexual intercourses. They should be encouraged by their clinicians who are treating them, to have sex only with people they are committed to and trust after getting themselves completely treated, but still with full protection during intercourse with them (e.g., constant use of latex condoms). Clinicians in STD clinics should put in more effort and follow up with these patients on their sexual activities and sexual networks for some amount of time, probably every 6 months. This could help them in being safe during their sexual intercourse and also making sure their sexual partners are people they know and trust rather than random people. This could stop the spread of syphilis among their sexual networks and reduce the risks in contracting HIV as well.

Adolescents and young adults who are patients with syphilis who attend STD clinics should be educated by their clinicians and also given counseling by public health officers on how people who have syphilis are more likely to be infected with syphilis again compared to gonorrhea which could place them at higher risk in getting infected by HIV, if they do not practice safe sex.

CHAPTER 3.

STUDY 2: NETWORK CHARACTERISTICS OF PATIENTS WITH SYPHILIS OR GONORRHEA: THE SOCIAL AND SEXUAL NETWORK (SSN) STUDY, BALTIMORE

ABSTRACT

Background: The spread of sexually transmitted diseases (STDs) are strongly associated with social networks as sexual transmission of infections follows routes of sexual contact. The aims of this study were to (1) estimate associations between the network characteristics of the sexual partners or non-sexual partners of the patients and the presence of syphilis vs. gonorrhea, (2) estimate associations between the network characteristics of the sexual partners or non-sexual partners of the patients and the presence of syphilis vs. gonorrhea, among sexual partners of index patients with syphilis and gonorrhea who were traced back to the study, (3) describe differences in associations between sexual characteristics and presence of syphilis vs. gonorrhea by different types of networks (more sexual networks than non-sexual networks and vice versa), and (4) estimate associations between some sexual behaviors and presence of syphilis vs. gonorrhea among men having sex with men (MSM) from this study.

Methods: The Social and Sexual Network (SSN) data from 526 respondents who were patients with syphilis or gonorrhea (index cases) and networking data from a total of 3309 social contacts were used to address the research questions of this study. Parameter estimates (adjusted odds ratios [aORs]), 95% confidence intervals (CIs), and p-values were generated using SPSS 18.0. aORs were used to estimate associations adjusted for the effects of confounders. Four separate 'generalized linear models (GLM)' analyses were performed while controlling for selected confounders

Results: Results indicated that patients with male networks were less likely to have syphilis (vs. gonorrhea) compared to female networks (aOR=0.80, 95%CI: 0.67, 0.97) but patients with networks aged 15-19 years (aOR=1.73, 95%CI: 1.16, 2.57) and networks aged 20-24 years (aOR=1.98, 95%CI: 1.40, 2.78) were more likely to have syphilis (vs. gonorrhea) compared to networks aged 55 years and above. Among sexual partners who were traced back to the study (n=172), results indicated that patients with male networks (aOR=1.38, 95%CI: 0.97, 1.97) and who had regular sexual partners (aOR=1.44, 95%CI: 0.89, 2.33) were more likely to have syphilis (vs. gonorrhea) compared to female networks and having non-sexual networks. Among individuals with more sexual partners than non-sexual partners, results indicated that patients who did not have vaginal sex in the past 90 days (aOR=0.08, 95%CI: 0.02, 0.30) and who had no more than 1 sexual partner in the past 90 days (aOR=0.37, 95%CI: 0.09, 1.61) were less likely

to have syphilis (vs. gonorrhea) than those who had vaginal sex and had more than 1 sexual partner. Among individuals with more non-sexual networks than sexual networks, results indicated that patients who had anal sex (aOR=1.58, 95%CI: 1.16, 2.14), vaginal sex (aOR=2.14, 95%CI: 1.38, 3.31) and oral sex (aOR=2.08, 95%CI: 1.68, 2.58) all in the past 90 days, had 2 or more sexual partners in the past 90 days (aOR= 1.56, 95%CI: 1.26, 1.93) and who were 14 years and more when they had sex the first time (aOR=2.06, 95%CI: 1.65, 2.56) were more likely to have syphilis (vs. gonorrhea) compared to those who did not have anal, vaginal or oral sex and those who had no more than 1 sexual partner in the past 90 days. Among individuals who are MSM, results indicated that those who had no more than 1 sexual partner in the past 90 days (aOR=0.10, 95%CI: 0.02, 0.60) were less likely to have syphilis (vs. gonorrhea), compared to those who had 2 or more different sexual partners in the past 90 days.

Public Health Implications: Clinicians could help syphilis patients who are MSM (based on the types of their networks (more sexual networks than non-sexual networks and vice versa) in educating them on possible re-infections which could place them in higher risk for co-infection with HIV.

Keywords: Syphilis, Gonorrhea, Individuals named as part of a sexual or non-sexual network, Networking data, MSM, SSN study

BACKGROUND

The spread of sexually transmitted diseases (STDs) are strongly associated with social networks as sexual transmission of infections follows routes of sexual contact. Thus, patterns of infections within populations depend on who has sex with whom.³⁰

Thomas Parran was the first Commissioner of Health for the state of New York and the sixth Surgeon General of the United States (US). He was the one person who has most influenced US efforts to control STDs. He has outlined thoroughly in his classic book, 'Shadow on the Land',¹³² the principles of STD control for syphilis, by promoting timely diagnosis and treatment, screening for unsuspected infection, partner notification and public education. Partner notification is essential to identify and treat undiagnosed sexually transmitted infections (STIs). The main objective of partner notification is to break the chains of STI transmission.^{132,133}

Partner notification methods begin when a public health worker counsels an STD patient to identify partners who may have been exposed to the infection in order that they can be evaluated and treated.¹³⁴ Partner notification serves 3 main purposes, which are epidemiology, ethics and case finding: epidemiology when socio-context and sexual networks are revealed in which transmission takes place; ethics when persons exposed are warned on possible serious infections; and case finding when contacts are identified, examined and treated.¹³⁵

In a study where the researchers conducted a record review of cases of early syphilis among patients reporting men having sex with men (MSM) or with women in Georgia, and compared contact tracing outcomes, they found that interviews of MSM case patients resulted in higher mean numbers of contacts named and located compared to men who have sex with women only.³⁰

An interesting study conducted in Baltimore compared meeting venues and residences of sex partners of syphilis cases.³⁴ Meeting venue information was collected from a subset of individuals who were more likely to engage in high-risk activities. The study indicated that syphilis cases from Baltimore often met sex partners outside their own neighborhoods. Another study that focused on the selections of sex partners (sexual mixing patterns) in the spread of gonorrhea and chlamydia, found that partnerships contradictory in terms of race, age, education and number of partners were associated with significant risk for gonorrhea and chlamydial infection.³²

Those who have syphilis and gonorrhea who have partners from multiple localities may function as network bridges, hence facilitating geographical dissemination. A study that investigated how surveillance and sexual networks relate to each other for syphilis outbreaks in

rural counties of North Carolina found that the county that is most affected by the outbreak is strongly connected to networks, consistent with large incidence.¹³⁶

A study conducted in Chicago on network mixing and network influences linked to human immunodeficiency virus (HIV) infection had findings that showed that network mixing on risk behaviors was more assortative (preference to attach with others who are similar in some way) in the sexual network compared to the non-sexual network.³³

Social network methods that identify and screen friends, family and close associates of an infected individual are reported to be effective in identifying infected members of STI outbreaks. This study aims to examine the role of social networking (sexual and non-sexual networks) on the transmissions of syphilis and gonorrhea in Baltimore.

This study is designed to address the research question: Are the network characteristics* of individuals named as part of a sexual or non-sexual network of the patients associated with the presence of syphilis vs. gonorrhea among people with syphilis or gonorrhea?

**Network characteristics-type of each sex partner in the past 90 days, age of the contacts, gender of their contacts, employment status of the contacts, distance from the contacts and contacts using drugs*

Sub-question 1: Are the network characteristics* of individuals named as part of a sexual or non-sexual network of the patients associated with the presence of syphilis vs. gonorrhea among individuals named as part of a sexual network of index patients with syphilis and gonorrhea who were traced back to the study?

Sub-question 2: Are sexual characteristics# of patients with more sexual networks^α than non-sexual networks^β associated with the presence of syphilis vs. gonorrhea among people with syphilis or gonorrhea?

Sub-question 3: Are sexual characteristics# of patients with more non-sexual networks^β than sexual networks^α associated with the presence of syphilis vs. gonorrhea among people with syphilis or gonorrhea?

#Sexual characteristics- number of different sex partners in the past 3 months, sex practices (anal sex, vaginal sex and oral sex), have a main sexual partner, sexual identity and age when having sex for the first time.

^αSexual networks- individuals named as part of a sexual network of the patients

^βNon-sexual networks- individuals named as part of a non-sexual network of the patients (no sexual intercourse between the index patients and non-sexual networks)

Sub-question 4: Are there associations between some sexual behaviors and the presence of syphilis vs. gonorrhea among MSM from this study?

METHODS

Data Sources

The Baltimore syphilis epidemic facilitated this study. In 1997, over 25,000 clients attended the Baltimore City Health Department (BCHD) STD clinics for evaluation and treatment of STDs.^{70,71} During this year, the BCHD STD Program reported 941 early latent syphilis cases; 441 secondary syphilis cases; and 226 primary syphilis cases. This represented a case rate of primary and secondary (P&S) syphilis of 98/100,000 population.^{70,71} During 1998, BCHD clinical services improved and over 28,000 clients were seen. In Baltimore, 303 cases of secondary syphilis and 155 cases of primary syphilis were diagnosed. As expected, case rates for 1998 declined slightly with improved services, but remained high at 70/100,000.⁷¹ This study is a secondary data analysis of the 'Social and Secondary Network' (SSN) study data. It concentrates on the networking measures and sexual behaviors; and their impact on the two main STDs: syphilis and gonorrhea. The SSN survey data is cross-sectional, as the information collected are of a single point in time.

Study sites

Patients were recruited from BCHD's two STD clinics: Eastern STD clinic and Druid STD clinic. Interviews were conducted at the Social Network Research Clinic (The Lighthouse), which is a row house located five blocks from the BCHD Eastern STD clinic, and 2 miles from the BCHD Druid STD Clinic. The off-site social network interviews were found to provide a more controlled and confidential setting with more flexible hours than STD clinic-based interviews. Interviews were conducted in private rooms by trained interviewers who completed an interviewer-training course developed by the University of Michigan.

Standard STD Clinic Procedures

All patients diagnosed with primary/secondary/early latent syphilis and patients diagnosed with gonorrhea in the STD clinics are considered syphilis and gonorrhea index cases, and were treated on site. They received STD/HIV counseling. They were interviewed by trained 'Disease Intervention Specialists' (DIS) to obtain information regarding STD/HIV risk. All information on syphilis index patients was kept in a locked, confidential file in the BCHD Disease Registry according to standard procedures approved by the 'Centers for Disease Control and Prevention' (CDC).

Recruitment

Volunteers for this protocol were recruited from the BCHD STD Clinics. Potential participants were patients who are diagnosed as having primary/secondary stage syphilis and gonorrhea at their STD clinic visit. All study participants were asked to provide a urine specimen for gonorrhea testing using nucleic acid amplification tests (NAAT) and to have blood drawn for syphilis testing using Rapid Plasma Reagin (RPR) nontreponemal screening test with Fluorescent *Treponemal* Antibody-Absorbed (FTA-ABS) test confirmation. Criteria for diagnosis of P&S syphilis were according to the following standard clinic protocol below:

Primary syphilis: Patient presents with a genital lesion and secretions collected from the lesion are found to contain spirochetes consistent with *Treponema pallidum* by dark-field microscopic examination.

Secondary syphilis: Patient presents any constitutional symptoms consistent with secondary syphilis (fever, chills, myalgias, arthralgias, patchy alopecia, mucous patches) and/or rash (including condylomata lata) with reactive serologic-tests for syphilis [positive Rapid Plasma Reagin test (RPR) with confirmatory Fluorescent *Treponemal* Antibody-Absorbed test (FTA-ABS)].

Criteria for enrollment

Patients having primary/secondary/early latent syphilis and gonorrhea were eligible for study enrollment as syphilis and gonorrhea index cases. Any patient diagnosed with gonorrhea during the same time frame was eligible for study enrollment as gonorrhea index cases. All eligible patients were fully notified about the study protocol. Informed consent was obtained from all willing participants, and a certificate ensuring the patient's confidentiality was signed by the clinician and the patient. The clinician recorded all the patient's clinical signs and symptoms on standardized data collection forms, collected additional specimens from lesions or rashes and ordered an additional 5 milliliters of blood to be collected during routine phlebotomy. Unique study numbers on data collection forms and specimens were used to ensure the patient's confidentiality. If the patient had confirmed primary/secondary syphilis or gonorrhea according to the above routine criteria, she/he was treated and escorted to a DIS. The DIS interviewed each patient and recorded the names and addresses of all known, identified sex partners according to standard confidential operating procedures for partner notification purposes. Participants were escorted back to the study clinician. The study clinician then asked the participants if they were (1) willing to present to the 'Lighthouse' for a network interview and (2) willing to bring, or refer, at least 3 of their friends and all of their sex partners who they have

identified as members of their personal networks for interview. At the 'Lighthouse', consenting index participants were interviewed using standard forms about their opinions, knowledge, attitudes and lifestyle including drug use and sexual behavior and about friends and other people that constituted their social/sexual network. Both syphilis and gonorrhoea index patients were interviewed using standardized instruments. The procedures were repeated for all the individuals named as part of a sexual or non-sexual network of the index patients who were traced back and participated in this study.

Participation rates

The response rate for this study is 43.7%. The numerator is 'Numbers of patients that completed the interview' and the denominator is 'Total numbers of patients that completed the interviews, refusals and those who could not be contacted'. Cooperation rates are outcome rates among those eligible and usually slightly higher than the response rates.¹⁰⁷ The cooperation rate for this study is 48.1%. The numerator is 'Numbers of patients that completed the interview' and the denominator is 'Total numbers of patients that completed the interviews and refusals'. The refusal rate for this study is 47.2%. The numerator is 'Numbers of patients that refused to participate' and the denominator is 'Total numbers of patients that completed the interviews and the refusals'

Compensation for participants

The index patients were remunerated \$10 for enrollment in the specimen collection protocol and \$35 for enrollment and social interview completion.

Measures/Variables of Interest

The SSN survey data from 2001-2005 were used to address the research question and the sub-questions of this study. The survey design, sampling scheme, and all the survey questions were consistent all along the 5 years.

Network characteristics

Network questions were about all the different people in the lives of the participants that they might know in different ways: friends, family members, sex partners, professionals or any other people. The initial networking measures for the final analyses are: type of each sexual contact in the past 90 days, age groups of the contacts, gender of the contacts, contacts having a 9-5 constant job and distance from their contacts. Age groups of the contacts were grouped into

9 categories: “14 years and below”, “15-19 years”, “20-24 years”, “25-29 years”, “30-34 years”, “35-39 years”, “40-44 years”, “45-54 years” and “55 years and above”. ‘Contacts using drugs’ was computed by merging three primary variables from the survey which are: ‘*Does this person (contact)...inject/snort heroin/smoke crack?*’. The responses were dichotomized into no versus yes. Some categories were merged together for the variable ‘Distance from their contacts’. The categories were: Same household and same block merged with within my neighborhood (within 5 blocks), within 1 mile merged with same area of town, another area of town merged with greater than 5 miles and outside of the city merged with outside of the state.

As for analyses on 2 different types of networking groups: patients with more sexual networks (more individuals named as part of a sexual network) than non-sexual networks (more individuals named as part of non-sexual network) and vice-versa, a new variable ‘Social Networks’ from the primary networking variable, ‘*Subject’s relationship with their contacts*’ was computed. Sexual partners were grouped as sexual contacts (individuals named as part of a sexual network of the index patients) and friends; family and acquaintances were grouped together as non-sexual contacts (individuals named as part of a non-sexual network of the index patients). Patients who were men and having sexual relationships with their male social networks were carefully chosen from the data set and used for the analyses involving MSM.

Sexual characteristics

Sexual characteristics were measured by asking participants about their sexual behaviors in the last 90 days prior to the study. The desired measures for the analyses are: types of sex practices (anal/vaginal/oral), sexual identity, numbers of different sex partners in the past 90 days and having a main sexual partner. ‘Age when having sex for the first time’ was categorized into: “Less than 14 years” and “14 years and above”. These 2 categories were chosen for this study after obtaining the overall mean response for analysis (the mean age in years when having sex the first time for patients who have syphilis is 15.3 and 14.5 for patients who have gonorrhea), and also because of smaller cell counts that would occur if there were more categories. A study investigating the impact of a history of sexual abuse on high risk behaviors among female school attendees had a similar variable, ‘Sexual initiation before age 14’.¹⁰⁸ Numbers of different sexual partners in the past 90 days’ was categorized into: “No more than 1 sexual partner” and “2 or more sexual partners”.

Analyses

SPSS 18.0 was used for the analyses of these data. Frequencies of characteristics of the individuals named as part of a sexual or non-sexual network of patients with syphilis and gonorrhea, the N sizes for syphilis and gonorrhea patients with different types of network and information on MSM patients with syphilis and gonorrhea were summarized and tabulated accordingly. Logistic regression with generalized linear models (GLM) was used to estimate associations between the presence of syphilis vs. gonorrhea and network characteristics of the patients with syphilis or gonorrhea.

Primary independent variables (IVs) were selected based on my research questions and literature^{71,81,85}; potential confounders of the associations between the primary IVs and syphilis vs. gonorrhea were selected through literature and also through prior knowledge on some potential confounders suggesting that they could be predictive of syphilis/gonorrhea (gathered while discussing with primary investigator, Dr. Anne Rompalo at the time I was given the raw data set). The primary IVs and potential confounders chosen for this study are shown in Table 3.1 below.

**Table 3.1: The primary IVs and potential confounders chosen for Study 2
[Dependent variable: Syphilis (vs. gonorrhoea)]**

Research question/sub-questions	Primary IVs	Potential confounders
Main Research Question	<ul style="list-style-type: none"> • Gender of contacts • Contacts using drugs • Distance from each partner • Employment status of the contacts (9-5 jobs) • Type of each sexual contact in the past 90 days • Age of contacts 	<ul style="list-style-type: none"> • Having anal sex in the past 90 days • Having vaginal sex in the past 90 days • Having oral sex in the past 90 days • Number of different sexual partners in the past 90 days • Sexual identity
Sub-question 1	Same as main research question	Same as main research question
Sub-question 2	<ul style="list-style-type: none"> • Having anal sex in the past 90 days • Having vaginal sex in the past 90 days • Having oral sex in the past 90 days • Age having sex the first time • Number of different sexual partners in the past 90 days 	<ul style="list-style-type: none"> • Age of contacts • Contacts using drugs • Type of each sexual contact in the past 90 days
Sub-question 3	<ul style="list-style-type: none"> • Having anal sex in the past 90 days • Having vaginal sex in the past 90 days • Having oral sex in the past 90 days • Age having sex the first time • Sexual identity • Number of different sexual partners in the past 90 days 	<ul style="list-style-type: none"> • Age of contacts • Contacts using drugs • Type of each sexual contact in the past 90 days
Sub-question 4	<ul style="list-style-type: none"> • Having anal sex in the past 90 days • Age having sex the first time • Have a main sexual partner • Number of different sexual partners in the past 90 days 	<ul style="list-style-type: none"> • Contacts using drugs

Variables were then assessed for collinearity. I performed collinearity tests for all the selected IV's before starting the univariate analysis. If the value of correlation was close to +1 or -1, then that indicated that the selected variables were highly correlated, implying the presence of collinearity. I also carried out multicollinearity tests once all the variables were fit into the respective models. If the variance inflation factor (VIF) was between 1- 10, then there was no serious multicollinearity problem. A VIF between 5 and 10 indicates high correlation that may be problematic but the values of VIF obtained from all the variables chosen for this study were below 5. I also executed Fisher's Exact Test to test some primary IVs that I wanted to include in the statistical models as they either had very low cell or zero counts. I encountered this problem for sub-question 2 and sub-question 4. Due to zero cell counts confirmed through Fisher's Exact Test, 'Sexual identity' and 'Type of sexual contact in the past 90 days' that I intended to use in the analyses for both the sub-questions initially, could no longer be used in the models. All analyses were complete case analysis using list wise deletion in SPSS as missing cases for all variables in the multivariable models had less than 15% of missing data.

Logistic regression models with GLM were conducted to assess the associations between index patients and the attributes of their egocentric network members. GLM was used to account for the fact that index patients had multiple network partners that contributed to the analysis. This means that for example, if the participant listed 5 network members, each of these members was treated as an observation within the cluster of five. GLM provides a general, flexible approach in these situations, because it allows a wide variety of correlation patterns (or variance-covariance structures) to be explicitly modeled. GLM models use both fixed and random effects.¹³⁷ GLM can perfectly handle a variety of outcome distributions such as continuous, binary and count outcomes that are present in my data.

My goal was to obtain the least biased and least confounded estimates of association. Hence, I decided to carry out analyses for multiple models to assure I would not miss any possible associations and confounding effects. I had 1 model to obtain crude estimates and 3 other models for my final multivariable generalized linear model analyses. The models are:

1. **Model 1:** Crude (unadjusted)
2. **Model 2:** Each primary IV adjusted for the effects of all other primary IVs
 - This model assumes that all primary IVs are confounders of each other and that there are no other confounders.
 - For each primary IV-outcome association, none of the other primary IVs

are in the causal path between the primary IV and the outcome.

3. **Model 3:** Each primary IV adjusted for the effects of confounders (excluding the other primary IVs)
 - This model assumes that for each primary IV-outcome association, none of the other primary IVs are confounders and all of the covariates in the model meet the definition of confounding which means that they are associated with the primary IV, predictive of the outcome, and not in the causal path between the primary IV and the outcome.
4. **Model 4:** Each primary IV adjusted for the effects of all other primary IVs plus the potential confounders
 - This model assumes that for each primary IV-outcome association, all other primary IVs and “potential confounders” meet the criteria for confounding of that primary IV-outcome association.

Adjusted odds ratios (aORs) with 95% confidence intervals (CIs) were used to estimate associations

RESULTS

A total of 526 patients with syphilis or gonorrhea were analyzed for this study. A total of 2106 social networks of syphilis patients and a total of 1203 social networks of gonorrhea respectively were analyzed for the networking analyses for this study. From the total of 526 patients, 78 index patients reported details on all their contacts (n=172) who were successfully traced back and participated in the study. Network characteristics of the individuals named as part of a sexual or non-sexual network of patients with syphilis and gonorrhea are shown in Table 3.2. Table 3.3 presents the N sizes of syphilis and gonorrhea patients with different types of network while Table 3.4 presents some information on MSM that was obtained in this study.

For patients with syphilis: ‘Age of contacts’, mean (standard deviation [SD]) = 38.6 (19.09), median = 38.00. For patients with gonorrhea: ‘Age of contacts’, mean = 35.6 (19.40), median = 30.00.

(a) Results for main research question

When controlling for having anal sex in the past 90 days, having vaginal sex in the past 90 days, having oral sex in the past 90 days, number of sexual partners in the past 90 days and sexual identity, results from both Model 3 and Model 4 showed that that patients with male networks were less likely to have syphilis (vs. gonorrhea) compared to female networks but

patients with networks aged 15-19 years and networks aged 20-24 years were more likely to have syphilis (vs. gonorrhoea) compared to networks aged 55 years and above. Table 3.5 presents the resulting aORs and 95% CIs showing the associations between characteristics of the individuals named as part of a sexual or non-sexual network and presence of syphilis vs. gonorrhoea.

(b) Results for sub-question 1

For individuals named as part of a sexual network of patients with syphilis and gonorrhoea who were traced back to the study, after controlling for having anal sex in the past 90 days, having vaginal sex in the past 90 days, having oral sex in the past 90 days, number of sexual partners in the past 90 days and sexual identity for each primary IV (Model 3), results showed that patients with male networks were more likely to have syphilis (vs. gonorrhoea) compared to female networks but when controlling for the same set of potential confounders for all the primary IVs (Model 4), results showed that the estimate for patients who had male networks was attenuated toward the null relative to the crude estimate. Also, results from both models (Model 3 and Model 4) showed that those who had regular sexual partners were more likely to have syphilis (vs. gonorrhoea) compared to those who had non-sexual networks, yet the estimates were attenuated toward the null relative to the crude estimates. Table 3.6 shows characteristics of the individuals named as part of a sexual or non-sexual network and presence of syphilis vs. gonorrhoea among individuals named as part of a sexual network of patients with syphilis and gonorrhoea who were traced back to the study.

(c) Results for sub-question 2

For individuals with more sexual networks than non-sexual networks, when controlling for age of contacts, contacts using drugs and type of each sexual contact, results from Model 4 showed that patients who had no more than 1 sexual partner in the past 90 days were less likely to have syphilis (vs. gonorrhoea), yet the estimate was attenuated toward the null relative to the crude estimate. Table 3.7 presents the resulting aORs and 95% CIs showing the associations between sexual characteristics of patient's networks and presence of syphilis vs. gonorrhoea among patients with more sexual networks than non-sexual networks.

(d) Results for sub-question 3

For individuals with more non-sexual networks than sexual networks; when controlling for age of contacts, contacts using drugs and type of each sexual contact for each primary IV (Model 3), results showed that patients who had vaginal sex and oral sex in the past 90 days and who

had 2 or more different sexual partners in the past 90 days were more likely to have syphilis (vs. gonorrhea) compared to those who did not have vaginal and oral sex and no more than 1 sexual partner in the past 90 days. When controlling for the same set of potential confounders for all the primary IVs (Model 4), results were similar as above but this time patients who had anal sex in the past 90 days were more likely to have syphilis (vs. gonorrhea) compared to those who did not. Also, results showed that those who were 14 years and older when having sex the first time were more likely to have syphilis vs. gonorrhea. Table 3.8 presents the resulting aORs and 95% CIs showing the associations between sexual characteristics of patients' networks and presence of syphilis vs. gonorrhea among patients with more non-sexual networks than sexual network.

(e) Results for sub-question 4

For individuals who are MSM, for all the primary IVs (Model 4), results showed similar estimates where those who had no more than 1 sexual partner in the past 90 days were less likely to have syphilis (vs. gonorrhea) compared to those who had 2 or more different sexual partners in the past 90 days, but the estimates were attenuated toward the null relative to the crude estimates in the model where each primary IV (Model 3) was controlled for all the potential confounders. Also results showed that there is little association between having anal sex in the past 90 days with the presence of syphilis (vs. gonorrhea). Table 3.9 presents the resulting aORs and 95% CIs showing the associations between sexual characteristics of patients' networks and presence of syphilis vs. gonorrhea among individuals who are MSM.

Table 3.2: Number (percent) of the individuals named as part of a sexual or non-sexual network of patients with syphilis (N=330) and patients with gonorrhoea (N=196) by disease status and characteristics of networks

Characteristics of networks	Networks of patients with syphilis (Total networks=2106)	Networks of patients with gonorrhoea (Total networks=1203)
	n*(%)	n*(%)
Types of each sexual contact in the past 90 days		
Regular sex partners	275 (13.1)	169 (14.0)
Occasional sex partners	223 (10.6)	183 (15.2)
New sex partners	59 (2.8)	48 (4.0)
Others (non-sexual)	1549 (73.6)	803 (66.7)
Age of Contacts		
≤ 14 years	120 (6.3)	49 (4.4)
15-19 years	139 (7.2)	133 (11.8)
20-24 years	226 (11.8)	232 (20.6)
25-29 years	179 (9.3)	135 (12.0)
30-34 years	167 (8.7)	92 (8.2)
35-39 years	231 (12.0)	88 (7.8)
40-44 years	245 (12.8)	97 (8.6)
45-54 years	305 (15.9)	141 (12.5)
≥ 55 years	309 (16.1)	161 (14.3)
Gender of contacts		
Male	883 (45.2)	433 (37.7)
Female	1072 (54.8)	715 (62.3)
Relationship with contacts		
Family	883 (45.7)	532 (46.3)
Friend	392 (20.3)	186 (16.2)
Sex Partners	553 (28.6)	403 (35.1)
Acquaintances	106 (5.5)	28 (2.9)
Employment status		
Have a 9-5 job	1023 (56.1)	648 (61.5)
Jobless	800 (43.9)	406 (38.5)

Table 3.2 (continued):

Characteristics of networks	Networks of patients with syphilis (Total networks=2106)	Networks of patients with gonorrhea (Total networks=1203)
	n*(%)	n*(%)
Distance from contacts		
Same household	654 (34.7)	288 (26.2)
Same block/within 5 blocks	200 (10.6)	155 (14.1)
Within 1 mile/same area of town	336 (17.8)	234 (21.3)
Another area/greater than 5 miles	455 (24.2)	275 (25.0)
Outside of city/state	170 (9.0)	108 (10.0)
Contacts using drugs^a		
Yes	155 (7.5)	41 (3.4)
No	1924 (92.5)	1162 (96.6)
Education level of contacts		
High school	341 (23.0)	207 (22.4)
Grad school	33 (2.2)	12 (1.3)
High school dip/GED	903 (61.0)	566 (61.2)
Some college/Uni.	205 (13.8)	140 (15.1)

*Percentages are rounded to one decimal place, category-specific estimates may not equal overall total due to differences in missing values.

^aDrugs-snorting heroin/smoking crack/injecting any kinds of drugs

Table 3.3: The N sizes for syphilis and gonorrhea patients with different types of network

Disease	Total N	N size for patients with more sexual^a networks	N size for patients with more non-sexual^b networks	N size for patients with equal sexual and non-networks
Syphilis	330	34	275	21
Gonorrhea	196	38	131	26

^aSexual networks- individuals named as part of a sexual network of index patients

^bNon-sexual networks- individuals named as part of a non-sexual network of index patients (no sexual network between them)

Table 3.4: Number (percent) of ‘men having sex with men’ (MSM) by disease status and sexual characteristics/behaviors

Sexual characteristics/ behaviors	Patients with syphilis Total, N=38 n*(%)	Patients with gonorrhea Total, N=8 n*(%)
Having anal sex in the past 90 days No Yes	15 (40.5) 22 (59.5)	3 (37.5) 5 (62.5)
Having oral sex in the past 90 days No Yes	8 (21.6) 29 (78.4)	0 (0) 8 (100)
Sexual identity Straight Bisexual Gay	7 (19.4) 6 (16.7) 23 (63.9)	4 (50.0) 2 (25.0) 2 (25.0)
Numbers of different sexual partners in the past 3 months None 1 partner 2- 10 partners > 10 partners	2 (5.3) 17 (44.7) 16 (42.1) 3 (7.9)	0 (0) 2 (25.0) 5 (62.5) 1 (12.5)
Age having sex for the first time < 14 years ≥ 14 years	17 (45.9) 20 (54.1)	1 (12.5) 7 (87.5)
Total sexual networks 1 person 2-3 persons 4-6 persons	13 (34.2) 22 (57.9) 3 (7.9)	3 (37.5) 4 (50.0) 1 (12.5)
Have ever been sexually forced in lifetime No Yes	28 (73.7) 10 (26.3)	7 (87.5) 1 (12.5)

*Percentages are rounded to one decimal place, category-specific estimates may not equal overall total due to differences in missing values.

Table 3.5: Estimated associations (crude and adjusted odds ratios [aORs] and 95% confidence intervals [CIs]) of some characteristics of the individuals named as part of a sexual or non-sexual network of patients with syphilis and gonorrhea (primary independent variables [IVs]) with having syphilis (vs. gonorrhea): Results from simple and multivariable generalized linear model (GLM) analyses

Measures (Primary IVs)	Syphilis (vs. Gonorrhea)			
	Crude OR (95% CI) {Model 1}	aOR (95% CI) {Model 2}	aOR (95% CI) {Model 3}	aOR (95% CI) {Model 4}
Gender of contacts				
Male	0.74 (0.63-0.85)	0.79 (0.67-0.93)	0.76 (0.64-0.90)	0.80 (0.67-0.97)
Female	Ref	Ref	Ref	Ref
Age of contacts				
≤ 14 years	0.74 (0.53-1.15)	1.21 (0.78-1.89)	0.78 (0.51-1.18)	1.16 (0.72-1.88)
15-19 years	1.84 (1.35-2.49)	1.69 (1.18-2.40)	1.72 (1.23-2.43)	1.73 (1.16-2.57)
20-24 years	1.97 (1.51-2.57)	1.92 (1.42-2.61)	1.86 (1.38-2.50)	1.98 (1.40-2.78)
25-29 years	1.45 (1.08-1.94)	1.44 (1.03-2.01)	1.33 (0.98-1.85)	1.38 (0.95-2.00)
30-34 years	1.06 (0.77-1.45)	1.01 (0.71-1.45)	0.96 (0.67-1.37)	0.94 (0.64-1.40)
35-39 years	0.73 (0.54-1.00)	0.80 (0.57-1.14)	0.71 (0.50-1.00)	0.80 (0.54-1.18)
40-44 years	0.76 (0.56-1.03)	0.83 (0.60-1.16)	0.88 (0.63-1.23)	0.95 (0.66-1.37)
45-54 years	0.89 (0.67-1.17)	0.95 (0.70-1.29)	0.96 (0.70-1.30)	1.05 (0.75-1.47)
≥ 55 years	Ref	Ref	Ref	Ref

Model 1: Unadjusted

Model 2: Adjusted for the effects of all other primary IVs

Model 3: Adjusted for potential confounders[#] (excluding the other primary IVs)

Model 4: Adjusted for the effects of all other primary IVs plus all the potential confounders[#]

^aHaving sex anally, vaginally or orally with main partner or others

[#]Potential confounders for all the primary IVs are: Having anal sex^a in the past 90 days, Having vaginal sex^a in the past 90 days, Having oral sex^a in the past 90 days, Numbers of different sexual partners in the past 90 days and Sexual identity

Table 3.6: Estimated associations (crude and adjusted odds ratios [aORs] and 95% Confidence Intervals (CIs) of some characteristics of the individuals named as part of a sexual or non-sexual network (primary independent variables [IVs]) with having syphilis (vs. gonorrhea) among individuals named as part of a sexual network of index patients with syphilis and gonorrhea who were traced back to the study: Results from simple and multivariable generalized linear model (GLM) analyses

Measures (Primary IVs)	Syphilis (vs. Gonorrhea)			
	Crude OR (95% CI) {Model 1}	aOR (95% CI) {Model 2}	aOR (95% CI) {Model 3}	aOR (95% CI) {Model 4}
Gender of contacts				
Male	1.30 (0.96-1.75)	1.27 (0.91-1.78)	1.46 (1.06-2.00)	1.38 (0.97-1.97)
Female	Ref	Ref	Ref	Ref
Type of each sexual contact in the past 90 days				
Regular sex partners	1.75 (1.16-2.60)	1.60 (1.01-2.52)	1.61 (1.06-2.44)	1.44 (0.89-2.33)
Occasional sex partners	2.07 (1.25-3.43)	1.66 (0.87-3.18)	1.86 (1.09-3.18)	1.36 (0.68-2.73)
New sex partners	0.75 (0.28-2.18)	0.31 (0.04-2.48)	0.45 (0.15-1.37)	0.17 (0.02-1.41)
Non-sexual partners	Ref	Ref	Ref	Ref

Model 1: Unadjusted

Model 2: Adjusted for the effects of all other primary IVs

Model 3: Adjusted for potential confounders[#] (excluding the other primary IVs)

Model 4: Adjusted for the effects of all other primary IVs plus all the potential confounders[#]

^aHaving sex anally, vaginally or orally with main partner or others

[#]Potential confounders for all the primary IVs are: Having anal sex^a in the past 90 days, Having vaginal sex^a in the past 90 days, Having oral sex^a in the past 90 days, Numbers of different sexual partners in the past 90 days and Sexual identity

Table 3.7: Estimated associations (crude and adjusted odds ratios [aORs] and 95% Confidence Intervals (CIs) of some sexual characteristics (primary independent variables [IVs]) with having syphilis (vs. gonorrhoea) among individuals with more sexual networks than non-sexual networks: Results from simple and multivariable generalized linear model (GLM) analyses

Measures (Primary IVs)	Syphilis (vs. Gonorrhoea)			
	Crude OR (95% CI) {Model 1}	aOR (95% CI) {Model 2}	aOR (95% CI) {Model 3}	aOR (95% CI) {Model 4}
Having vaginal sex in the past 90 days^a				
No	0.12 (0.05-0.31)	0.09 (0.03-0.28)	0.10 (0.03-0.30)	0.08 (0.02-0.30)
Yes	Ref	Ref	Ref	Ref
Number of different sexual partners in the past 90 days				
≤1 partner	0.58 (0.19-1.76)	0.67 (0.18-2.50)	0.32 (0.10-1.04)	0.37 (0.09-1.61)
≥2 partners	Ref	Ref	Ref	Ref

Model 1: Unadjusted

Model 2: Adjusted for the effects of all other primary IVs

Model 3: Adjusted for potential confounders[#] (excluding the other primary IVs)

Model 4: Adjusted for the effects of all other primary IVs plus all the potential confounders[#]

^aHaving sex anally, vaginally or orally with main partner or others

[#]Potential confounders for all the primary IVs are: Age of contacts, Contacts using drugs and Type of each sexual contact in the past 90 days

Table 3.8: Estimated associations (crude and adjusted odds ratios [aORs] and 95% Confidence Intervals (CIs) of some sexual characteristics (primary independent variables [IVs]) with having syphilis (vs. gonorrhoea) among individuals with more non-sexual networks than sexual networks: Results from simple and multivariable generalized linear model (GLM) analyses

Measures (Primary IVs)	Syphilis (vs. Gonorrhoea)			
	Crude OR (95% CI) {Model 1}	aOR (95% CI) {Model 2}	aOR (95% CI) {Model 3}	aOR (95% CI) {Model 4}
Having anal sex in the past 90 days^a No Yes	Ref 1.05 (0.83-1.34)	Ref 1.63 (1.22-2.20)	Ref 0.99 (0.77-1.27)	Ref 1.58 (1.16-2.14)
Having vaginal sex in the past 90 days^a No Yes	Ref 4.04 (2.78-5.88)	Ref 2.20 (1.43-3.38)	Ref 4.07 (2.78-5.96)	Ref 2.14 (1.38-3.31)
Having oral sex in the past 90 days^a No Yes	Ref 1.97 (1.64-2.37)	Ref 1.99 (1.62-2.45)	Ref 1.91 (1.58-2.31)	Ref 2.08 (1.68-2.58)
Age having sex the first time < 14 years ≥ 14 years	Ref 1.46 (1.21-1.75)	Ref 1.79 (1.45-2.21)	Ref 1.66 (1.37-2.01)	Ref 2.06 (1.65-2.56)

Table 3.8 (continued):

Measures (Primary IVs)	Syphilis (vs. Gonorrhoea)			
	Crude OR (95% CI) {Model 1}	aOR (95% CI) {Model 2}	aOR (95% CI) {Model 3}	aOR (95% CI) {Model 4}
Number of different sexual partners in the past 90 days ≤1 partner ≥2 partners	Ref 1.94 (1.63-2.30)	Ref 1.61 (1.32-1.96)	Ref 1.87 (1.56-2.24)	Ref 1.56 (1.26-1.93)

Model 1: Unadjusted

Model 2: Adjusted for the effects of all other primary IVs

Model 3: Adjusted for potential confounders[#] (excluding the other primary IVs)

Model 4: Adjusted for the effects of all other primary IVs plus all the potential confounders[#]

^aHaving sex anally, vaginally or orally with main partner or others

[#]Potential confounders for all the primary IVs are: Age of contacts, Contacts using drugs and Type of each sexual contact in the past 90 days

Table 3.9: Estimated associations (crude and adjusted odds ratios [aORs] and 95% Confidence Intervals (CIs) of some sexual characteristics (primary independent variables [IVs]) with having syphilis (vs. gonorrhoea) among individuals who are men having sex with men (MSM): Results from simple and multivariable generalized linear model (GLM) analyses

Measures (Primary IVs)	Syphilis (vs. Gonorrhoea)			
	Crude OR (95% CI) {Model 1}	aOR (95% CI) {Model 2}	aOR (95% CI) {Model 3}	aOR (95% CI) {Model 4}
Having anal sex in the past 90 days^a No Yes	1.07 (0.32-3.53) Ref	1.34 (0.33-5.45) Ref	0.99 (0.30-3.32) Ref	1.01 (0.24-4.37) Ref
Number of different sexual partners in the past 90 days ≤1 partner ≥2 partners	0.26 (0.06-1.27) Ref	0.13 (0.02-0.76) Ref	0.24 (0.05-1.17) Ref	0.10 (0.02-0.60) Ref

Model 1: Unadjusted

Model 2: Adjusted for the effects of all other primary IVs

Model 3: Adjusted for potential confounders[#] (Excluding the other primary IVs)

Model 4: Adjusted for the effects of all other primary IVs plus all the potential confounders[#]

^aHaving sex anally with main partner or others

[#]Potential confounders for all the primary IVs are: Contacts using drugs

DISCUSSION

Network epidemiologic analysis is an approach to research that is distinctively suited to describing, exploring, and understanding structural and relational aspects of health. It is both a methodological device and a hypothetical worldview that permits us to stance and answer imperative environmental inquiries in general wellbeing. Network epidemiology offers a comprehensive way of thinking about individual sexual behavior and its consequences for STDs, as behaviors that transmit STDs directly involve at least two people and the links either of these persons might have to others.

This study found that patients with networks who were females and aged between 15 to 19 years and 20-24 years were more likely to have syphilis (versus gonorrhea). Even though the rate of P&S syphilis has increased each year since 2001, mostly in men, the rate has also increased in women from 2004-2005, with an increase of 12.5 percent from 2004 to 2005 (from 0.8 per 100,000 population to 0.9)¹³⁸ and consistent with results obtained from this study that was conducted in the same timeline. This increase was driven by increased rates among black women which is relevant to this study population which is made of a majority of African-Americans.¹³⁸ In 2006, the rate of P&S syphilis among African Americans was highest among women aged between 20 to 24 years¹³⁸ and this is similar to the findings from this study. Individuals who were part of a sexual network of the index patients with syphilis and gonorrhea who were traced back to this study with networks who were males were more likely to have syphilis (versus gonorrhea), and this was relevant to the rate of P&S syphilis that increased 11.8% among men between 2005-2006.¹³⁸ This study also found that those who had regular sexual partners were more likely to have syphilis (vs. gonorrhea) but even with the uncertainty in the exact magnitude of effect as reflected in the wide CI, it was similar to a study that investigated predictors of risky sexual behaviors among women bar drinkers that found rates of risky sexual behavior were higher with regular sexual partners and had lower STD prevention assertiveness.¹³⁹

Most sexual partnerships are relatively assortative with respect to demographic characteristics, in the sense that partners tend to have similar ages, race/ethnicity, educational backgrounds, and religious affiliations.¹⁴⁰ This is merely because sex partners are usually drawn from among the people with whom one comes into contact in social situations. Thus, people's sex partners generally resemble the social composition of their immediate social networks. This study found that among patients who had more sexual networks than non-sexual networks, those who did not have vaginal sex in the past 90 days were less likely to have syphilis (versus gonorrhea). Also, those who had zero or 1 sexual partner in the past 90 days were less likely to have syphilis (versus gonorrhea) but there is uncertainty in the exact magnitude of effect as reflected in the wide CI. These findings explain how their sexual partners play roles in their preferred sexual practices and the effect of having sex at such

young ages. Evidence suggests that patterns of sexual networks may differ between black versus white populations.⁸⁷ One difference is that, among black persons, more frequent sexual contact occurs between those with many partners. Another is that, because black persons are more likely to choose other black persons as sex partners, the sexual networks of black persons are more racially segregated than those of other racial or ethnic groups.⁸⁷ A study among black MSM found similar findings with this study where those who were less than 12 years when they had sex the first time and had more than 3 different sexual partners were more likely to have HIV compared to those who do not have HIV.¹⁴¹

In comparison to patients who had more non-sexual networks than sexual networks, this study found that those who had anal, vaginal and oral sex in the past 90 days and had 2 or more different sexual partners in the past 90 days were more likely to have syphilis (versus gonorrhea). These findings were similar to a study that found among adults with HIV, those who reported any oral, vaginal or anal sex in the past 12 months were more likely to be tested positive for syphilis compared to those who did have any sexual activity¹⁴², and another study that found those who had 3 or more different sexual partners in the past 6 months were more likely to have syphilis compared to gonorrhea.¹⁴³ Another finding was that those who were 14 years and more when they had sex the first time were more likely to have syphilis (versus gonorrhea) compared to those who were under 14 years old. Chapter 2 had a contradictory finding where those who were under 14 years when they had sex the first time were more likely to have syphilis (versus gonorrhea). The differences in both the findings could be possibly due to the sexual network analysis in this study, as the results for Chapter 2 were accessed only by using the data obtained from the lifestyle questionnaire without the data on their network characteristics obtained from the networking questionnaire for the SSN project (using only multivariable logistic regression analyses) whereas for this study, results were accessed by using data on the network characteristics that was merged with data from the lifestyle questionnaire (using multivariable GLM regression analyses). Non-sexual network relationships (peers/close friends, relatives and acquaintances) often bring people to social situations; people may choose to participate in the events like hanging out or attending parties because of the people they know.¹⁴⁰ For example, as they hang out with their peers, they tend to be vulnerable and be influenced by the sexual lifestyles of their peers, hence leading them to have random sexual partners who were referred to them by their peers. This may explain the findings among patients who have more non-sexual contacts than sexual contacts from this study.

This study found that among patients who were MSM, those who had zero or 1 different sexual partner in the past 90 days were less likely to have syphilis (vs. gonorrhea), compared to

having 2 or more different sexual partner in the past 90 days. A report on the national plan to eliminate syphilis from the US by the CDC stated that high rates of new sex partner acquisition and partner change rates with high rises in unprotected penetrative sex leading to the infections of syphilis/HIV, have been documented across the US.¹⁴⁴

Limitations

This study had some limitations. Firstly, this study is based on secondary analysis from a cross-sectional study. The study has already been designed and carried out. Data collections are completed as well. This is a common limitation in any secondary analysis. At times, data may not be able to facilitate a particular research question. There was an interest to find out if the meeting venues between the index patients and their sexual networks are geographically different than their residences, as mutual meeting venues especially those associated with high-risk activities could enhance traditional case-finding techniques by identifying previously unknown cases³⁴, yet this could not be achieved in this study as this study has already been carried out and completed. The SSN study was a cross-sectional study hence, causal associations between the dependent and independent variables should not be inferred.

Although the overall sample sizes for the networks were fairly large, some of the groups and specific findings included small numbers of respondents. Sample sizes from sub-groups, groups with more sexual networks than non-sexual networks and MSM were rather small, resulting in less power for detecting associations and lower precision of the estimates. Low power studies are more likely to provide a wide range of estimates of the magnitude of an effect which is known as ‘vibration of effects’ (situation in which a study obtains different estimates of the magnitude depending on the analytical options it implements).¹⁴⁵ Small studies like this could still be valuable as the results obtained could be used to design larger confirmatory studies.¹⁴⁶

The participation rate for this study is not too high and could account for a type of selection bias; volunteer bias. Volunteer bias usually occurs when those who volunteer to participate in a study differ systematically with regard to either exposure or disease status from those who did not volunteer. A lower participation rate might result in bias due to differences in the exposure effect between participants and non-participants. The aORs in my study might not be that affected by the low participation rates. Participation rate alone does not determine the extent of bias present in any study and low participation rates do not always indicate a high level of bias essential in a study.^{121,122} What matters most are the differences in factors that affect exposure effect. Most studies have found little evidence for substantial bias as a result of non-

participation that decreases the participation rates.¹²³ However, participation should still be enhanced as much by probably targeting a larger population with more variations in the race, increasing monetary incentives and using web-based modes of data collection allowing respondents to complete surveys at a time and place convenient for them.

The major limitation of any network study would be the incompleteness of the data. It is not possible to know characteristics of unreported sexual partners and not all reported sexual partners could be located for the study. Un-interviewed sexual partners can affect the application of findings beyond this study population because they might pose risk of syphilis or gonorrhea to their respective index patients, which could explain the results that were biased toward the null for sample that consist of only 172 sexual partners of the index patients who were traced back to this study. Given the cross-sectional study design, whether participants' networks were altered as a result of disclosure or to prevent disclosure is not known. Disclosure could have strengthened some relationships or weakened some others.

Another disadvantage on social networking would be that, it is not always possible for an individual no matter how cooperative she or he may be, to give enough information about any given sexual partner.⁹⁰ This study used self-reported data as not all the networks of the patients who participated were interviewed and the analyses completely relied on the patients' knowledge of all their networks, and there is the possibility of differential reporting of certain characteristics of the networks (e.g., distance from their networks, if their contacts did drugs or the education level of their contacts). It is plausible in this study for example, if their respective contacts did drugs or not, to be underestimated by the patients who took part in this study due to social desirability. This could have caused possible non-differential misclassification given that everyone in this study had an STD. Hence, the aORs from this study involving these variables could be slightly biased towards the null.

Self-reported bias has been criticized when it involves sexual networking studies as sexuality is a sensitive topic. Thus, individuals may adapt responses rendering to social desirability which could be explained easily by ('I will tell you what you want to hear'). For example, researchers have questioned the inconsistency of self-reported age when having sex the first time.¹⁴⁷ Men may over-report as having sex represents a prestige among peers but women may under-report as it is considered disgraceful for them to be sexually active in societies where virginity is still rewarded. Another variable which could face the same social desirability bias would be number of sexual partners in the past 90 days, and the type of sexual partners in the past 90 days. Thus, the aORs from this study involving these variables could

have been slightly affected which could lead to bias towards the null. Applying standardized and validated methods and using objective measures can help reduce information inaccuracies.

Confounding is another type of bias that could occur in this study. This study focuses on sexual behaviors and also network characteristics of all the participants and their associations to the presence of syphilis vs. gonorrhea among persons with either syphilis or gonorrhea. There were few questions from the network questionnaire that could not be used in the analyses due to missing data and scarcity in the frequencies. Sufficient data for questions like: 'Where did you meet your sexual partner?', 'How often did you have sex with each of your sexual partner?', 'How often you use a condom with each of your sex partner?' and 'How often you talk or see each sexual network listed?' would have been truly valuable for this study because they could be either primary IVs or potential confounders in this study.

There were 3 multivariable models for the analyses in this study because of not being sure about a single models specification that would give the least confounded estimates. The possible differences in point estimates between models were probably due to random variability that is shown in the width of most CIs because of low sample sizes and low cell counts for certain categories or possibly due to the differences in the covariates across the models. Model misspecification could have occurred possibly due to covariates that aren't confounders and also because of the differences in assumptions about associations between the covariates and associations of covariates with syphilis vs. gonorrhea. For this study, Model 4 would be the best model to deliver results closest to the truth in comparison to Model 3. This would be because some of the primary IVs were also potential confounders and Model 4 controls for all the chosen primary IVs along with the chosen potential confounders that were selected for this study based on relevant studies^{71,81,85} and prior knowledge. Yet, the estimates from Model 4 would still be a little biased due to residual confounding because I was not able to control for some variables that might be predictive of syphilis/gonorrhea as I did not have the data, and over-adjustment as not all the primary IVs were potential confounders, only some of them were, thus precision is generally reduced. An example for possible over-adjustment would be that, 'Contacts using drugs', 'Gender of contacts' and 'Age of contacts' (other primary IVs) could predict the type of each sexual contact in the past 90 days (main primary IV) as well as the presence of syphilis vs. gonorrhea. But, the other primary IVs (distance from each contact and employment status of the contacts) do not associate with type of each sexual contact. Nevertheless, even though some potential confounders could not be accessed due to absence of data on them, I made full effort to identify all the potential confounders which had sufficient data in this study based on literature or prior knowledge and had them controlled for in all analyses.

Another conceivable limitation of this study is that the sampled population limits the generalizability. The target population in this study is people with syphilis or gonorrhea and the associations between the IVs and syphilis vs. gonorrhea in this target population are likely very different from the associations between IVs and syphilis that would be observed in populations that include people without gonorrhea and vice versa for the associations between the IVs and gonorrhea. Thus, the results would not be generalizable to lower risk populations, people in established couple relationships or general population samples not seeking STD care. Moreover, as the analyses were based on single snapshots and is therefore incapable to account for the changing and sustaining dynamics of all the networks over time. Nonetheless, results from this study are consistent with other studies which are more population based.

Strengths

One strength of this study would be that the STDs among all participants of this study (index patients and their sexual networks who were traced back to the study) were diagnosed clinically as opposed to be depending on self-report that may underestimate STDs because of social desirability bias (tendency of survey respondents to answer in a manner that will be viewed favorably by others: e.g., over-reporting a good behavior or under-reporting a bad behavior) in reporting and undiagnosed infections.¹²⁷ Another strength would be that all the sexual partners who were traced back to the study were interviewed personally by the DIS and not by gathering information based on the index patients' knowledge of their partners. Even though approximately 13% were traced back and interviewed personally, information on their respective networks could be obtained in this study. This study investigates multiple characteristics of individuals named as part of a sexual or non-sexual network and this is quite unique as most sexual networking studies focus on how the networks are connected to the index cases but not on specific characteristics of the networks that could contribute to risky sexual behaviors which might lead to high prevalence of STDs. Another strength to look at would be that this study focused on patients with syphilis or gonorrhea and their recent sexual and non-sexual networks, thus enabling focus on those acquiring and transmitting STD. The thorough approach in all the analyses that were carried out in this study would add in to the strengths of this study. Even though this study is a small study, it could be still valuable because it was carefully designed by the primary investigator, Dr. Anne Rompalo after the outbreak of syphilis from 1993-1995.⁷⁴ She made sure the Baltimore STD clinics' computerized patient tracking system was enhanced in order to identify as many networks of the index patients as possible to examine the role of social networks (sexual and non-sexual) on syphilis or gonorrhea

transmission in Baltimore, thus being one strength of this study. Lastly, I performed my analyses with 3 multivariable models with different assumptions so that I could attain the least confounded estimates to address the research and sub-questions of this study.

Conclusions and Public Health Implications

In conclusion, this study was a distinctive one as it provided important information on characteristics of the individuals named as part of a sexual or non-sexual network among patients diagnosed with either syphilis or gonorrhea. The relative importance of the characteristics of networks of the index patients and individual sexual activities (e.g., types of sexual practices, age having sex the first time, number of sexual partners and sexual identity) in STD diagnosis has always been unclear as most studies either focus on how each person is connected in the sexual network (e.g., the relationships with all their sexual partners/types of all their sexual partners) and how this is associated to the transmission of STDs or, on the geographic distribution of the index patients and their sexual networks but this study has revealed some important associations between all network characteristics and sexual behaviors/characteristics with the presence of syphilis (versus gonorrhea) among people with syphilis or gonorrhea.

Although, some of my findings for this study had uncertainty in the exact magnitude of the effect due to a complex data set with small sample size/low cell counts for some independent variables, these findings are still valuable for some public health interventions, as this study is distinctive and investigates the differences between patients with syphilis and patients with gonorrhea, and also on their network characteristics. In general, my findings are consistent with those which are more population based even though they could not be directly compared to these studies due to the unique sample for this study. 'Non-significant' results do not mean 'no-effect' and if my study could be replicated in larger populations and in studies with less potential selection bias and confounding in the near future, besides getting estimates with narrower width in the confidence intervals, we could also determine if the estimates from these new studies are consistent with the estimates obtained from this study. Implications discussed below could be the baseline for future implications specifically for patients diagnosed with STDs or HIV in the US, as these patients are the beginning of the transmissions of STDs/HIV through their sexual networks.

From 2000-2014, the rise in the P&S syphilis rate was primarily associated to increased cases among men, especially among MSM.¹⁴⁸ However, during 2013-2014, the rate increased both among men (14.4%) and among women (22.7%) and the increase among women is of

specific concern because congenital syphilis cases tend to parallel increased rate of P&S syphilis among women.¹⁴⁸ Even though syphilis is easily curable in its primary or secondary stages, if untreated, it can lead to serious complications in health even death and congenital syphilis could cause still birth, death soon after birth or physical deformity and neurological complications in children who survive. Besides all these, reported cases of P&S syphilis continue to be characterized by a high rate of HIV co-infection especially among MSM.¹⁴⁸

Findings from this study suggest that among patients who had more sexual networks; who had vaginal sex in the past 90 days and had 2 or more different sexual partners in the past 90 days and among patients who had more non-sexual networks; who had anal, vaginal and oral sex in the past 90 days and also had 2 or more different sexual partners in the past 90 days, had higher odds of syphilis compared with gonorrhea. This is consistent with the rise in P&S syphilis by sex and sex behavior where the rates increased among both men and women.¹⁴⁸ Few studies have examined how many patients with syphilis recognized their symptoms or, if they do, how many present for medical attention, and one study has reported that about 45% of partners of identified syphilis patients stated that they had not sought medical care despite identifying symptoms of syphilis.⁶⁸ Hence, it is important for state and local health departments to monitor and work towards increasing the proportion of those found to have an STD and STD clinic attenders who receive a screening test for syphilis according to recognized standards.¹⁴⁴ Clinicians and health practitioners could play vital roles in identifying the reasons why some patients come in during the later stages of syphilis rather than coming in earlier even after noticing some obvious symptoms. They could prepare follow up questions for these patients on why they are hesitant to come in earlier for diagnosis and earlier treatment, and also if have they referred their sexual partners to STD clinics for screening and diagnosis. This could help to assist patients like this and their networks to get early treatment on syphilis and also screening to screen for HIV and help curb the spread of the infections through the sexual networking pathway.

Lastly, findings from this study suggest that patients who are MSM, who had 2 or more different sexual partners in the past 90 days and had anal sex in the past 90 days, had higher odds of syphilis (compared with gonorrhea). Some individual risk behaviors such as high numbers of lifetime sexual partners as well as cultural factors such as difficulty accessing quality health care contribute to inequalities in the sexual health of gay and bisexual men. Complex issues like homophobia and stigma could make it difficult for this sexual minority group to find culturally-sensitive and appropriate care and treatment.¹⁴⁹ Hence, state and local health departments should enhance access to syphilis screening probably by extending operating times

and establishing MSM clinical sessions as well as augmenting syphilis education and sexual health promotion with MSM within STD clinics.

CHAPTER 4.

STUDY 3: COMORBIDITY OF DEPRESSION AND DRUG ABUSE WITH THE PRESENCE OF SYPHILIS VS. GONORRHEA. THE SOCIAL AND SEXUAL NETWORK (SSN) STUDY, BALTIMORE

ABSTRACT

Background: Depression, drug use and sexual abuse play important roles in the epidemiology of sexually transmitted diseases (STDs) like syphilis and gonorrhea. The aims of this study were to (1) estimate the comorbidity of depression and drug abuse with the presence of syphilis vs. gonorrhea among people with syphilis or gonorrhea, (2) describe differences in the associations of drug abuse with syphilis vs. gonorrhea between people with different types of networks (more sexual networks than non-sexual networks and vice versa) and, (3) estimate associations between depression and sexual abuse among people with syphilis or gonorrhea.

Methods: The Social and Sexual Network (SSN) data from 526 respondents who were patients with syphilis or gonorrhea (index cases) and networking data from a total of 3309 social contacts were used to address the research questions of this study. Parameter estimates (adjusted odds ratios [aORs]), 95% confidence intervals (CIs), and p-values were generated using SPSS 18.0. aORs were used to estimate associations adjusted for the effects of confounders and two types of multivariable analyses were performed: multivariable logistic regression and multivariable generalized linear model (GLM) while controlling for selected confounders.

Results: Patients with syphilis have lower odds of depression (aOR=0.85, 95% CI: 0.57, 1.25) and drug abuse (aOR=0.60, 95% CI: 0.47, 0.75) compared to patients with gonorrhea. Among patients with more sexual networks than non-sexual networks, results indicated that those who had used marijuana in past month to 1 year ago (aOR=3.56, 95% CI: 1.19, 10.67) were more likely to have syphilis (vs. gonorrhea) but those who had used cocaine more than a year ago (aOR=0.18, 95% CI: 0.05, 0.73) were less likely to have syphilis (vs. gonorrhea) compared to those who never used them before. Among patients with more non-sexual networks than sexual networks, those who had used marijuana in past month to 1 year ago (aOR=1.87, 95% CI: 1.42, 2.45) and used cocaine more than a year ago (aOR=1.62, 95% CI: 1.08, 2.43) were more likely to have syphilis (vs. gonorrhea) but those who used crack more than a year ago (aOR=0.56, 95% CI: 0.37, 0.84) were less likely to have syphilis (vs. gonorrhea); compared to those who never used them before. Lastly, patients with syphilis or gonorrhea who were not forced to have sex in their lifetime (aOR=0.28, 95% CI: 0.10, 0.79) and those who were never forced for sex by anyone in their lifetime (aOR=0.28, 95% CI: 0.11, 0.79) were less likely to have depression

compared to those who were forced and those who had 2 or more people who forced sex in their lifetime.

Public Health Implications: Health departments should improve programs that could help patients with STDs to overcome mental illness and work with drug treatment centers to improve treatment and rehabilitation programs for STD patients who are also addicted to drugs.

Keywords: Syphilis, Gonorrhea, Depression, Drug abuse, Sexual abuse, Types of networks

BACKGROUND

Depression and substance abuse are common among people with sexually transmitted infections (STIs).¹⁵⁰ Investigating the associations between depression and substance abuse with STIs, especially in populations with sexual and social networks could have important public health implications.

Depression is often co-morbid with some sexually transmitted diseases (STDs) as depressed people are more vulnerable to sickness. A study examining the relationship between psychiatric disorders and sexual behaviors among adolescents receiving mental health treatment found that adolescents meeting criteria for major depressive, generalized anxiety and post-traumatic stress disorders were more likely to report a lifetime history of vaginal and anal sex.¹⁵¹ Another similar study in a African-American cohort of female adolescents that investigated the associations between depressive symptoms and sexual risk behavior found that high levels of depressive symptoms were independently associated with increased numbers of lifetime sexual partners.⁴⁷

A retrospective chart review on relationships among depressive symptoms and STIs among African-American adolescent girls found that those with a history of depressive symptoms were more likely to have a history of STI.⁴⁶ A 3-year prospective study among male to female transgender persons found that gender abuse along with depressive symptoms predicted high-risk sexual behavior (unprotected receptive anal intercourse) and the incidence of human immunodeficiency virus (HIV) infection and STI.⁴⁹

Mental problems like depression could play an important role in either promoting or preventing partner notification. Some studies show that mental health factors contribute to the transmission of STIs. Individuals who have greater psychological distress are more likely to engage in behaviors that can get them infected with certain STIs. A study examining the association between psychosocial and cognitive factors, and patient referral found that a lower level of depression was associated with higher degrees of self-efficacy (the confidence about convincing each partner to get an STI check-up).¹⁵²

Studies that examine the associations between risky sexual behavior and substance abuse show higher rates of unprotected sex, sex with multiple partner and STI diagnoses among STD clinic patients who report high levels of substance abuse.⁶⁴ A study that reviewed 16 epidemiological studies that examined drug use, sexual behavior and STDs found 8 studies that outlined the association between crack and STD and 7 studies that found STD to be related with other drugs or cocaine use.¹⁵³ Another study on crack/cocaine addiction and HIV high risk

behavior found that crack users reported more sexual partners, more STDs in their lifetime, exchanging sex for drugs and having sex with injection drug users and greater current depression, anxiety and social isolation were associated with earlier initiation into alcohol use.⁶¹

Studies have found a relationship between substance abuse and greater number of partners and greater number of casual partners. Substance abuse may have either direct or indirect influence on notification rates depending on the number and type of partner. A study seeking to describe rates of partner notification found that participants with one time partners were more likely to use marijuana compared to those with regular partners and participants with casual partners were more likely to use alcohol compared to those with regular partners.¹⁵²

Little attention has been given to the impact of factors related to mental illness such as trauma on STDs and HIV risk behaviors. A community-based study in South Africa reported depression was strongly associated with experiences of forced sex and transactional sex.¹⁵⁴ Another study discovered that having a history of sexual abuse substantially increased sexual risk behaviors among female adolescents attending alternative schools.¹⁰⁸ A study examining relationships between timing of gay-related developmental milestones, early abuse, and emergence of poor health outcomes in adulthood among gay/bisexual men in the 'Urban Men's Health Study', found that participants who developed early were more likely, compared to others, to experience forced sex and gay-related harassment before adulthood and also were more likely to be HIV seropositive and experience gay-related victimization, partner abuse and depression during adulthood.¹⁵⁵

Childhood sexual abuse (CSA) has been correlated with sexual victimization including intimate partner violence (IPV).¹⁵⁶ A study reported gay and bisexual men had higher odds of reporting CSA compared with heterosexual men and for sexual minority men, CSA histories were associated with higher HIV and STD incidences.¹⁵⁷ In a study investigating the relation of CSA, IPV and depression to risk factors for HIV among black men who have sex with men (MSM), nearly a third of the participants who experienced any unwanted sexual activity or sex with someone at least 5 years older, between the ages 12 and 16 years, also experienced emotional abuse.¹⁴¹

Depression, drug abuse and sexual abuse play important roles in the epidemiology of STDs like syphilis and gonorrhea. It is important to study possible predictors for STDs among patients with social networks (sexual and non-sexual networks) from various age groups and ethnicities for future interventions for the control of STDs like syphilis and gonorrhea.

This study is designed to address the research question: Are depression and drug abuse co-morbid with the presence of syphilis vs. gonorrhea among people with syphilis or gonorrhea?

Sub-question 1: Are there differences in the associations of drug abuse with syphilis vs. gonorrhea between people with different types of networks (more sexual networks* vs. more non-sexual networks#)?

**Sexual networks- individuals named as part of a sexual network of the patients (sexual intercourse present between participants and their sexual networks)*

#Non-sexual networks- individuals named as part of a non-sexual network of the patients (no sexual intercourse between participants and their non-sexual networks)

Sub-question 2: Is sexual abuse associated with depression among people with syphilis and gonorrhea?

METHODS

Data Sources

The Baltimore syphilis epidemic facilitated this study. In 1997, over 25,000 clients attended the Baltimore Health City Department (BCHD) STD clinics for evaluation and treatment of STDs.^{70,71} During this year, the BCHD STD Program reported 941 early latent syphilis cases; 441 secondary syphilis cases; and 226 primary syphilis cases. This represented a case rate of primary and secondary (P&S) syphilis of 98/100,000 population.^{70,71} During 1998, BCHD clinical services improved and over 28,000 clients were seen. In Baltimore, 303 cases of secondary syphilis and 155 cases of primary syphilis were diagnosed. As expected, case rates for 1998 declined slightly with improved services, but remained high at 70/100,000.⁷¹ This study is a secondary data analysis of the Social and Sexual Network (SSN) study data. It focuses on the demographic measures, sexual behaviors and networking measures; and their impact on the two main STDs: syphilis and gonorrhea. The SSN survey data are cross-sectional, as the information collected is from a single point in time.

Study sites

Patients were recruited from BCHD's two STD clinics: Eastern STD clinic and Druid STD clinic. Interviews were conducted at the Social Network Research Clinic (The Lighthouse), which is a row house located 5 blocks from the BCHD Eastern STD clinic, and 2 miles from the BCHD Druid STD Clinic. The off-site social network interviews were found to have provided a more controlled and confidential setting with more flexible hours than do STD clinic-based

interviews. Interviews were conducted in private rooms by trained interviewers who have completed the interviewer-training course developed by the University of Michigan.

Standard STD Clinic Procedures

All patients diagnosed with primary/secondary/early latent syphilis and patients diagnosed with gonorrhea in the STD clinics were considered syphilis and gonorrhea index cases, and were treated on site. They received STD/HIV counseling. They were interviewed by trained 'Disease Intervention Specialists' (DIS) to obtain information regarding STD/HIV risk. All information on index patients was kept in a locked, confidential file in the BCHD Disease Registry according to standard procedures approved by the 'Centers of Disease Control and Prevention' (CDC).

Recruitment

Volunteers for this protocol were recruited from the BCHD STD Clinics. Potential participants were patients diagnosed as having primary/secondary stage syphilis and gonorrhea at their STD clinic visit. All study participants were asked to provide a urine specimen for gonorrhea testing using nucleic acid amplification tests (NAAT) and to have blood drawn for syphilis testing using Rapid Plasma Reagin (RPR) nontreponemal screening test with the Fluorescent *Treponemal* antibody-absorbed (FTA-ABS) test for confirmation. Criteria for diagnosis of P&S syphilis were according to the following standard clinic protocol below:

Primary syphilis: Patient presents with a genital lesion and secretions collected from the lesion are found to contain spirochetes consistent with *Treponema pallidum* by dark-field microscopic examination.

Secondary syphilis: Patient presents any constitutional symptoms consistent with secondary syphilis (fever, chills, myalgias, arthralgias, patchy alopecia, mucous patches) and/or rash (including condylomata lata) with reactive serologic-tests for syphilis [positive Rapid Plasma Reagin test (RPR) with confirmatory Fluorescent Treponemal Antibody-Absorbed test (FTA-ABS)].

Criteria for enrollment

Patients having primary/secondary/early latent syphilis and gonorrhea were eligible for study enrollment as syphilis and gonorrhea index cases. Any patient diagnosed with gonorrhea during the same time frame was eligible for study enrollment as gonorrhea index cases. All eligible patients were fully notified about the study protocol. Informed consent was obtained

from all willing participants, and a certificate ensuring the patient's confidentiality was signed by the clinician and the patient. The clinician recorded all the patient's clinical signs and symptoms on standardized data collection forms, collected additional specimens from lesions or rashes and ordered an additional 5 milliliters of blood to be collected during routine phlebotomy. Unique study numbers on data collection forms and specimens were used to ensure the patient's confidentiality. If the patient had confirmed primary or secondary syphilis according to the above routine criteria, she/he was treated and escorted to a DIS. The DIS interviewed each patient and recorded the names and addresses of all known, identified sex partners according to standard confidential operating procedures for partner notification purposes. Participants were escorted back to the study clinician. The study clinician then asked the participants if they were (1) willing to present to the 'Lighthouse' for a network interview and (2) willing to bring, or refer, at least 3 of their friends and all of their sex partners who they have identified as members of their personal networks for interview. At the 'Lighthouse', consenting index participants were interviewed using standard forms about their opinions, knowledge, attitudes and lifestyle including drug use and sexual behavior and about friends and other people that constituted their social/sexual network. Both syphilis and gonorrhoea index patients were interviewed using standardized instruments.

Participation rates

The response rate for this study is 43.7%. The numerator is 'Numbers of patients that completed the interview' and the denominator is 'Total numbers of patients that completed the interviews, refusals and those who could not be contacted'. Cooperation rates are outcome rates among those eligible and usually slightly higher than the response rates.¹⁰⁷ The cooperation rate for this study is 48.1%. The numerator is 'Numbers of patients that completed the interview' and the denominator is 'Total numbers of patients that completed the interviews and refusals'. The refusal rate for this study is 47.2%. The numerator is 'Numbers of patients that refused to participate' and the denominator is 'Total numbers of patients that completed the interviews and the refusals'

Compensation for participants

The index patients were remunerated \$10 for enrollment in the specimen collection protocol and \$35 for enrollment and social interview completion.

Measures/Variables of Interest

The SSN survey data from 2001-2005 were used to address the research question and the sub-questions of this study. The survey design, sampling scheme, and all the survey questions were consistent all along the 5 years.

Depression

The patients were asked to complete the 'Depression Screening' questionnaire from the Center for Epidemiologic Studies Depression (CES-D) that was included in the Lifestyle Questionnaire. The CES-D is a 20-item scale commonly used to evaluate current depressive symptom severity with a score range of 0-60 (higher scores reflect increased symptom severity). Item responses range from 0 to 3, where 0=rarely or none of the time (less than 1 day in the past week), 1=some or a little of the time (1-2 days), 2=occasionally or a moderate amount of the time (3-4 days), and 3=most or all of the time (5-7 days). This scale was found to have very high internal consistency and adequate test-retest repeatability.¹⁵⁸ There are various ways of analyzing the CES-D score: the standard cutoff of 16 and a more stringent cutoff at 23.^{159,160} For this study, the standard cutoff score of 16 was used. The responses were dichotomized into not depressed versus depressed.

Drug abuse

Drug use was assessed by asking participants, "*When was the last time you (smoked marijuana/took stimulants/took sedatives/injected heroin/snorted heroin/injected speedball/snorted cocaine/injected cocaine/smoked crack/used other drugs)?*" and responded on a nine-point scale, ranging from "0=No", "1=More than 10 years ago", "3=5-10 years ago" until "9=in the past month". 'Smoked marijuana' and "smoked crack" were initial variables from the questionnaire. "Injecting heroin" and "Snorting heroin" were collapsed together into 1 variable, "Using heroin" and "Snorted cocaine" and "Injecting cocaine" were collapsed into "Using cocaine". This was done because of low cell counts on the primary categories. The responses for all the 4 drugs chosen for the analyses to investigate the associations of drug abuse with syphilis vs. gonorrhea between people with different types of networks (more sexual networks vs. non-sexual networks), were initially merged into: "1= Never", "2= Past month", "3= 1 month-1 year ago" and "4=more than 1 year." Fisher's exact tests were performed and the cell counts for category 2 and category 3 were too low for analyses. Thus, category 2 was then merged in category 3. The final categories for all the 4 drugs were: "1= Never", "2= Past month-1 year ago" and "3= more than 1 year ago. For the analyses to investigate on co-morbidity of drug

abuse and the presence of syphilis compared to gonorrhea, all the kinds of drugs were collapsed to 1 variable, 'Drug abuse' and the responses were dichotomized into "0=Never used" and "1=Used in lifetime".

Sexual abuse

Two primary variables were used to define sexual abuse. "*Has anyone ever forced sex on you in your lifetime?*" has dichotomized responses; yes versus no. "*How many different people have forced you to have sex with them?*" has responses: "0=none", "1=one", "2= 2 to 3", "3=4 to 5" and "4=6 to 7". For final analyses using multivariable regression, the responses for "*How many different people have forced you to have sex with them?*" were merged into: "0=none", "1=1 person" and "2= 2 and more people". This was done because of smaller cell counts that would occur if there were more categories

Sexual characteristics

Sexual characteristics were measured by asking participants on their sexual behaviors in the last 90 days prior to the study. The desired measures for the analyses for this study are: sexual identity and numbers of different sexual partners in the past 90 days. 'Age when having sex for the first time' was categorized into: "Less than 14 years" and "14 years and above". These two categories were chosen for this study after obtaining the overall mean response for analysis (the mean age in years when having sex the first time for patients who have syphilis is 15.3 and 14.5 for patients who have gonorrhea), and also because of smaller cell counts that would occur if there were more categories. A study investigating the impact of a history of sexual abuse on high risk behaviors among female school attendees had a similar variable, 'Sexual initiation before age 14'.¹⁰⁸ Numbers of different sexual partners in the past 90 days' was categorized into: "No more than 1 sexual partner" and "2 or more sexual partners".

Network characteristics

Network questions were about all the different people in the lives of the participants that they might know in different ways: friends, family members, sex partners, professionals or any other people. The initial networking measure for the final analyses for this study is: type of each sexual contact in the past 90 days. 'Contacts using drugs' was computed by merging three primary variables from the survey which are: '*Does this person (contact)...inject/snort heroin/smoke crack?*'. The responses were dichotomized into no versus yes. As for analyses on 2 different types of networking groups: patients with more sexual networks (more individuals

named as part of a sexual network) than non-sexual networks (more individuals named as part of non-sexual network) and vice-versa, a new variable 'Social Networks' from the primary networking variable, '*Subject's relationship with their contacts*' was computed. Sexual partners were grouped as sexual contacts (individuals named as part of a sexual network of the index patients) and friends; family and acquaintances were grouped together as non-sexual contacts (individuals named as part of a non-sexual network of the index patients).

Analyses

SPSS 18.0 was used for the analyses of these data. Frequencies of characteristics of the individuals named as part of a sexual or non-sexual network of patients with syphilis and gonorrhea, the N sizes for syphilis and gonorrhea patients with different types of network and information on MSM patients with syphilis and gonorrhea were summarized and tabulated accordingly. Logistic regression was used to estimate the comorbidity of depression and drug abuse with the presence of syphilis vs. gonorrhea.

Primary independent variables (IVs) were selected based on my research questions and literature^{43,45,54,55}; potential confounders of the associations between the primary IVs and syphilis vs. gonorrhea were selected from literature and through prior knowledge on some potential confounders suggesting that they could be predictive of syphilis/gonorrhea (gathered while discussing with primary investigator, Dr. Anne Rompalo at the time I was given the raw data set). Table 4.1 below shows the Primary IVs and potential confounders for the main research question and sub-questions.

Table 4.1: The primary IVs and potential confounders chosen for Study 3

Research question/sub-questions	Primary IVs	Potential confounders
Main Research Question <i>(Dependent variable: Presence of Depression)</i>	<ul style="list-style-type: none"> • Presence of STD (syphilis vs. gonorrhoea) 	<ul style="list-style-type: none"> • Forced to have sex in a lifetime • Numbers of different people forcing sex • Sexual identity
Main Research Question <i>(Dependent variable: Drug abuse)</i>	<ul style="list-style-type: none"> • Presence of STD (syphilis vs. gonorrhoea) 	<ul style="list-style-type: none"> • Number of different sexual partners in the past 90 days • Presence of depression • Contacts using drugs
Sub-question 1 <i>[Dependent variable: Syphilis (vs. gonorrhoea)]</i>	<ul style="list-style-type: none"> • Using marijuana • Using crack • Using heroin • Using cocaine 	<ul style="list-style-type: none"> • Age having sex the first time • Forced to have sex in a lifetime Presence of Depression • Contacts using drugs • Type of each sexual contact in the past 90 days
Sub-question 2 <i>(Dependent variable: Presence of depression)</i>	<ul style="list-style-type: none"> • Forced to have sex in a lifetime • Numbers of different people forcing sex 	<ul style="list-style-type: none"> • Sexual identity • Number of different sexual partners in the past 90 days • Using crack

Variables were then assessed for collinearity. I performed collinearity tests for all the selected IV's before starting the univariate analysis. If the value of correlation was close to +1 or -1, then that indicated that the selected variables were highly correlated, implying the presence of collinearity. I also carried out multicollinearity tests once all the variables were fit into the respective models. If the variance inflation factor (VIF) was between 1- 10, then there was no serious multicollinearity problem. A VIF between 5 and 10 indicates high correlation that may

be problematic but the values of VIF obtained from all the variables chosen for this study were below 5.

Logistic regression models with generalized linear models (GLM) were conducted to access the associations between index patients and the attributes of their egocentric network members. GLM was used to account for the fact that index patients had multiple network partners that contributed to the analysis. This means that for example, if the participant listed 5 network members, each of these members was treated as an observation within the cluster of five. GLM provides a general, flexible approach in these situations, because it allows a wide variety of correlation patterns (or variance-covariance structures) to be explicitly modeled. GLM models use both fixed and random effects.¹³⁷ GLM can perfectly handle a variety of outcome distributions such as continuous, binary and count outcomes that are present in my data. All analyses were complete case analysis using list wise deletion in SPSS as missing cases for all variables in the multivariable models had less than 15% of missing data.

My goal was to obtain the least biased and least confounded estimates of association. Hence, I decided to carry out analyses for multiple models in assurance of not to miss any possible associations and confounding effects. I had 1 model to obtain crude estimates and 3 other models for my final multivariable generalized linear model analyses. The models are:

1. **Model 1:** Crude (unadjusted)
2. **Model 2:** Each primary IV adjusted for the effects of all other primary IVs
 - This model assumes that all primary IVs are confounders of each other and that there are no other confounders.
 - For each primary IV-outcome association, none of the other primary IVs are in the causal path between the primary IV and the outcome.
3. **Model 3:** Each primary IV adjusted for the effects of confounders (excluding the other primary IVs)
 - This model assumes that for each primary IV-outcome association, none of the other primary IVs are confounders and all of the covariates in the model meet the definition of confounding which means that they are associated with the primary IV, predictive of the outcome, and not in the causal path between the primary IV and the outcome.
4. **Model 4:** Each primary IV adjusted for the effects of all other primary IVs plus the potential confounders

- This model assumes that for each primary IV-outcome association, all other primary IVs and “potential confounders” meet the criteria for confounding of that primary IV-outcome association.

Adjusted odds ratios (aORs) with 95% confidence intervals (CIs) were used to estimate associations.

RESULTS

A total of 526 patients with syphilis and gonorrhea were analyzed for this study and a total of 2106 social networks of patients with syphilis and a total of 1203 social networks of patients with gonorrhea were analyzed for the networking analyses for this study. Information of drug abuse among patients with syphilis and gonorrhea are shown in Table 4.2 and 4.3 respectively. Information on presence of depression among patients with syphilis or gonorrhea is shown in Table 4.4 and Table 4.5 presents information on possible sexual abuse among patients with syphilis or gonorrhea.

(a) Results for main research question

When controlling for ‘Forced to have sex in a lifetime’, ‘Numbers of different people forcing sex’ and ‘Sexual identity’, patients with syphilis have the lower odds of depression as those with gonorrhea. After adjusting for ‘Numbers of different sexual partners in the past 90 days’, ‘Presence of depression’ and ‘Contacts using drugs’, patients with syphilis have lower odds of drug abuse compared to patients with gonorrhea. Table 4.6 and Table 4.7 present the resulting aORs and 95% CIs showing the associations between the presence of depression and drug abuse and presence of STD (syphilis compared to gonorrhea). Results also show that over 60% of persons with either syphilis or gonorrhea were depressed (by the CES-D) criteria as shown in Table 4.4.

(b) Results for sub-question 1

For patients who have more sexual networks than non-sexual networks: after controlling for ‘Age having sex the first time’, ‘Forced to have sex in a lifetime’, ‘Presence of depression’, ‘Contacts using drugs’ and ‘Types of sexual partners in the past 90 days’, results showed similar estimates in both Model 3 and Model 4; patients who had used marijuana in between past month to a year were more likely to have syphilis (vs. gonorrhea) compared to those who never used it before but those who had used cocaine more than a year ago were less likely to have syphilis (vs. gonorrhea) compared to those who never used it before. Table 4.8 presents the

resulting aORs and 95%CIs showing the associations between drug abuse/depression of patients with more sexual networks than non- sexual networks and presence of syphilis vs. gonorrhea. For patients who have more sexual networks than non-sexual networks: after controlling for ‘Age having sex the first time’, ‘Forced to have sex in a lifetime’, ‘Presence of depression’, ‘Contacts using drugs’ and ‘Types of sexual partners in the past 90days’, results showed similar estimates in both Model 3 and Model 4; those who had used marijuana in between past month to a year ago and those who had cocaine more than a year ago were more likely to have syphilis (vs. gonorrhea) compared to those who never used them before while those who used crack more than a year ago were less likely to have syphilis (vs. gonorrhea) compared to those who never used it before. Results from Model 4 showed that those who never used cocaine before were less likely to have syphilis (vs. gonorrhea) compared to those who used it more than 1 year ago but the estimate from Model 3 showed the contrary. Table 4.9 presents the resulting aORs and 95%CIs showing the associations between drug abuse/depression of patients with more non-sexual networks than sexual networks and presence of syphilis vs. gonorrhea.

(c) Results for main sub-question 2

When controlling for ‘Sexual identity’, ‘Numbers of different sexual partners in the past 90 days’ and ‘Using crack’, results showed similar estimates in both Model 3 and Model 4 indicating that patients with syphilis or gonorrhea who were not forced to have sex in their lifetime were less likely to have depression compared to those who were forced. Those who were never forced for sex by anyone in their life were less likely to have depression compared to those who had 2 or more people who forced sex in their lifetime. Table 4.10 presents the resulting aORs and 95%CIs showing the associations between presence of depression and sexual abuse.

Table 4.2: Number (percent) of patients with syphilis (N=330) by duration of drug abuse and type of drugs

Type of drugs	Never used n*(%)	Used in the past month-1 year ago n*(%)	Used more than 1 year ago n*(%)
Marijuana	44 (14.7)	82 (27.3)	174 (58.0)
Crack	233 (77.7)	34 (11.3)	33 (11.0)
Heroin	204 (68.0)	52 (17.3)	44 (14.7)
Cocaine	224 (74.7)	28 (9.2)	49 (16.1)

*Percentages rounded to first decimal place, category-specific estimates may not equal overall total due to differences in missing values.

Table 4.3: Number (percent) of patients with gonorrhea (N=196) by duration of drug abuse and type of drugs

Type of drugs	Never used n*(%)	Used in the past month-1 year ago n*(%)	Used more than 1 year ago n*(%)
Marijuana	34 (17.3)	93 (47.4)	69 (35.3)
Crack	174 (89.2)	10 (5.2)	11 (5.6)
Heroin	171 (87.7)	9 (4.6)	15 (7.7)
Cocaine	174 (89.2)	4 (2.1)	17 (8.7)

*Percentages rounded to first decimal place, category-specific estimates may not equal overall total due to differences in missing values.

Table 4.4: Number (percent) of patients with syphilis or gonorrhea, by disease status and presence of depression

Depression^a	Patients with Syphilis Total, N=330	Patients with Gonorrhea Total, N=196
	n*(%)	n*(%)
Yes	200 (60.6)	118 (60.5)
No	130 (39.4)	77 (39.5)

*Percentages rounded to first decimal place number, category-specific estimates may not equal overall total due to differences in missing values.

^aDepression is present when the CES-D score ≥ 16 and Depression is absent when the CES-D score < 16 .

Table 4.5: Number (percent) of patients with syphilis or gonorrhea, by disease status and information on possible sexual abuse

Information on possible sexual abuse	Patients with Syphilis Total, N=330	Patients with Gonorrhea Total, N=196
	n*(%)	n*(%)
Forced to have sex in the lifetime		
Yes	82 (24.9)	30 (15.4)
No	247 (75.1)	165 (84.6)
Number of different people forcing sex in the lifetime		
None	229 (73.6)	163 (84.5)
1 person	57 (18.3)	22 (11.4)
2 or more people	25 (8.1)	8 (4.1)

*Percentages rounded to first decimal place number, category-specific estimates may not equal overall total due to differences in missing values.

Table 4.6: Crude and Adjusted Odds Ratios (aORs) and 95% Confidence Intervals (CIs) between presence of depression and the presence of syphilis (vs. gonorrhea) among patients with syphilis or gonorrhea: Results from simple and multivariable* logistic regression analyses

Measures (Primary IV)	Crude OR (95%CI)	aOR (95% CI)
Presence of STD		
Syphilis	1.00 (0.70-1.44)	0.85 (0.57-1.25)
Gonorrhea	Ref	Ref

*Final model for logistic regression contains: Presence of STD. The primary IV is adjusted for: Forced to have sex in a lifetime, Numbers of different people forcing sex and sexual identity.

Table 4.7: Crude and Adjusted Odds Ratios (aORs) and 95% Confidence Intervals (CIs) between drug abuse and the presence of syphilis (vs. gonorrhea) among patients with syphilis or gonorrhea: Results from simple and multivariable* generalized linear model (GLM) analyses

Measures (Primary IV)	Crude OR (95%CI)	aOR (95% CI)
Presence of STD		
Syphilis	0.76 (0.61-0.94)	0.60 (0.47-0.75)
Gonorrhea	Ref	Ref

*Final model for GLM contains: Presence of STD. The primary IV is adjusted for: Numbers of different sexual partners in the past 90 days, Presence of depression and Contacts using drugs.

Table 4.8: Estimated associations (crude and adjusted odds ratios [aORs] and 95% Confidence Intervals (CIs) of drug abuse (primary independent variables [IVs]) with having syphilis (vs. gonorrhea) among individuals with more sexual networks than non-sexual networks: Results from simple and multivariable generalized linear model (GLM) analyses

Measures (Primary IVs)	Syphilis (vs. Gonorrhea)			
	Crude OR (95% CI) {Model 1}	aOR (95% CI) {Model 2}	aOR (95% CI) {Model 3}	aOR (95% CI) {Model 4}
Using Marijuana				
Past month-1 year ago	2.14 (0.88-5.20)	3.57 (1.44-8.86)	1.87 (0.65-5.39)	3.56 (1.19-10.67)
>1 year ago	0.81 (0.33-1.99)	1.36 (0.54-3.40)	0.46 (0.15-1.35)	0.76 (0.25-2.37)
Never Used	Ref	Ref	Ref	Ref
Using Cocaine				
Past month-1 year ago	0.16 (0.06-0.41)	0.30 (0.10-0.94)	0.16 (0.07-0.36)	0.45 (0.13-1.52)
>1 year ago	0.19 (0.09-0.40)	0.39 (0.13-1.20)	0.31 (0.10-0.95)	0.18 (0.05-0.73)
Never Used	Ref	Ref	Ref	Ref

Model 1: Unadjusted

Model 2: Adjusted for the effects of all other primary IVs

Model 3: Adjusted for potential confounders* (excluding the other primary IVs)

Model 4: Adjusted for the effects of all other primary IVs plus all the potential confounders*

*Potential confounders for all the primary IVs are: Age having sex the first time, Forced to have sex in a lifetime, Presence of Depression, Contacts using drugs and Type of each sexual contact in the past 90 days

Table 4.9: Estimated associations (crude and adjusted odds ratios [aORs] and 95% Confidence Intervals (CIs) of drug abuse (primary independent variables [IVs] with having syphilis (vs. gonorrhea) among individuals with more non-sexual networks than sexual networks: Results from simple and multivariable generalized linear model (GLM) analyses

Measures (Primary IVs)	Syphilis (vs. Gonorrhea)			
	Crude OR (95% CI) {Model 1}	aOR (95% CI) {Model 2}	aOR (95% CI) {Model 3}	aOR (95% CI) {Model 4}
Using Marijuana Past month-1 year ago >1 year ago Never Used	1.64 (1.28-2.12) 0.54 (0.42-0.70) Ref	1.83 (1.41-2.37) 0.60 (0.47-0.78) Ref	1.67 (1.29-2.18) 0.52 (0.40-0.67) Ref	1.87 (1.42-2.45) 0.58 (0.45-0.76) Ref
Using Crack Past month-1 year ago >1 year ago Never Used	0.41 (0.28-0.62) 0.53 (0.39-0.71) Ref	0.85 (0.52-1.39) 0.57 (0.37-0.84) Ref	1.93 (1.41-2.63) 0.87 (0.53-1.44) Ref	0.93 (0.56-1.52) 0.56 (0.37-0.84) Ref
Using Cocaine Past month-1 year ago >1 year ago Never Used	0.10 (0.05-0.22) 0.71 (0.55-0.92) Ref	0.24 (0.10-0.55) 1.65 (1.10-2.46) Ref	1.39 (1.08-1.80) 0.15 (0.07-0.34) Ref	0.25 (0.11-0.60) 1.62 (1.08-2.43) Ref

Model 1: Unadjusted

Model 2: Adjusted for the effects of all other primary IVs

Model 3: Adjusted for potential confounders* (excluding the other primary IVs)

Model 4: Adjusted for the effects of all other primary IVs plus all the potential confounders*

*Potential confounders for all the primary IVs are: Age having sex the first time, Forced to have sex in a lifetime, Presence of Depression, Contacts using drugs and Types of each sexual contact in the past 90 days

Table 4.10: Estimated associations (crude and adjusted odds ratios [aORs] and 95% Confidence Intervals (CIs) of sexual abuse (primary independent variables [IVs]) with presence of depression among patients with syphilis or gonorrhea: Results from simple and multivariable logistic regression analyses

Measures (Primary IVs)	Crude OR (95% CI) {Model 1}	aOR (95% CI) {Model 2}	aOR (95% CI) {Model 3}	aOR (95% CI) {Model 4}
Forced to have sex in a lifetime No Yes	0.61 (0.39-0.95) Ref	0.25 (0.09-0.66) Ref	0.59 (0.36-0.98) Ref	0.28 (0.10-0.79) Ref
Number of different people forcing sex in the lifetime None 1 person 2 or more people	0.25 (0.09-0.65) 0.31 (0.11-10.89) Ref	0.25 (0.09-0.66) 0.31 (0.11-10.89) Ref	0.28 (0.10-0.79) 0.37 (0.12-1.13) Ref	0.28 (0.11-0.79) 0.37 (0.12-1.13) Ref

Model 1: Unadjusted

Model 2: Adjusted for the effects of all other primary IVs

Model 3: Adjusted for potential confounders* (excluding the other primary IVs)

Model 4: Adjusted for the effects of all other primary IVs plus all the potential confounders*

*Potential confounders for all the primary IVs are: Sexual identity, Number of different sexual partners in the past 90 days and Using crack

DISCUSSION

Mental illness and substance abuse are frequently linked to high-risk sexual behaviors and higher odds in acquiring STDs like syphilis and gonorrhea. Several studies have shown that sexual risk behaviors and STDs are associated with alcohol and drug abuse but the association between them and mental illness such as depression has always received little attention.¹⁵³ The rise of the drug culture within poor black communities is known to be worsened by segregation and poverty, thus effecting sexual networks and transmission of STDs.⁹⁴ Crack cocaine use spread widely throughout many urban areas of the United States (US) during the 1980s.¹⁶¹ Being highly addictive, crack cocaine has directly altered sexual networks through increased sexual exploitation of women and high-risk sexual behavior, including increased numbers of sex partners and the exchange of sex for drugs, and has been found to promote heterosexual transmission of HIV infection.⁹⁵

In this study, it appears that there was no difference in depression for persons with syphilis compared to those with gonorrhea, but this study had over 60% of patients with either syphilis or gonorrhea who were depressed (by the CES-D) criteria. Another finding was that patients with syphilis have lower odds of drug abuse compared to patients with gonorrhea and even though direct comparison to previous studies is not possible, these findings were consistent to a study in Brooklyn that found patients with gonorrhea only or patients with gonorrhea and chlamydia were more likely to use marijuana several times a week or more.¹⁵²

This study also found that among patients with more sexual networks than non-sexual networks, those who had used marijuana in between past month and a year ago were more likely to have syphilis (vs. gonorrhea). This finding is consistent to a study among MSM in New York that found those who had syphilis were more likely to use marijuana in the past 6 months compared to those who do not have syphilis.¹⁶² Another finding was that those who had used cocaine more than a year ago were less likely to have syphilis (vs. gonorrhea). This finding could be because of the longer time interval of using cocaine more than 1 year ago which could be too long to reflect the cocaine addiction during the period immediately before infection for the syphilis patients. This was explained in a study investigating the risk factors for syphilis (cocaine and prostitution) where the time interval of 3-month period before the STD clinic visit was chosen so that it is short enough for accurate recall but long enough to reflect behavior during the period immediately before infection for most patients.⁵⁹

Among patients with more non-sexual networks than sexual networks, those who used marijuana in between past month and 1 year ago (similar to the finding among patients with more sexual networks) and those who used cocaine more than a year ago were more likely to

have syphilis (vs. gonorrhea) compared to those who never used it before. The difference in the findings on cocaine use between patients with more sexual networks and patients with more non-sexual networks could be possible due to the two different sub-groups. The sample size for patients with more sexual networks than non-sexual networks were very small compared to the sample size for patients with more non sexual networks, and this could be the reason for the differences in my findings. Those who had used crack more than a year ago were less likely to have syphilis (vs. gonorrhea) and this was consistent to a study among heterosexual males attending public STD clinics in 3 cities, that found those who were high on crack and cocaine before or during sex were more likely to be diagnosed with syphilis.¹⁶³

Several research studies investigating associations between history of sexual abuse and sexual risk-taking behaviors have found that these two are related.¹⁶⁴ A model proposed by Finkelhor and Browne in 1985 described how children who have experienced CSA learn inappropriate risky sexual behaviors which later leads to acquisition of STDs.¹⁶⁵ This study found that those who were not forced to have sex in their lifetime were less likely to have syphilis or gonorrhea compared to those who were forced to have sex which relates to the other finding that found those who were never forced for sex by anyone in their lifetime were less likely to have depression compared to those who had 2 or more people who forced sex in their lifetime. This finding was similar to a study on gay men and a study on MSM, which found that being forced to have sex at early ages and experiencing CSA when aged 12-16 years were associated with depression.^{139,155}

Limitations

The findings of this study should be interpreted in the context of several limitations. First of all, this study is based on secondary analysis from a cross-sectional study. The study has already been designed and carried out. Data collections are completed as well. This is a common limitation in any secondary analysis. At times, data may not be able to facilitate a particular research question. There were interests to investigate the associations between variables such as: ages of sexual partners who forced sex, ages when they were sexually abused and any forms or IPV (emotional or physical abuse, being stalked or pressured for sex always, with the presence of depression among the STD patients in this study^{156,157}, yet this could not be achieved in this study as this study has already been carried out and completed. Studies have shown that alcohol use may contribute to elevated rates of sexual risk taking, thus leading to acquisition of STDs¹⁶⁶ but again, this study lacked detailed information on alcohol consumption of the

participants of this study. The SSN study was a cross-sectional thus, precluding any causal inferences.

Although the overall sample sizes for the networks were fairly large, some of the groups and specific findings included small numbers of respondents. Sample sizes for sub-groups with more sexual networks than non-sexual networks were rather small, resulting in relatively less power for detecting associations and lower precision of the estimates. Low power studies are more likely to provide a wide range of estimates of the magnitude of an effect which is known as 'vibration of effects' (situation in which a study obtains different estimates of the magnitude depending on the analytical options it implements).¹⁴⁵ Then again, low powered studies (small studies) are not always of low quality.

It is important to note that depression was measured using CES-D (self-report) which is not clinically diagnostic, and so these findings cannot be interpreted as definitive data on the prevalence or correlates of depression. This could lead to over-reporting this mental illness by symptoms that may be related to other psychiatric disorders such as anxiety, leading to slightly over-estimated or underestimated aORs compared to the true value. However, the unmodified CES-D can be useful in maintaining the psychometric integrity of the measure.¹⁵⁹

The participation rate for this study is not too high and could account for a type of selection bias; volunteer bias. Volunteer bias usually occurs when those who volunteer to participate in a study differ systematically with regard to either exposure or disease status from those who did not volunteer. A lower participation rate might result in bias due to differences in the exposure effect between participants and non-participants. The aORs in my study might not be that affected by the low participation rates. Participation rate alone does not determine the degree of bias present in any study while low participation rates do not always indicate a high level of bias essential in a study.^{121,122} Differences in factors that affect exposure effect matter most. Most studies have found little evidence for substantial bias as a result of non-participation that decreases the participation rates.¹²³ Yet, participation should still be enhanced as much by probably targeting a larger population with more variations in the predictor variables such as race.

Use of self-report measures for sexual behaviors/characteristics, drug abuse and on possible sexual abuse may have influenced the under-reporting or over-reporting of these stigmatized experiences and behaviors. Thus, individuals may adapt responses rendering to social desirability where answers were based on what others would want to hear which would not embarrass them or which would make them seem prestigious. For example, some participants could have under-reported details on questions related to sexual abuse due to sheer

shame and trauma or some of them could have under-reported the details on drug abuse due to embarrassment of being addicted to drugs. Thus, the aORs from this study involving these variables could have been slightly affected which could lead to bias towards the null due to possible non-differential misclassification of the IVs. Applying standardized and validated tools such as 'Audio Computer-Assisted Self-Interviews' (ACASI)¹²⁶ and using objective measures which could help reduce information inaccuracies.

Selection bias could possibly occur if among persons with syphilis or gonorrhea, drug users (marijuana/crack/heroin/cocaine) are more or less likely than non-users to be seen for care in the STD clinic. However, patients in this study were patients who presented themselves voluntarily to the STD clinics and were as likely to report drug use as were patients detected by the health department partner notification efforts and screening.⁵⁹

There were 3 multivariable models for the analyses in this study because of not being sure about a single model specification that would give the least confounded estimates. The possible differences in point estimates between models were probably due to random variability that is shown in the width of most CIs because of low sample sizes and low cell counts for certain categories or, due to the differences in the covariates across the models. Model misspecification could have occurred possibly due to covariates that aren't confounders and also because of the differences in assumptions about associations between the covariates and associations of covariates with syphilis vs. gonorrhea. Model 4 would be the best model to deliver results closest to the truth in comparison to Model 3 for this study. The estimates in this study were however not biased due to over-adjustment as per the other 2 studies because all the primary IVs chosen for all the analyses were also potential confounders of each other, thus Model 4 estimates were closer to the truth as Model 4 controls for all the chosen primary IVs along with the chosen potential confounders that were selected for this study based on relevant studies^{43,45,54,55} and prior knowledge. However, the estimates from Model 4 would still be a little biased due to residual confounding because I was not able to control for some variables that might be predictive of syphilis/gonorrhea and depression such as data on the use of the methamphetamine (meth) drugs and data on IPV, as I did not have the data. Nevertheless, even though some potential confounders could not be accessed due to absence of data on them, I made full effort to identify all the potential confounders which had sufficient data in this study based on literature or prior knowledge and had them controlled for in all analyses.

Another possible limitation of this study is that the sampled population limits the generalizability. The target population in this study is people with syphilis or gonorrhea who were from STD clinics in Baltimore. The associations between the IVs and syphilis vs. gonorrhea

in this target population are likely very different from the associations between IVs and syphilis that would be observed in populations that include people without gonorrhea and vice versa for the associations between the IVs and gonorrhea. Thus, the results would not be generalizable to other health care settings, to lower risk populations, people in established couple relationships or general population samples not seeking STD care. However, results from this study are consistent with other studies which are more population based compared to this study.

Strengths

One strength of this study would be that the STDs among all participants of this study (index patients and their sexual networks who were traced back to the study) were diagnosed clinically as opposed to be depending on self-report that may underestimate STDs because of social desirability bias (tendency of survey respondents to answer in a manner that will be viewed favorably by others, e.g., over-reporting a good behavior or under-reporting a bad behavior) in reporting and undiagnosed infections.¹²⁷ Another strength is that this study focused on patients with syphilis or gonorrhea and their recent sexual and non-sexual networks, thus enabling to focus on those acquiring and transmitting STD. Lastly, the detailed approach in all the analyses that were carried out in this study would add in to the strengths of this study. I performed my analyses with 3 multivariable models with different assumptions just so that I could attain the least confounded estimates to address the research and sub-questions of this study.

Conclusions and Public Health Implications

Despite the limitations, this study has provided some important information on associations between drug abuse, depression, and possible sexual abuse among patients with syphilis or gonorrhea who attended STD clinics in Baltimore. The findings of the study suggested that approximately 60% of syphilis or gonorrhea patients had depression. Syphilis has more neuropsychological impact compared to gonorrhea⁶⁸ and could possibly exacerbate symptoms of depression and also lead to the use of excessive drugs just to control the symptoms but my findings were contradictory to this. This could be due to some differences in the methodology in this study (e.g., low sample size, possible recall or information bias) or maybe they had already been referred and were already receiving treatment prior to this study. A study among women recruited from clinical settings and the community in Western Pennsylvania found that high levels of depression were associated with gonorrhea or chlamydia¹⁶⁷, and this is consistent with the finding on depression and syphilis or gonorrhea from this study. Patients

with STDs like syphilis and gonorrhea who attend STD clinics for treatment should also be screened for substance abuse as well as mental illness to aid in behavioral interventions for troubled patients. Behavioral interventions are evidence-based psychotherapies such as ‘Interpersonal Psychotherapy (IPT)’ or ‘Cognitive Behavioral Therapy (CBT)’.¹⁶⁸ Thus, improved diagnosis and care for depression are needed not only because depression is a public health concern by itself but also because addressing depression may lead to improved physical and mental health. Clinicians who identify severe mental illness in their patients with STDs should refer them to mental health professionals. Mental health professionals should incorporate health promoting strategies that could reduce stigma associated with the therapies, among these patients.

The findings on the associations between drug abuse and the presence of syphilis (versus gonorrhea) in this study suggest that among patients who had more sexual networks than non-sexual networks, those who used marijuana in between past month and 1 year ago and, among patients who had more non-sexual networks than sexual networks, those who used marijuana in between past month and 1 year ago and cocaine more than a year ago, have higher odds for syphilis compared to gonorrhea. Recreational drug uses have acted as co-factors for syphilis transmissions.¹³¹ Crack cocaine use was a co-factor for syphilis transmission in the early 90s and still remain as one of the factor for disease spread among poor heterosexuals.^{162,165} There has been increases in sexual risk behaviors of MSM being driven by recreational drug use and abuse and poor mental health.¹³¹ Besides, HIV infection is more prevalent among heterosexual blacks in inner cities and cocaine use is found to lead to increased sexual transmission of HIV along with syphilis being an important co-factor in HIV transmission.¹⁶⁹ Therefore, tools of disease control such as targeted screening and presumptive treatment could be useful especially in defined populations and settings as the STD clinics in the US. Barriers which prevent drug users with STDs like syphilis from obtaining medical care should be removed. State and local health departments should focus in creating partnerships with local drug treatment centers and programs, thus clarify pathways for treatment and rehabilitation for drug abuse for those patients with diagnosed STDs. This study showed that both groups (patients with more sexual networks than non-sexual networks and vice-versa) had recent marijuana use associated with syphilis (versus gonorrhea) thus, clinicians and psychiatrists (dealing with drug addiction/abuse) could contribute by getting information on the types of networks in their patients’ lives (more sexual networks than non-sexual networks or vice versa) when they come in for treatments. They could focus on follow ups, probably every six months to learn on their networks and how that influences the drug abuse and increase their risk in possible re-infection

of syphilis or susceptibility to HIV. This could lead to interventions for patients with both types of networks, such as getting them into counseling and therapy sessions with psychiatrists and public health officers to help them in rehabilitation from any current drug addiction and also from possible re-infection of syphilis.

Clinicians who treat patients with syphilis should talk in a friendly manner with their patients and find out information (probably by asking them to fill out a short questionnaire on their drug use while still talking to them in a friendly manner), if their patients use drugs like cocaine, crack and marijuana especially in the current time of their visit or within the year. They could then help them to get into local drug treatment centers and programs while constantly keeping track on their progress. A lot of people who are addicted to drugs lack emotional support from their family or friends and continue to indulge in drugs and be vulnerable to STDs like syphilis and also HIV.

Finally, the findings on depression and sexual abuse suggest that patients with syphilis or gonorrhea who were forced for sex and had 2 or more people who forced sex in a lifetime have higher odds of depression. Studies have shown that those with history of forced sexual activity are more likely to engage in riskier sexual behaviors due to the depression caused by the ordeal being forced into sex before, thus increasing the risks of acquiring STDs.^{155,156} Mid-level clinicians such as nurses, nurse practitioners and physician assistants could act as advocates for sexual abuse awareness and prevention programs in STD clinics for patients infected with syphilis who are also severely depressed. Nurses who diagnose and treat clients for an STD should be responsible to screen them for depression and offer affordable and accessible mental health services.

CHAPTER 5.

CONCLUSION

Social factors of all kinds like education, occupation, neighborhoods, migration, media, religion, substance use, incarceration, and urbanization can influence sexual behaviors, partnerships formation, and sexual networks. Causes of STDs include lack of preventive knowledge, lack of preventive behavior, lack of prompt and effective health care, and social network patterns that facilitate STD dissemination. This dissertation concentrated on associations between behaviors of sexual risk, peer influences, networking risks, drug and sexual abuse and presence of depression, with syphilis versus gonorrhea among patients with syphilis or gonorrhea from STD clinics in Baltimore. The findings covered in the 3 research studies emphasized on all the possible associations between these predictors on the presence of syphilis and gonorrhea.

The first study sought to determine the associations between the presence of syphilis vs. gonorrhea and sexual behaviors among these patients with syphilis or gonorrhea, determine the associations between the presence of syphilis vs. gonorrhea and peer influences on condom use before any sexual intercourse and determine the associations between the presence of syphilis vs. gonorrhea and sexual behaviors among individuals named as part of a sexual network of the index patients who were traced back to this study through 'partner notification'. The second study attempted to determine the associations between the presence of syphilis vs. gonorrhea and the network characteristics of the individuals named as part of a sexual or non-sexual network of the index patients, determine the associations between the presence of syphilis vs. gonorrhea and the network characteristics of the individuals named as part of a sexual or non-sexual network among individuals named as part of a sexual network of index patients, describe differences in associations between sexual behaviors and presence of syphilis vs. gonorrhea by different types of networks (more sexual networks than non-sexual networks and vice versa) and determine the associations between some sexual behaviors and presence of syphilis vs. gonorrhea among men having sex with men (MSM) from this study. Finally, the third study aimed to determine if depression and drug abuse are comorbid with the presence of syphilis vs. gonorrhea among patients with syphilis or gonorrhea, to describe differences in the associations of drug abuse with syphilis vs. gonorrhea between people with different types of networks, and to determine if sexual abuse is associated with depression among these patients.

The findings from the 3 studies covered in this dissertation did confirm the associations on (1) some risky sexual behaviors among index patients and also among sexual networks of the

index patients who were traced back, and peer influences being associated with the presence of syphilis vs. gonorrhea, (2) existence of differences in associations between some sexual characteristics or behaviors and presence of syphilis vs. gonorrhea, by different types of networks (more sexual networks than non-sexual networks and vice versa), (3) associations on some sexual characteristics among MSM and the presence of syphilis vs. gonorrhea and, (4) comorbidity between drug abuse with presence of syphilis compared to gonorrhea, drug abuse being associated with the presence of syphilis vs. gonorrhea among patients with more sexual networks than non-sexual networks and vice-versa and associations between sexual abuse with depression among these patients. All 3 studies serve as the basis for future longitudinal studies involving networking analysis and partner notification process that could be essential to the management of successful STD prevention programs.

In conclusion to all 3 studies among predominantly African-American patients; those who were gay, had sex the first time under 14 years old, not having a main sexual partner, having male and female networks, networks aged between 15-24 years, networks who were regular sexual partners, involved with anal, oral, and vaginal sex in the past 3 months, having more than 2 sexual partners in the past 3 months, using marijuana among patients with more sexual networks than non-sexual networks and using marijuana and cocaine in the past month to a year ago or more than a year ago among patients with more non-sexual networks than sexual networks, had higher odds of syphilis compared to gonorrhea. Patients with syphilis or gonorrhea who were forced into sex in a lifetime and having more than 2 people who have forced sex were more likely to have depression.

Reported diagnoses of syphilis may fluctuate more dramatically than gonorrhea given the changes in the sexual behaviors of the populations and risk groups. Based on STD surveillance report for year 2014¹⁴⁸, in 2014, among 49 states in the United States (US) that submitted data in the race and ethnicity categories, the rate of primary and secondary (P&S) syphilis cases remained highest among blacks (5.4 times the rate among whites), the rates among American Indians/Alaska Natives were 2.2 times the rate among whites, and the rates among Native Hawaiians/Other Pacific Islanders were 2 times the rate among whites. Also, P&S syphilis continue to be categorized by a high rate of HIV co-infection and in 2014, 26 states in the US reported both sex of sex partner and HIV status for at least 70% of P&S syphilis cases and 51.2% of cases were among MSM who were HIV positive. Given the data on syphilis rates among people from the US in 2014, which is still similar thus far, findings from all three studies could be a baseline guide to clinicians at all STD clinics, local and state health departments in the US to aid patients with syphilis to understand on the possibility of re-infection of syphilis

and increased susceptibility of HIV while educating them on the risks of having different types of networks (more sexual networks than non-sexual networks, and vice-versa). Besides these, they should also focus on the possible drug abuse, presence of depression and possible sexual abuse among syphilis patients during their visits to STD clinics by screening them completely for substance abuse and severe mental illness and then help them by referring them to mental health and substance abuse specialists. These interventions could be the beginning in the gradual but possible elimination of the bridges linking index syphilis patients and their sexual networks and so forth in the spread of syphilis/HIV.

The 'Special Focus Profiles' from the CDC¹⁴⁸ emphasized trends and distribution of STDs in populations of particular interest to STD and HIV prevention programs in state and local health departments, such as: women and infants, adolescents and young adults, racial and ethnic minority groups, and gay and bisexual men and other men who have sex with men (MSM), who are most vulnerable to STDs and often lack adequate access to healthcare services. In 2013, in the US, older adults (65 years and older) and children (19 years and under) were most likely to have health insurance while working adults (19 years to 64 years) had higher uninsured rates.^{170,171} Thus, those who are at high risk for syphilis and HIV usually encounter trouble to receive proper clinical services and health programs such as HIV screening (everyone who is 15–65 years old, pregnant, and at higher risk), STD counseling (for all sexually active adolescents and higher-risk adults), and syphilis screening (for pregnant women and adults at higher risk). Nevertheless, even though health insurance coverage has been expanded for most groups, including both men and women, and for most race and ethnic groups, evidence¹⁷¹ still suggests that disparities in health insurance coverage and access to STD services remain and so this factor needs to be looked into by the health department in the US to ensure people at high risk for syphilis and HIV get the attention and treatment they deserve regardless their insurance status.

These studies could be a kick off for future studies involving data on the STD patients and their sexual networks. Results from these 3 studies should be used as pilot studies to design larger confirmatory studies. Continued development and research into network-related concepts will definitely help reach the goal of being able to anticipate how STDs may spread. More studies should be carried out in other parts of the US including rural areas with large geographical distances as well as in Hawaii and the Pacific region because of higher rates of syphilis that could be observed in these other parts of the US. Studies with larger populations and studies with less potential selection bias and confounding in the near future are needed to determine less biased and more precise estimates compared to these 3 studies.

Enhanced surveillance is crucial for planning and evaluation. Monitoring the proximate and fundamental determinants of STD epidemics may lead STD prevention programs to a better understanding of the factors that influence trends in morbidity and to better expectations of future changes in these factors. Therefore, it is hoped that all these studies would inspire researchers to continue from where this dissertation leaves off, in order to make more meaningful contributions especially on sexual network analysis and partner notification process in larger populations with higher response and participation rates.

APPENDIX.

HUMAN SUBJECTS PROTECTION DOCUMENTS



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Title:
Impact of Social Networks on Syphilis Transmission: Network Member Interview

Number: NA_00029242

Principal Investigator: Anne Rompalo

IRB Committee:
IRB-3

Study Expiration Date:
2/8/2015

Review Type:
Expedited

Initial Approval Date:
6/16/2009

Date Submitted: 5/29/2009

Last Scheduled Review:

IRB Review Items:

Review Date	Review Type	Outcome	Letter Sent	Agenda Topic	Project Submission
There are no items to display					

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Activity	Author	Activity Date
Continuing Review First Reminder Sent to Study Team	Admin, System	1/6/2014 1:26 AM

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Date: Friday, July 11, 2014 11:56:56 AM

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Application
NA_00029242
Anne Rompalo

1 - General Information

ID: NA_00029242

1. * Principal Investigator:

Click Select to choose PI:

Anne Rompalo

2. * Will the PI obtain consent for this study?

Yes No

3. * Indicate the PI's primary affiliation:

(Select "Other (Affiliation Not Listed)" if the PI's primary affiliation is not listed):

4. * Title of Study:

Impact of Social Networks on Syphilis Transmission: Network Member Interview

5. * Provide a BRIEF statement of your research question and plan:

Syphilis eradication is a national public health priority. Despite overall low national rates, hyperendemic foci of disease persist in several areas, particularly in Baltimore, which leads the nation for primary and secondary infectious syphilis. Understanding transmission patterns is critical for developing successful intervention and control. Traditional tracing and treatment of sexual contacts of infectious syphilis patients has been criticized as an expensive, time-intensive, and effectual mode of syphilis control. Social network methods that identify and screen friends, family and close associates of an infected individual are reported to be as good as the traditional mode in identifying infected members of small syphilis outbreaks. We propose to examine the role of social context and social influence on syphilis transmission in Baltimore. The goals of this study are, first, to examine the social context of syphilis risk through the assessment of social and sexual network characteristics. Social context data will be confirmed by biologically-based strain typing. Restriction fragment length polymorphism (RFLP) analysis will be used in conjunction with contact tracing data to define epidemic strain types and to derive probable routes of transmission. This will be the first time that a biological marker of transmissions will serve to validate epidemiologically defined transmission groups and thus improve our ability to delineate the sexual, social and personal network characteristics associated with syphilis transmission. A second goal will be to compare the social context of syphilis risk to that of gonorrhea risk and to determine and compare the role of drug use in the social context of both sexually transmitted diseases. Third, we propose to compare the efficacy of detecting early infectious (primary, secondary and early latent stage) syphilis cases by screening social network members of early syphilis index cases compared to that of standard sexual partner notification techniques. The proposed project seeks a total of five years of support to map, analyze and compare syphilis cases within social and sexual networks, and to examine and compare the relationship between social network characteristics of individuals newly infected with syphilis and gonorrhea in high prevalence areas of Baltimore. We are currently funded to examine the role of social context and influence on gonorrhea transmission and risk reduction (NICHD 1R01HD 33982). The Baltimore STD clinics' computerized patient tracking system has allowed us to identify patients with newly acquired gonorrhea and members of their networks who seek treatment at one of the city's two STD clinics or whose morbidity reports are received by the health department's surveillance unit. We will apply this model to identify and interview patients with primary, secondary and early latent syphilis. All referred sexual and social network members will be screened and tested for newly acquired syphilis. We will collect and store blood and primary/secondary syphilis lesion specimens from the all index patients and sexual and social network participants identified with early syphilis for restriction fragment length polymorphism (RFLP) analysis. Using Geographic Information System (GIS), we will map the social and sexual networks of syphilis patients. This will allow us to track and compare possible syphilis transmission through both network types and to examine social structural factors, especially drug use, which may be associated with disease transmission and risk behaviors. We will compare the rates of identifying new syphilis cases through screening of social versus network members.

6. * Select the type of review requested:

If you are unsure what review type to request, please use the Review Type Wizard.

Expedited

7. * Is this a retrospective chart review only?

Yes No

<https://e-irb.jhmi.edu/eirb2/ResourceAdministration/Project/PrintSmartForms?Project=co...> 7/11/2014

8. * Is this a resubmission of an expired, terminated, withdrawn or disapproved application?
 Yes No

9. * Previously approved JHM IRB Protocol Number:
 98-10-21-03

10. * Is this a conversion of an active study already approved by a Hopkins/Affiliates IRB (including the JHM All Children's Hospital IRB)?
 Yes No

12. * Progress Report:
 Click **Add** to upload a new document. Click **Update** to upload a revised version of the existing document. Do **not** delete existing documents. (Click **History** to see all uploaded versions of an existing document.)

Title	Date Modified	Version	Status
View Progress Report(0.01)	5/18/2009 6:31 PM	0.01	Submitted

13. * What is the current status of your study?

- Active Enrollment
- Active follow-up continues but not active treatment (e.g., weekly clinic visits)
- Enrollment Closed and participants are receiving study intervention [Participants receiving drugs, Participants receiving other research related procedures (including protocol-specified testing, radiation, etc.)]
- Enrollment Closed (Open for collection of follow-up data, data analysis)
- Enrollment has not started

14. * Estimated time to complete this study:
 2011

15. Study Team Members:

Click **Add** to add new Study Team members. Click **Update** to modify existing Study Team member information.

Last	First	Degrees	JHED Dept	Primary Affiliation	Role	Consenting Hopkins participants	Receive Notifications	Agree To Participate
View Thieman	Laurel	MSED	SOM Ped Infectious Disease		Study Coordinator	no	yes	yes
View Jennings	Jacky	Ph.D., M.P.H.	SOM Ped Bay Bayview Pediatric Unit		Co-Investigator	no	yes	yes
View Ellen	Jonathan	M.D.	ACH Pediatrics		Co-Investigator	no	yes	yes
View WYLIE	CHARLEEN	n/a	SOM DOM ID BCHD		Consent Designee	no	no	yes

Application
 NA_00029242
 Anne Rompalo

2 - Study Team Compliance Training

1. All Study Team Members listed below must complete indicated training requirements

PIs of active IRB Protocols must complete the REWARDS training (Research Ethics Workshops) or equivalent. PIs have one year from the date of their first eIRB submission to complete the REWARDS requirement.

For studies with a Prospective Reimbursement Analysis document (PRA), Clinical Research Billing Orientation (CRBO) training is required for study team members who have a role in the consenting process. Clinical Research Support Services will notify those members by email. The IRB cannot take final action until all training is complete.

<https://e-irb.jhmi.edu/eirb2/ResourceAdministration/Project/PrintSmartForms?Project=co...> 7/11/2014

1.

Principal Investigator

Last Name	First Name	HSR Required	Date	H&R Required	Date	COI Required	Date	Date REwards Completed	CRBO Required	Date CRBO Completed
Rompalo	Anne	yes	3/14/2012	yes	4/6/2003	yes	12/15/2003	5/5/2004	no	9/15/2010

Study Team:

Last Name	First Name	HSR Required	Date	H&R Required	Date	COI Required	Date	Date REwards Completed	CRBO Required	Date CRBO Completed
Thieman	Laurel	yes	2/2/2001	yes	3/23/2003	yes	10/21/2003	9/15/2003		6/24/2008
Jennings	Jacky	yes	2/15/2012	yes	4/10/2003	yes	9/5/2003	7/25/2006		
Ellen	Jonathan	yes	2/15/2012	yes	3/28/2003	yes	9/4/2003	6/5/2006		8/2/2008
WYLIE	CHARLEEN	yes	9/18/2006	yes	4/2/2003	yes	10/22/2003	3/22/2004		7/1/2008

2. If the dates above are blank or incorrect, upload copies of training certificates or myLearning Report and the JHM IRB staff will enter the dates for you.

Click **Add** to upload a new document. Click **Update** to upload a revised version of the existing document. Do not delete existing documents. (Click **History** to see all uploaded versions of an existing document.)

Title	Date Modified	Version	Status
There are no items to display			

Application
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5 – Protocol Information

1. * Type of protocol:

- JHM-IRB eForm A
- Outside Sponsor
- Investigator-Initiated

2. * Check the option that best describes this protocol:

- Protocol written by a Hopkins investigator/researcher
- Protocol written by a consortium or cooperative group not at Hopkins
- Protocol written by a federal sponsor
- Protocol written by a commercial sponsor
- Protocol written by a non-profit sponsor

3. * Clean Protocol:

Click **Add** to upload a new clean document. Click **Update** to upload a clean revised version of the existing document. (Click **History** to see all uploaded versions of an existing document.)

Title	Date Modified	Version	Status
View protocol(0.01)	5/18/2009 6:36 PM	0.01	Submitted

4. Track Changes Protocol or Summary of Changes

Click **Add** to upload a new track change document. Click **Update** to upload a track change revised version of the existing document. (Click **History** to see all uploaded versions of an existing document.)

Title	Date Modified	Version	Status
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5. Enter the sponsor protocol title if different from this study title:

6. Appendices/Sub-study protocol/Letter of Amendment

<https://e-irb.jhmi.edu/eirb2/ResourceAdministration/Project/PrintSmartForms?Project=co...> 7/11/2014

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7. * Did this study receive a non-IRB scientific review?
 Yes No

10. Additional pilot data or relevant publications

Click Add to upload a new document. Click Update to upload a revised version of the existing document. (Click History to see all uploaded versions of an existing document.)

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There are no items to display			

11. * Check All of the below that apply to this study:

- There are procedures in this protocol that attempt to induce new symptoms in research participants, such as: procedures to provoke an allergic reaction (pulmonary, nasal, or GI), use of a glucose clamp or exercise stress test, or drugs being used to provoke a reaction.
- Normal volunteers or participants with a condition will undergo high risk, invasive procedures, such as: bronchoscopy, cardiac catheterization, or insertion of an arterial line.
- Participants will be placed at increased risk due to the circumstances under which they will be enrolled, consented, or undergo study related procedures, (for example: participants will be consented in the ER prior to emergency treatment, or participants will receive interventional procedures in an emergency situation where a waiver of consent has been granted).
- The protocol includes rescue medications for the experimental intervention.
- This is the first time you have been listed as PI on a more than minimal risk application.
- None of the above.

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6 - Clinical Trials Information

1. * Is this a clinical trial?
 Yes No

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7 - Conflict of Interest

1. Does the PI or any study team member (or their spouse, domestic partner, or dependent children) have a financial interest or fiduciary relationship that

- 1) could be affected by the research, or
- 2) is in an entity that could be affected by the research?

This applies to current interests/relationships and those within the past 12 months.

- Yes No

All conflicted individuals must disclose potential conflicts of interest to the Office of Policy Coordination (OPC) before this application can be approved.

5. * To the best of your knowledge, does Johns Hopkins have a financial interest that 1) could be affected by the research or 2) is in an entity whose financial interest could be affected by the research?

- Yes No

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8 - Support Information

1. * Check all sources of support (pending or awarded):

- Monetary
- Material or Equipment (e.g., drugs or devices)
- None of the above

3. * Will data from this study be submitted to a Genome Wide Association Studies (GWAS) NDH database (e.g., dbGaP)?

- Yes No

9. * Will you apply to the Bayview Institute for Clinical and Translational Research - Clinical Research Unit (ICTR-CRU) (formerly GCRC) or JHH ICTR-CRU (includes NBRU) for funding or use of facilities?

- Yes No

10. If ORA has requested IRB review of your grant or you have funding from the Maryland Stem Cell Research Fund, submit a copy of the complete grant, including the face page but excluding the appendices:

Click [Add](#) to upload a new document. Click [Update](#) to upload a revised version of the existing document. (Click [History](#) to see all uploaded versions of an existing document).

Title	Date Modified	Version	Status
There are no items to display			

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9 - Study Location

1. Check all sites where this research will be conducted:

- Johns Hopkins Sites
- Johns Hopkins Community Physicians (JHCP) sites (Click on the [help link](#) for guidance and to download the JHCP Research Review Form.)
- Johns Hopkins ICTR-CRU sites
- Johns Hopkins Clinical Research Network (CRN) Sites
- Other sites with reciprocity or review agreements (e.g., NIA, NIDA, Medstar Facilities, BCHD)
- Multicenter sites where another PI will conduct the research
- Non-Hopkins/Affiliates sites where you will conduct the research

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10 - Sample Size

1. * Will this research involve intervention/interaction with participants?

- Yes No

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11 - Participant Information

1. * Will you obtain identifiable data, records, specimens, or samples, or have access to codes, links or identifiers?

- Yes No

2. * Age ranges of participants (e.g., 0-17, 18-100):
15-65

3. * Study population - check all that apply:

- Male adults (18+)
- Female adults (18+)
- Male children (<18)
- Female children (<18)

4. Special Study Populations - check all populations that may be enrolled:

- Adults lacking capacity to consent
- Pregnant Women
- Non-viable neonates/neonates of uncertain viability
- Prisoners
- Non-English speakers
- Children who are in foster care or wards of the state

5. * Will you enroll healthy volunteers?

Yes No

6. Hopkins Study Populations - check all populations that you will directly recruit and/or review charts/records:

- JHH/JHBMC adult emergency department patients/records
- JHH employees/records
- JHU School of Medicine residents/interns/records
- JHU School of Medicine students/records
- Other JHU students/records
- Hopkins/Affiliates inpatients
- Hopkins/Affiliates outpatients
- JHH obstetric patients

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12 - Recruitment Information

1. * Check all sources of recruitment for this study:

- No intervention/interaction with participants (e.g., chart record review)
- Individuals who are clinical patients of the PI or co-investigators
- Review of clinical records of individuals who are not clinical patients of the PI or co-investigators prior to their consent
- Referral of individuals by treating clinicians not on the study team
- Prior Hopkins/Affiliates study participants
- Individuals who learn about the study through advertisements or peer/network recruiting

2. * Describe the process for recruiting these individuals, including:

- individual(s) responsible for approaching participant(s)
- where and when recruitment will take place
- how privacy issues will be addressed in recruitment process

5. Are you submitting recruitment materials and/or telephone screening scripts for review?

Yes No

8. Data Sources:

- Hopkins/Affiliates clinical databases or medical charts/records (including EPIC, EPR, department databases,

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patient registry logs,
etc.)

Non-Hopkins/Affiliates clinical databases or medical charts/records (including EPIC,EPR, department databases, patient registry logs, etc.)

JHM IRB approved studies or research databases

Non-Hopkins IRB approved studies

Public databases/registries/repositories

Administrative/claims data from Johns Hopkins Healthcare LLC

Cancer registry data elements

Imaging Data collected for research

Other

10. Provide any additional information about your recruitment process:

11. JHM-IRB waiver of privacy authorization (HIPAA Form 4)

Required for:

- Chart/record review of individuals who are not patients or former study participants of the PI or study team
- Receiving PHI from a referring Clinician not on the study team
- Conducting telephone screening prior to obtaining written consent

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Application
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13 - Consent and Waivers

1. * Check the type(s) of consent planned for this study:

- Written Consent
- Oral Consent
- Consent Waiver
- Survey/questionnaire research

1. *In vitro* diagnostics

- None of the above

Application
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16 - Assent and Waivers - Children

1. * Check the type of assent planned for this study:

- Assent statement in consent form
- Written assent
- Oral assent
- Waiver or alteration of assent
- No assent/waiver/alteration required

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19 - Supplemental Study Documents

1. Upload supplemental study document(s) requiring a JHM IRB approval logo:

Click Add to upload a new document. Click Update to upload a revised version of the existing document. Do not delete existing documents. (Click History to see all uploaded versions of an existing document)

Title	Date Modified	Version	Status
There are no items to display			

2. Upload supplemental study document(s) not requiring a JHM IRB approval logo:

Click Add to upload a new document. Click Update to upload a revised version of the existing document. Do not delete existing documents. (Click History to see all uploaded versions of an existing document)

Title	Date Modified	Version	Status
There are no items to display			

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21 - Devices

1. * Will any devices be studied in this research (including devices which are FDA-approved for marketing)?

Yes No

2. * Will any investigational devices (non-FDA-approved for marketing or used according to non-FDA-approved indications) be used in this research?

Yes No

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22 - Human Biological Samples

1. * Will human biological samples (e.g., blood, cells, tissue, urine) be used in this research?

Yes No

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33 - SKCCC CRO

1. * Is this study cancer related (e.g., cancer prevention, screening, therapeutic, diagnostic, etc.), involving cancer patients, using cancer center facilities/resources?

Yes No

* Does this study involve a drug that will be administered/dispensed in the Weinberg IDS?

Yes No

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35 – Data Confidentiality

1. * I confirm that all the procedures listed below will be used to protect the confidentiality of data and samples collected and stored for research purposes:
 Yes No

- Only authorized persons will be granted access
- Only authorized persons may enter and view study data
- Passwords and system IDs will not be shared
- Physical security of the workstations/files will be maintained
- Adequate back-up plan is in effect
- Staff trained on data entry system and importance of security procedures
- Workstations with databases will not be left unattended

3. * Will a Certificate of Confidentiality be obtained for this study?
 Yes No

Study Team Information

1. * Study team member:
Laurel Thieman
2. * Study team role:
Study Coordinator
3. Primary Affiliation:
4. * Will this study team member be consenting participants for this study?
 Yes No

Study Team Information

1. * Study team member:
Jacky Jennings
2. * Study team role:
Co-Investigator
3. Primary Affiliation:
4. * Will this study team member be consenting participants for this study?
 Yes No

Study Team Information

1. * Study team member:
Jonathan Ellen
2. * Study team role:
Co-Investigator
3. Primary Affiliation:
4. * Will this study team member be consenting participants for this study?
 Yes No

Study Team Information

1. * Study team member:
CHARLEEN WYLIE
2. * Study team role:
Consent Designee
3. Primary Affiliation:
4. * Will this study team member be consenting participants for this study?
 Yes No

Study Team Conflict of Interest

Study team member:

Laurel Thieman

1. Does this study team member have a conflict of interest?
2. Will this study team member server as a non-conflicted designee?

Study Team Conflict of Interest

Study team member:

Jacky Jennings

1. Does this study team member have a conflict of interest?
2. Will this study team member server as a non-conflicted designee?

Study Team Conflict of Interest

Study team member:

Jonathan Ellen

1. Does this study team member have a conflict of interest?
2. Will this study team member server as a non-conflicted designee?

Study Team Conflict of Interest

Study team member:

CHARLEEN WYLIE

1. Does this study team member have a conflict of interest?
2. Will this study team member server as a non-conflicted designee?

IRB approval from University of Hawaii, Mānoa



UNIVERSITY
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MĀNOA

Office of Research Compliance
Human Studies Program

August 22, 2014

TO: Vinogiri Krishnan
Principal Investigator
Public Health (Epidemiology)

FROM: Denise A. Lin-DeShetler, MPH, MA
Director

A handwritten signature in black ink, appearing to read "Denise A. Lin-DeShetler".

SUBJECT: CHS #22411- "Comparison of Behavioral and Sexual Networking Risks Among
Adult Men and Women with Syphilis or Gonorrhea. The Social
and Sexual Network (SSN) Study, Baltimore"

This letter is your record of the Human Studies Program approval of this study as exempt.

On August 22, 2014, the University of Hawai'i (UH) Human Studies Program approved this study as exempt from federal regulations pertaining to the protection of human research participants. The authority for the exemption applicable to your study is documented in the Code of Federal Regulations at 45CFR 46.101(b)(Exempt Category 4).

Exempt studies are subject to the ethical principles articulated in The Belmont Report, found at <http://www.hawaii.edu/irb/html/manual/appendices/A/belmont.html>.

Exempt studies do not require regular continuing review by the Human Studies Program. However, if you propose to modify your study, you must receive approval from the Human Studies Program prior to implementing any changes. You can submit your proposed changes via email at uhirb@hawaii.edu. (The subject line should read: Exempt Study Modification.) The Human Studies Program may review the exempt status at that time and request an application for approval as non-exempt research.

In order to protect the confidentiality of research participants, we encourage you to destroy private information which can be linked to the identities of individuals as soon as it is reasonable to do so. Signed consent forms, as applicable to your study, should be maintained for at least the duration of your project.

This approval does not expire. However, please notify the Human Studies Program when your study is complete. Upon notification, we will close our files pertaining to your study.

If you have any questions relating to the protection of human research participants, please contact the Human Studies Program at 956-5007 or uhirb@hawaii.edu. We wish you success in carrying out your research project.

1960 East-West Road
Biomedical Sciences Building B104
Honolulu, Hawai'i 96822
Telephone: (808) 956-5007
Fax: (808) 956-8683

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