UNIVERSITY OF CALGARY

The Use of Social Network Analysis to Quantify the Importance of Social Venues in an Infectious Syphilis Outbreak in Calgary, Alberta: A pilot study

by

Rhonda Lynne Fur

A THESIS

SUBMITTED TO THE FACULTY OF GRADUATE STUDIES

IN PARTIAL FULFILMENT OF THE REQUIREMENTS FOR THE

DEGREE OF MASTER OF SCIENCE

DEPARTMENT OF COMMUNITY HEALTH SCIENCES

CALGARY, ALBERTA

MAY 2010

Abstract

Objective: The purpose of this study was to explore the use of social network analysis as both an epidemiological and methodological tool to determine the relative importance of venues where people meet sex partners to the transmission of syphilis.

Subjects and Methods: Cases and named contacts of infectious syphilis aged 18-75 were identified and enrolled at an Alberta Sexually Transmitted Disease clinic, between April-August, 2009. In addition to standard contact tracing information, participants were asked to list all venues attended in the last six months where sexual partnering occurred. Sexual affiliation networks were constructed by linking individuals to sex partner meeting venues. Algebraic measures of network position and permutation statistical methods were used to determine what type of venue connected the most individuals.

Results: A total of 154 network members comprised of 46 cases of infectious syphilis and 108 named sexual contacts were connected to 52 venues. A densely connected network of 94 gay men linked together by 21 venues was identified. In this sexual affiliation network, Internet venues had significantly higher degree centrality than non-Internet venues ($p<0.05$). The three most central Internet venues, connected two thirds of all infectious syphilis cases in the network.

Conclusion: Network analysis identified key venues that connected individuals who were infected with syphilis. These venues would be an ideal target for preventive interventions to prevent further dissemination of disease.

Acknowledgements

This thesis would not have been possible without the support and contributions of many great people. To my supervisor, Dr. Elizabeth Henderson, I express my sincere gratitude for granting me the opportunity to undertake this research and for her tremendous support, encouragement, and guidance during my graduate studies and in the preparation of this thesis.

I also extend my deepest gratitude to my co-supervisor Dr. Ronald Read for generously giving his time and sharing his wisdom to assist me. His ardent dedication to the control of syphilis has been inspiring.

It is a pleasure to thank Dr. Jenny Godley, without whose vision and knowledge this research project would not have been possible. Genuine appreciation is also due to the other members of my supervisory committee, Ms. Colleen Roy and Ms. Kathryn Bush of Alberta Health Services, for their unremitting support, comments and insightful suggestions.

I am extremely grateful to Dr. Alberto Nettel-Aguirre for his advice regarding aspects of the statistical analyses and to Dr. Ameeta Singh, who as external examiner provided constructive feedback and thoughtful comments.

Finally, a heartfelt thank you is extended to the staff of the Calgary Sexually Transmitted Disease clinic for their overwhelming support and enthusiasm in the project, and for giving their valuable time to assist with participant recruitment and aspects of data collection.

Dedication

To my husband John and our two beautiful daughters Alyssa and Robyn-Lynn; your endless love is a constant source of inspiration.

Table of Contents

List of Tables

List of Figures and Illustrations

List of Symbols, Abbreviations and Nomenclature

Graph Symbols	**Definition**
X	A sociomatrix X is a gxg matrix
G (N, $\mathcal{L}$)	A graph consisting of a set of nodes N and lines $\mathcal{L}$
$\mathcal{L} = \{l_1, l_2, \ldots l_L\}$	Set of lines in a graph
N, $= \{n_1, n_2, \ldots n_g\}$	Set of nodes in a graph
i ➔ j	Tie from node *i* to node *j*
X_{ij}	Value of the tie from node *i* to node *j*
n (n-1)/2	Theoretical maximum distinct lines in a an undirected graph with n points
C_B (n_i)	Node-level betweenness centrality index
C_D (n_i)	Node-level degree centrality index
d (n_i)	The degree of node *i*
g_{jk} (n_i)	The frequency of geodesics linking two individuals (*j*, *k*) that contain individual *i*
g_{jk} (n_i)/g_{jk}	The proportion of geodesics involving individual *i* for all possible shortest paths between *j* and *k*
Vertices	Also known as points, nodes, or actors (social networks)
Edge	Also known as lines, or in social networks ties or links
Adjacency	Two vertices are adjacent if there is an edge that connects them
Undirected graph	The relation has no direction
Directed graph (digraph)	The relation has direction, represented with an arrowhead May be used to represent the flow of infection
Valued graph	The relation or link has a numerical value (e.g. the frequency of men connecting two venues)
One-mode network	Single set of actors or nodes in a network (sexual network)
Two-mode network	Two sets of actors in a network (individuals and venues
Matrix concept of transpose	The rows and columns of the original matrix are interchanged in the transposed matrix so that the rows become columns and the columns become rows, i.e. an *n* x *m* matrix becomes a *m* x *n* matrix

Abbreviations

AIDS	Acquired immunodeficiency syndrome
HIV	Human immunodeficiency virus
MSM	Men who have sex with men
STD	Sexually transmitted disease
STI	Sexually transmitted infection
UAI	Unprotected anal intercourse

Graph notation/terminology adapted from Wasserman S, Faust K. Social Network Analysis: Methods and Applications: Cambridge University Press; 1994. [1]

Chapter One: Introduction

1.1 Study context and motivation

Unlike many infectious diseases, transmissibility of sexually transmitted infections (STIs) is impacted significantly by behaviour. Thus in STI epidemiology, understanding sexual risk behaviour is critical for gaining insight into STI/human immunodeficiency virus (HIV) transmission, identifying populations at risk for infection, and evaluating prevention programs. Social network analysis is one avenue to determine the topography of sexual behaviour and its affect on STI transmission. The social network approach is an extension of the standard epidemiologic model where attributes of the individual are the singular explanation for acquiring a STI. The network perspective provides a framework to model the complex patterns and structure of sexual and social interactions with others to further our understanding of STI transmission. This approach can provide important information on STI epidemics that conventional epidemiological methods do not capture.

There is an increasing body of literature that has shown that sexual network structure is a determinant of STI dissemination.[2-9] However, obtaining comprehensive data on sexual networks is difficult. The notion that sex partner meeting places may play a central role in sexual network formation and transmission dynamics of STIs has generated considerable interest. In 2007, Frost [10] introduced the term "sexual affiliation networks" to differentiate these networks from sexual networks. A sexual affiliation network is a network of persons and the venues they frequent to seek sex partners. Identifying sexual affiliations may enhance understanding of proliferation patterns of sexually transmitted infections.

Syphilis is a sexually transmitted infection with substantial associated morbidity. Despite public health efforts to control rates, Alberta, like many health jurisdictions in Canada, is faced with a concerning resurgence of infectious syphilis. The escalating incidence, considerable associated morbidity [11] and the risk of HIV transmission [12] necessitates the control of syphilis as an important public health goal. Attaining syphilis elimination will call for health regions to implement innovative approaches to enhance efforts for case finding. Social network methodology has the potential to quantify the role places of social aggregation play in transmission of syphilis based on a network approach. Furthermore, information on locations where syphilis may have been acquired could elucidate key determinants of syphilis transmission not ascertainable by the identity of sex partners alone.

1.2 Study objective and research questions

The primary research purpose of this pilot study was to explore the use of social network analysis as both an epidemiological and methodological tool to determine the relative importance of sex partner meeting places to the transmission of syphilis, in a sustained infectious syphilis outbreak in the Calgary Health Region. The study objectives were: 1) to describe the sexual and affiliation networks of persons infected with syphilis; 2) compare the network structure of persons connected through sexual contact with the network structure of persons connected through venues; 3) and determine what type of venue connected the most individuals as measured by graph-theoretic algebraic calculations of point degree and betweenness centrality. Specifically, social network analysis was employed to address the following research questions:

1) Do social venues connect persons infected with syphilis?
2) Does the network structure of persons infected with syphilis change when the link considered is a sexual contact versus a social venue?

1.3 Thesis overview

To facilitate interpretation and critical appraisal by reviewers and readers, this thesis follows the progression recommended by the STROBE statement on **ST**rengthening the **R**eporting of **OB**servational studies in **E**pidemiology.[13, 14] First the scientific rationale for the study being reported is explained in *Chapter Two (Background)*. *Chapter Three (Methods)* follows with key elements of the study design including, setting, participants, data collection, and the planned analysis. Efforts to mitigate potential bias, and any deviations from the original plan are also addressed in this chapter. *Chapter Four (Results)* provides descriptive data on participants and networks and reports the main results of network and statistical analysis. Finally, the thesis concludes with *Chapter five (Discussion).* This chapter will revisit research objectives; provide an overall interpretation of results with consideration given to other pertinent research; discuss limitations, including direction and magnitude of potential bias and statistical imprecision; discuss the external validity of study findings and implications for practice and future research. This report uses the New England Journal of Medicine reference style.

Chapter Two: Background

2.1 Syphilis

Syphilis is a chronic sexually transmitted infection caused by the bacterium spirochete *Treponema pallidum*, sub species *pallidum*.[11] Syphilis has an extraordinary storied history; the origin and antiquity debated for centuries. The philosopher and physician Hieronymus Fracastorius first coined the name syphilis in his 1530 epic poem, *Syphilis sive morbus gallicus*, which means "Syphilis or The French Disease".[15] In the renaissance Latin poem, Apollo cursed the mythical shepherd "Syphilus" with the disease as punishment for worshiping king Alcithous instead of the Gods and the Sun.[15] Syphilis has long been known as the "the great imitator" because its variable clinical manifestations frequently mimic other diseases or infections.[11] Untreated syphilis infection will follow a progression that can be classified into primary, secondary, latent and tertiary stages.[11] However, symptoms can appear more than 30 years after exposure.[16] Primary and secondary stages are considered infectious. Latent syphilis can be subdivided into early and late latent infection. Early latent syphilis, which is defined as infection occurring within the previous year, is also considered infectious due to the possibility of relapse to the secondary stage.[16]

The impact of undetected syphilis can be profound and adverse. Untreated syphilis can lead to serious sequelae such as cardiovascular syphilis, neurosyphilis, late benign (gummatous) syphilis or death.[16] Congenital[a] syphilis underscores the serious consequences of untreated syphilis. Syphilis infection during pregnancy or a pregnancy that occurs in an infected woman can result in spontaneous abortion, premature delivery, stillbirth or perinatal death.[11] Also, co-infection with syphilis may facilitate the transmission of HIV.[12]

2.1.1 Transmission

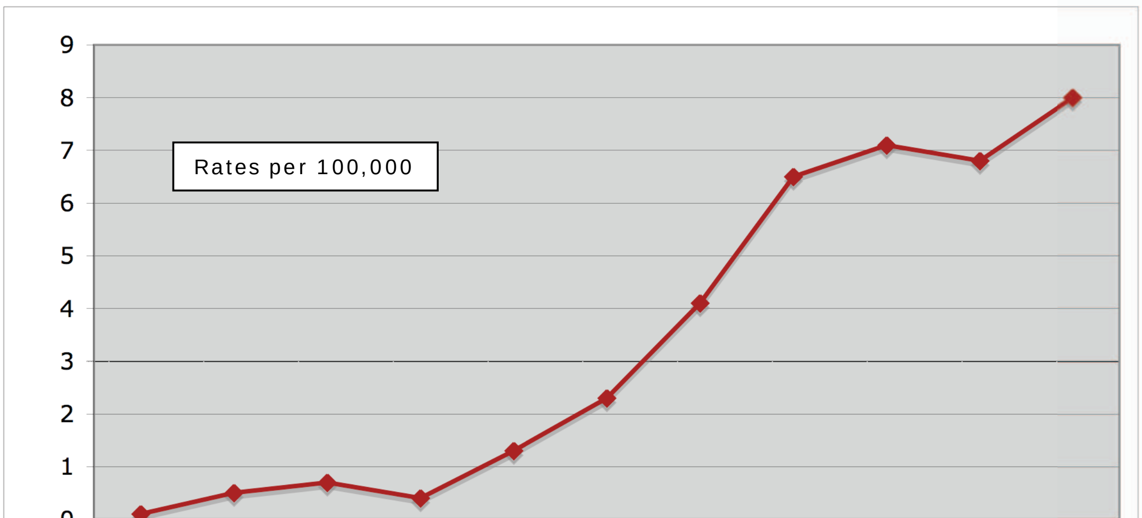
Although transmission of syphilis through kissing, blood products and accidental inoculation has been documented, the primary mode of transmission is by direct sexual contact through oral, vaginal and anal sex.[11] The estimated transmission probability per partner is approximately 60%.[17] Another important mode of transmission is transplacental treponemal infection to the fetus in utero and to a lesser extent by contact with a syphilitic lesion during childbirth.[18] The probability of vertical transmission in pregnancy can be as high as 100%.[11]

2.1.2 Epidemiology

Despite the accessibility of screening tests, and widely available antibiotics to cure infection, public health efforts to eradicate syphilis have been unsuccessful. The national rates of infectious syphilis among males and females have been rising progressively since 2000, with a greater disease burden among males. Between 2000 and 2008, reported rates of infectious syphilis among males increased from 0.7 per 100,000 to 7.3 per 100,000.[19] During this time, the reported rate among women increased from 0.4 per 100,000 to 1.1 per 100, 000.[19] Alberta, like many health jurisdictions in Canada, is faced with a

[a] Congenital syphilis is when an infant, born to a mother with untreated or inadequately treated syphilis, becomes infected with syphilis either in utero or at birth.[11]

concerning resurgence of infectious syphilis. In Alberta, there had not been any locally acquired infectious syphilis cases for a number of years prior to 2000.[20] **Figure 2-1** shows that between 2000 and 2009, reported rates of infectious syphilis increased from 0.5 per 100,000 (15 cases) [19] to a preliminary rate of 8 per 100,000 [22] (267 cases confirmed with several more still under investigation); about 67% of cases were among men (Alberta Health and Wellness, April 1 2010, unpublished data). Aboriginal persons are disproportionately affected, accounting for about 30 % of cases in 2008.[21] Traditional means of disease control have fallen short, resulting in twenty-three cases of congenital syphilis reported in the province since 2005 and five ensuing neonatal deaths (Alberta Health and Wellness, April 1 2010, unpublished data).



	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009
Rate	0.1	0.5	0.7	0.4	1.3	2.3	4.1	6.5	7.1	6.8	8

Public Health Agency of Canada.[19] Note 2009 data are preliminary.[22]

Figure 2-1: Rates of infectious syphilis in Alberta, 1999-2009

In March 2007, Alberta's Chief Medical Officer of Health officially declared a syphilis outbreak.[20] These disease rates are well above the Canadian target of syphilis reduction to no more than 0.5 per 100,000 population and the national goal to prevent all cases of endemic congenital syphilis.[23]

2.1.3 Local characteristics of syphilis outbreak

In 2009 there were 115 infectious cases reported in the Calgary Health region, accounting for 43% of infectious syphilis cases in Alberta. Among health regions in the province, the number of cases reported in Calgary was the highest (Alberta Health and Wellness, April 1 2010, unpublished data). Since the start of the outbreak in Alberta in 2002, it has shifted from the men who have sex with men (MSM) population to the heterosexual population. The proportion of MSM among cases in Calgary has decreased from 68% in 2006 to 33% in 2009 (Alberta Health and Wellness, April 1 2010, unpublished data). A comparable pattern was observed in the syphilis outbreak that occurred in Calgary between 2000 and 2002. During the first phase of the outbreak, syphilis was diagnosed in MSM exclusively. During the second phase, syphilis through heterosexual contact surfaced.[24]

2.1.4 Treatment and follow-up

There are no effective vaccines available and without treatment *T. pallidum* can endure in the human host for decades. Further, previously treated persons can be re-infected. Nevertheless syphilis infection is curable and treatment prevents further transmission and progression to tertiary stages provided that appropriate and adequate antibiotic regimens are given.

Penicillin, first shown to be effective in 1943 in the treatment of four men with primary syphilis,[25] remains the drug of choice for treatment of all stages of syphilis infection. However, the preferred preparation, route, dosage and duration of treatment are dependent on the stage of infection, and other clinical considerations such as disease manifestation and HIV co-infection. The Canadian Guidelines on Sexually Transmitted Infections [26] recommended treatment regimen for adults with infectious syphilis (primary, secondary and early latent of less than one year duration) is a single dose of benzathine penicillin G-long acting 2.4 million units given by intramuscular injection in two sites. In Canada, benzathine penicillin G-long acting injectable suspension is widely available in commercially prepared pre-filled syringes. This single dose regimen is highly effective and has been reported to achieve cure rates of 95-97% in patients with early syphilis.[27, 28]

Some experts recommend a longer course of treatment for pregnant women (2 weekly doses for a total of 4.8 million units) and individuals co-infected with HIV (three weekly doses for a total of 7.2 million units).[26] A more extensive treatment regimen (with different penicillin preparations used) administered intravenously is required for the treatment of syphilis infection of the brain or spinal cord and congenital syphilis.[26]

Because HIV co-infection alters the clinical management including treatment and follow-up, all individuals testing positive for syphilis should have HIV testing.[26] It is generally recommended that patients with infectious syphilis have repeat syphilis serology testing at 1, 3, 6, and 12 months after treatment to ensure an adequate serologic response and a cure was achieved.[26] Based on the incubation periods associated with each stage of infectious syphilis, all sexual contacts within the following time periods are located for testing and treatment: three months prior to the onset of symptoms for primary syphilis, six months prior to the onset of symptoms in secondary stage and one year prior to the diagnosis of early latent syphilis.[26] Under the *Public Health Act*, the attending physician can determine if contacts of infectious syphilis are treated immediately or on the basis of clinical and/or laboratory findings.[29] However, the Canadian guidelines recommend that all sexual contacts in the preceding 90 days be treated.[30]

2.1.5 Traditional partner notification

The cornerstone of STI control in Canada is contact tracing and partner notification. Infectious syphilis is reportable under the *Public Health Act* in all provinces and territories. Infected persons are interviewed to elicit names of sexual partners who are then located for testing and treatment. In Alberta, the *Public Health Act* mandates that all syphilis infections are reportable by all sources to the Provincial Chief Medical Officer within 48 hours.[29] Thus, all cases and sexual contacts of infectious syphilis are reported by the attending health care professional to Alberta Health and Wellness STI services using a standard Sexually Transmitted Infection form and an enhanced syphilis surveillance form. Laboratories are also legally required to report all positive tests to the provincial health program.

However, there are inherent limitations to conventional partner notification activities for syphilis control.[31-36] In a recent review of the empirical evidence on the effectiveness of case finding, Brewer [36] found that for approximately every four to five STI index cases interviewed, only one newly diagnosed case was found and brought to treatment; and this was similar across all bacterial STIs. In point of fact, the number of new cases found per index case may be substantially lower for defined subgroups of the population such as MSM.[37] Lack of case finding has been due in part to an inability to accurately obtain identifying information on sexual contacts. Paradoxically, many infected cases simply forget a substantial amount of their sexual partners.[35] Anonymous sexual partnering adds another degree of complexity. Hogben and colleagues [37] found 65% of MSM diagnosed with syphilis reported anonymous partners. This implies that many infected persons go undetected and in consequence endemicity is maintained in the population. Thus, attaining syphilis elimination will require innovative strategies to prevent infection and improve case finding. Mathematical models for transmission can inform public health strategies for prevention and control measures.

2.2 Basic model of infection transmission

A fundamental concept in epidemiology is the basic reproductive rate of an infection. Formally introduced by George Macdonald within the context of malaria,[38] the basic reproductive rate refers to the expected number of secondary infections produced by a single typical infected case in a completely susceptible population. In 1987, May and Anderson [39] applied this concept to HIV transmission. Their basic model for describing the success of sexually transmitted infection propagation was as follows:

$$R_0 = \beta Dc$$

Where the reproductive rate represents the average number of secondary infections produced by an individual infected with a STI. β denotes the probability of infecting a susceptible individual during one sexual contact, D indicates the duration of infectiousness of an individual who has acquired an STI, and c is the number of new susceptible sexual contacts per unit of time. If R_0 is > 1 then the STI will spread and if the number is < 1, prevalence will diminish.[39]

Public health interventions such as screening and early treatment, and strategies to increase condom use can reduce the values of one or more of these parameters.[40] However, over time there have been modifications to this model and recognition that social and sexual networks influence this basic reproductive number. A full understanding of the interplay between infection dynamics and sexual network structure is required to understand STI epidemics and implement effective intervention and health promotion strategies.[41]

2.3 Social network approach to infection transmission

The social network approach posits that dissemination of syphilis is socially constructed and that the risk of acquiring or transmitting the disease is a consequence of structured social and sexual interaction in a population. For these reasons, the utility of the social network approach for syphilis investigation and control has been proposed.[42] Given that the risk and behaviour in a social milieu may affect individual risk for acquisition of infection, this approach moves beyond the infected person, to others in their social or sexual circle who may be important to the transmission of disease.[42] A complex interplay of social and sexual interactions may shape the transmission of syphilis. Standard transmission models fail to capture the complexity of these social interactions in populations. The network approach may expand investigator knowledge of disease dissemination and factors associated with an epidemic. Following the same line of reasoning, this approach is well suited for identifying high-risk individuals or 'core groups' important in the transmission of the infection, who may be missed by standard investigative measures.[43]

2.4 The concept of a sexually transmitted disease core

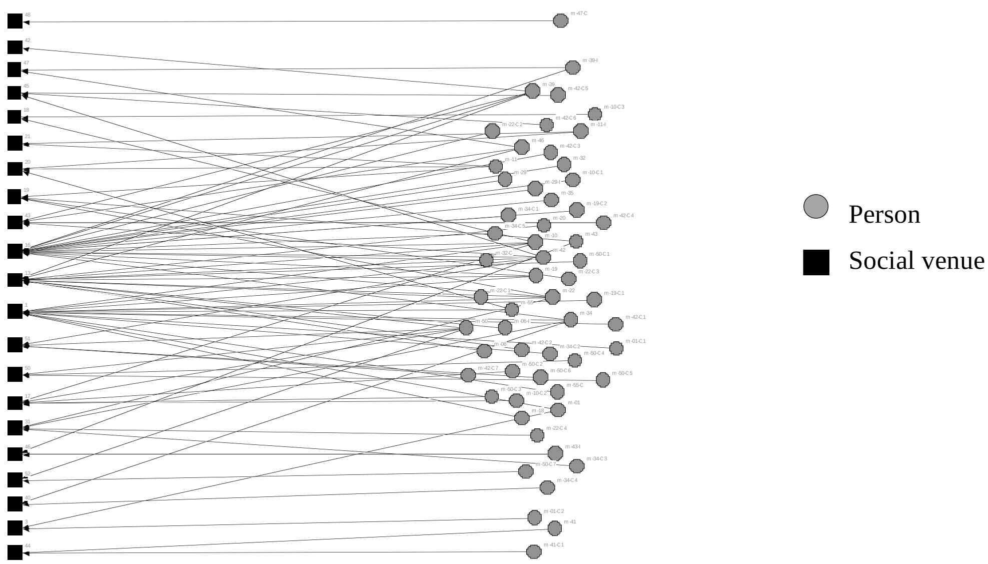
Yorke et al.[44] first explicated the notion of an STI 'core group' in 1978. Since that time the STI core group has been a central concept in STI epidemiology with regard to STI acquisition and proliferation. Core STI groups are small subgroups within a population that are characterized by extremely high rates of infection.[45] The STI core has been defined in terms of geographical location,[46-48] group prevalence,[44] and high-risk behaviors.[49] This subset of the population is thought to disproportionately contribute to STIs in the population as a whole. STIs remain endemic outside the core only through sexual contact with the core.[44] Given that theoretically, elimination of an STI from the core would eliminate the infection from the population, efforts to identify core groups has been enthusiastically promoted. Social network analysis is a methodological tool to study sexual network structure and examine core groups.

2.5 Social network analysis

The last decade has seen rapid growth in the interest of social network concepts and social network analysis. Social network analysis is both a theoretical model used to explain social phenomena and a methodological tool for examining patterns in the relationship or structure between data points (actors).[50-52] Social network analysis as an approach to research has become pervasive in recent years with application in sociology, physics, communication, economics, management, and biology. Social network methodology is an emerging field for studying epidemic transmission of infectious disease. In addition to this application, public health has seen enormous progress in the development of the network approach to study the dissemination of health information, the affect of social capital and social support on health, and for examining organizational networks to plan and evaluate public health programs.[52] The recent publications of the textbook by Wasserman and Faust [1] and Scott's [50] handbook have provided researchers with the lexicon for application of social network analysis.

The following overview is adapted from the two aforementioned publications.[1, 50] In social network analysis, data are collected on relationships as well as on actors. An actor can be any social entity such as an individual or an organization. The dyad, which is a pair of actors and the tie between them, is the unit of observation. Ties are relational links between actors and can be binary (such as sexual contact yes/no) or have value (number of people connecting two sex partner meeting places). A social network then, is a distinct group of actors linked directly or indirectly together by defined social ties. A network can be one-mode, consisting of single set of actors (i.e. individuals) or two-mode, containing two sets of actors (i.e. places and people). In network analysis, a network is viewed as a mathematical graph consisting of vertices (actors or nodes) and edges (connections or links). The network analysis method to investigate relational data consists of examination of ties at the node level or both quantitative and qualitative measures of network structure among subgroups or among the entire network. Mathematical concepts are used to quantify structural properties of the connection between nodes. Analyses of networks draws on three areas of mathematics; mathematical relations, graph theory and matrix algebra. Important advances have also been made in statistical methods to analyze network data.

Visual representation of the mathematical graph is an important aspect of social network analysis. The actors are represented as points or nodes and the tie or link are shown as lines. Network software offer spatial positioning important for qualitative interpretation of the network. For, example a two-mode affiliation network can be represented by a bipartite graph where nodes are divided into two distinct independent sets (people and places); every line connects a node from each set (**Figure 2-2**). However, spatial positioning is absent in the mathematical representation of a bipartite graph, making the graph difficult to interpret.[53]



The squares represent sex partner meeting places and the circles are individuals

Figure 2-2: Bipartite graph representation of two-mode sexual affiliation data

Social network analysis has been proposed as a novel approach to understanding the behavioural epidemiology of syphilis.[42] While the utility of social network analysis was extensively recognized in the social sciences, it was the AIDS epidemic that propelled the expansion of social network theory to the transmission of STIs. The relational approach has made important advances as an alternative to traditional epidemiologic theory, such as the epidemic curve, in examining outbreaks of syphilis.[43, 54, 55] The rate and scope of STI propagation is dependent on the structure of the social and sexual connections within the population.[2-9] Consequently, knowledge of the structure can provide opportunity for breaking the chain of infection. The implicit assumption is that network structure plays a pivotal role in syphilis outbreaks. However collecting data on sexual networks presents a formidable challenge. First, the aforementioned poor sex partner recall, anonymity and pseudo-anonymity (partial information about sex partners) challenge conventional contact tracing practices. Second, sexual networks are fluid due to high sex partner turnover. Stigum et al.[56] and Humblet and colleagues [57] provided evidence that membership in the STI core is continuously changing with a notably high annual migration rate moving in and out of the core. Intuitively, places where people meet partners may be easier to recall than people and are stationary. Thus sexual affiliation networks may be more stable.

2.6 From high-risk people to high-risk places

The notion that sex partner meeting places play a central role in transmission dynamics of STIs has generated considerable interest. Potterat et al.[58] initially recognized the importance of social venues in the establishment of sexual ‘core groups’. It is of some interest then, that Wylie and Jolly [59], who analyzed an exceptionally large sexual network of 4500 people in the province of Manitoba, found that sexually connected individuals were geographically widespread. Wylie and Jolly posited that this was suggestive of other factors, such as places of social aggregation, which may provide opportunity for establishing social and sexual networks.

Numerous recent observational and analytical studies have reported that individuals, particularly MSM, utilize social venues for seeking sex partners. Substantive examples of venues attended for the purpose of sexual partnering are extensive and include bathhouses,[24, 60-67] public cruising sites such as parks and bathrooms,[60, 61, 64-67] bars or nightclubs,[24, 60, 63, 65-68] and the Internet.[24, 60, 63, 65-67, 69-76] Venue sex seekers are more likely to be men and homosexual.[70, 71] Many of these reports consisted primarily of MSM, with the exception of two fairly large cross-sectional surveys [70, 71] and a sexual network analysis study,[68] where the majority of participants identified as heterosexual.

The vast use of venues for seeking sex partners is compelling. Three recent case control studies that examined risk factors associated with early syphilis in MSM are case in point. Niccolai and colleagues [66] found 52% of cases reported meeting sex partners at venues such as bars, the Internet, and adult bookstores. Imrie et al.[64] reported that 74% of cases and 65% of controls visited a public cruising site or bathhouse and a study in New York city found that almost 80% of all participants reported visiting at least one venue (bathhouse, bar, public cruising site, or sex/circuit party) with the intent of meeting a sex partner.[60] In a recent cross-sectional study in the United Kingdom, it was reported that 35% of MSM diagnosed with syphilis acquired the infection at a social venue.[67] Understanding the relationship between sexual risk behaviour and sex partner meeting places is of particular importance.

2.6.1 Sexual risk behaviour and sex partner meeting venues

Many epidemiological studies have examined the association between high-risk sex-related behaviour and places where sex partnering occurs. There appears to be a link between sex partner meeting venues and sexual risk behaviour such as drug use,[61, 72, 73] multiple partnering, [70, 71, 76] anonymous sex,[62, 73] previous STDs,[70, 71] and unprotected anal intercourse (UAI).[61, 62, 76, 77]

Increased risk of HIV transmission in men who seek partners at venues has also been investigated. Some studies have found that individuals using the Internet to find partners report more casual partners known to be HIV positive than those not finding partners on-line.[70, 74, 75] Current HIV infection has also been associated with meeting partners in venues. A cross-sectional study that examined the relationship between early syphilis infection and commercial sex venue use, found that MSM diagnosed with syphilis were twice as likely to be HIV positive (OR, 1.91: 95% CI, 1.36-2.68) if they met their sex partners at a bathhouse or sex club compared to those who did not meet their partners at these venues.[62] Though limited by study size, multivariate analysis in a recent case control study found recent HIV infection was associated with meeting sex partners on line (OR, 6.7: 95% CI, 1.6-27.7), at a bar/club (OR, 8.2: 95% CI, 1.5-45.7), or at a bathhouse/sex club (OR, 11.5: 95% CI, 1.7-77.2) [63] Although this finding is informative, the adjusted odds ratios necessitate a conservative interpretation considering the width and location of the confidence intervals.

It is important to highlight that observational studies have serious limitations in establishing the temporal sequence between cause and effect and most studies have not addressed the complex underpinnings of sex partner venue use. As such it is not completely clear whether venues create an environment for high-risk behaviour or whether those with a propensity for high-risk behaviour may be more likely to use venues for sexual partnering. This point is made in the meta-analysis by Liau et al.[77] Nevertheless, these data indicate that individuals with a high-risk of STI acquisition and proliferation do meet their partners at identifiable venues. Thus, it is intuitively reasonable that identification of sex partner meeting places may identify core STI transmitters and perhaps, those mostly likely to be infected with syphilis next. Furthermore, detection of venues rather than core groups based on individual characteristics (e.g. sex trade worker, intravenous drug user, MSM) reduces stigmatization. Arguably, this could provide public health officials with a target for primary and secondary prevention strategies to prevent further dissemination of disease.

2.6.2 Place-based interventions

The conception that places where sex partnering occurs may be useful markers for identifying core STI transmitters has led to efforts to target places. The PLACE intervention model was developed to identify places/geographic areas where targeted AIDS prevention programs could reach populations most at risk for HIV transmission.[78] The five-step approach in the PLACE methodology includes a step where 200-300 key informants are asked to list specific places where individuals go to meet sex partners. This method has been implemented in different settings with promising results.[79-82]

Michaud et al.[83] illustrated the potential of targeted intervention aimed at high-risk locations where sex partnering occurred. Although the number was modest, new cases of syphilis that had not been identified through conventional case-finding activities were reached at the targeted area.[83] More practical techniques are required to identify places important in syphilis transmission and to quantify the role they play in an outbreak.

2.6.3 Sexual affiliation network

A sexual affiliation network is a network of persons and the places they visit to seek sex partners. Analysis of a sexual affiliation network may provide important information about transmission dynamics and underlying sexual networks.[10] In the classical paper "The Duality of Persons and Groups", Breiger expands the sociometric notion that networks can only be defined by connections between homogenous nodes.[84] Through the application of matrix algebra, Breiger [84] illustrated an analytical technique that exemplified that nodes in one matrix could be links in a dual matrix. Put succinctly, he took a two-mode affiliation network (a person-to-social event network, where the rows in the matrix were persons, the columns social events, and the link the affiliation), and transformed it into two distinct one-mode networks (a person-to-person network where the nodes were persons and the link an affiliation to the same social event(s) and a social event-to-social event network where the nodes were social events and the link was the affiliation of persons to those events). The rationale for the application of Breiger's method to analyze an affiliation network is that it permits the connection of people through patronizing the same social event or conversely the connection of events through people, or both.[1] The connection of persons infected with syphilis through social venues is in the realm of applicability with the approach proposed by Breiger.

The empirical literature is relatively silent with regards to the analysis of a sexual affiliation network to quantify the role social venues play in an epidemic, with some exceptions. Although the approach used differed from that of Breiger,[84] Klovdahl et al.[85] conceived the notion of an outbreak network where the node of interest may be an individual or place and the line or tie any "epidemiologically-relevant" interface between them. In an outbreak of tuberculosis disease, standard contact investigation and fieldwork failed to connect 50 % of patients infected with the same DNA strain to another infected person. The index case could not be linked to anyone else in the outbreak.[85] Subsequent research used social network methods to connect the seemingly isolated cases through social venues. When an outbreak network was reconstructed (where nodes in the network could be either a person or place), connections between persons emerged to provide new insights into transmission of the tuberculosis infection in the outbreak. Analysis of the outbreak network revealed that the most important nodes (person or place) in the network, as measured by centrality scores, were a "pick-up" bar and a popular meeting place.[85] The authors of this study concluded the outbreak was "place-associated"; the spread of infection may not have occurred within the social venues, rather individuals may have recalled places better than people whom they had contact with.[86]

Similarly, in a network study of a gonorrhoea outbreak in northern Alberta, a social venue emerged as the key for understanding the spread of infection. A motel bar connected the geographically widespread distribution of sexually linked persons; some living more than 200 km apart.[68] The authors of the study demonstrated that individuals who attended the bar had higher network centrality scores (thus more likely to facilitate disease transmission) than those who did not patronize the bar, and also were the links between local networks and larger populations.[68] It is of particular interest that this network study corroborated the findings of an earlier case-control study involving the same outbreak; that the bar was the source of the epidemic.[87] More recently, the formation of high-risk networks around venues assisted in the understanding of infectious disease transmission patterns among intravenous drug users.[88]

2.7 Summary

Traditional syphilis-control measures have not been successful in reducing the rates of infectious syphilis in Canada; on the contrary rates are increasing considerably. Sex partner meeting places may be an important catalyst for disease dissemination. Social network analysis has the potential to provide quantitative evidence of the relative importance of places to the proliferation of STIs in the population, although empirical evidence is limited. Further research is necessary for evaluating the utility of social network analysis to quantify the role places of social aggregation play in syphilis transmission. Furthermore, analysis of a sexual affiliation network could provide valuable epidemiologic information needed to target venues for STI prevention and control.

Chapter Three: Methods

This section describes in detail the methodology used in this study including what was planned and any deviations from the original plan. Furthermore, efforts to address any sources of potential bias in the design stage are explained.

3.1 Study design

A snowball or link-trace network survey design was used. This network design is used when it is not possible to enroll the entire population of interest. This design is on the continuum of network sampling designs between complete network design, where the entire population of interest is enrolled and an egocentric design, that produces local (personal) network data only.[51] A network survey design requires revision of conventional survey methodology. The advantages of a network survey design are increasingly recognized.[51] Given that the goal of social network analysis is to analyze the structural properties of networks by examining the nature of the connections between nodes, the central unit of interest is the relation or link. Examining partnerships or links pose unique challenges with respect to sampling, instrument design and analysis that can be addressed using a network survey design.[51]

3.1.1 Network sampling

There are two sampling units in network sampling: the respondents and the links between them. The sampling frames for the individual and for the connections between individuals are nested.[51] Accordingly, this project employed two different sampling approaches to sample these two levels. The population of interest was individuals with infectious syphilis in the Calgary area. Identification of syphilis requires that infected individuals interface with the healthcare system. Thus, the sampling frame for the individual unit was all diagnosed infectious syphilis cases in the Calgary area during the four-month time period from April-August 2009. There are two separate relations of interest for the 'link' in this study: 1) the sexual encounter(s) of infectious syphilis cases and 2) the same affiliation(s) with a sex partner meeting place. The sampling frame for sexual partnerships and affiliations of positive syphilis cases is unknown. In network studies, the method used to sample relations is part of the survey instrument. The technique used, a "name generator", determines the sampling frame to be sampled in each successive generation of partnerships [51] and the sampling frame for the venue affiliations. A free recall [1] format was used to generate names. That is, no limits were placed on the amount of sexual partners or places named.

3.1.2 Network boundary

In network studies, network boundary specification is of particular importance. An appropriately defined boundary allows identification of the target population and permits the researcher to describe the population under study.[1] Inappropriate inclusion or exclusion of individuals may produce erroneous network measurements. When the boundary is unknown (such as a hidden population of syphilis cases), certain sampling techniques such as link-trace or snowball sampling, can be used to define network boundaries.[1]

3.1.3 Survey instrument

The Alberta Health and Wellness Syphilis History and Syphilis Contact Notification form (10/6/2006) was used to collect socio-demographic and relational data **(Appendix B)**. In addition, to generate names of social venues, subjects were asked to identify places they attended where sexual partnering may have occurred. This question was adapted from the work of De and colleagues [68] and Michaud et al.[83, 89] Since untreated persons infected with syphilis may be infectious for up to one year [11], subjects were asked to list places frequented in the last year. A semi-structured question was used to facilitate the collection of sufficient information to allow characterization of the social venue with confidence **(Appendix C)**. The question was read verbatim to each participant to prevent interviewer bias. The use of prompts to allow characterization of the venue was done only after a place was named. Participants were told that sexual contact did not need to occur at that venue for the place to be named.

Although, the researcher inquired about venues in the last year, only partner and venue information in the last six months was retained for analysis for four central reasons: 1) Although most partner interviews were done by the investigator, some patients who agreed to the study on a subsequent visit had their partners ascertained by the clinic staff. If the patient was known to have primary or secondary syphilis only sex partner data for the last six months was collected. 2) Very few participants could provide names of sex partners up to one year. 3) A fair comparison of the sexual and venue networks required that partner and venue information be collected over the same time period. 4) Very few sex partners and only five venues were lost when data was restricted to six months. This decision likely reduced the potential for bias due to memory error. Even among participants who intend to respond accurately, recall of past behaviour can be problematic. Memory recall is pivotal to the correctness of self-report of sexual behaviour.[90-92] Not surprisingly, the longer the recall period the more likely subjects are to forget sex behaviour information in general [90, 92, 93] and sex partners in specific.[35] Also, other researchers have agreed that targeted intervention at more recent venues may be more valuable for disease control.[89]

3.2 Study setting

This study recruited diagnosed infectious syphilis cases and their sexual contacts from the Calgary Sexually Transmitted Disease (STD) clinic in Alberta, Canada during a four-month time period from April 20, 2009 – August 25, 2009. The STD clinic was chosen as the recruitment site because it is the referral site for infectious syphilis cases in the Calgary area. The Calgary STD clinic is a free, confidential walk-in clinic that plays a key role in managing the spread and impact of syphilis in the Calgary area through: 1) early syphilis diagnosis; 2) provision of comprehensive treatment and monitoring of infected persons; 3) identification, location, and thorough follow-up of sexual partners of infected persons; 4) case surveillance; 5) health professional education and increased awareness; and 6) research.

As outlined in Chapter two, all laboratories and health care providers are legally required to report cases of syphilis infection to the Provincial Chief Medical Officer, Alberta Health and Wellness. Subsequently, Alberta Health and Wellness notifies the Calgary STD program of all infectious syphilis cases in the Calgary area that have been identified. Calgary STD clinic staff coordinates treatment and follow-up. Public health nurses employed at the clinic most often arrange for treatment and complete the interviewing and partner notification of these cases. In fact, 97-99% of all identified Calgary area infectious syphilis cases are interviewed and treated by the Calgary STD program staff (Colleen Roy, personal communication).

Shortly after we started recruitment it was recognized that some patients who met study eligibility criteria were not recruited because they were treated offsite through the STD clinic outreach program. These offsite locations included other places within the Alberta Health Services-Calgary and area boundaries such as, the Safeworks street van, other community agencies, other healthcare institutions, and patient's residences. A subsequent amendment to the study protocol to include offsite locations for patient recruitment was submitted and approved by the Conjoint Health Research Ethics Board.

3.3 Study procedure

Participants in this study were a convenience sample of individuals with diagnosed infectious syphilis and their sexual contacts identified through the Calgary STD clinic during the study period. All suspected infectious syphilis cases 18 years of age or older and their adult sexual contacts were eligible. For consenting purposes, reading English was also a study requirement.

To improve data quality, all interviews were conducted in person at the STD clinic by the principal investigator. Sampling began with an initial number of identified syphilis cases. This first generation of cases was interviewed to generate names of sexual partners. All named sexual partners were contacted by STD contact tracing nurses at the STD clinic and arrangements made for testing and follow-up at the STD clinic in the usual manner. Then individuals from the list of sex partners produced by each first generation case were interviewed next. Only those with syphilis infection had their sex partners enrolled in the subsequent generation. This link-trace procedure continued until the end of the four-month time period. In addition to standard contact tracing information, participants were asked to list all venues attended in the last 12 months where sexual partnering may have occurred.

Convenience and link-trace sampling violates the assumption of independence required for a random sample. However the general principles based on probability theory and the law of large numbers has not been proven with relational data.[50] The assumption of link-trace sampling in network studies is that the linked segment of the sample network is representative of the linked segments of the complete network.[50] Through a series of Monte Carlo simulations Johnson et al.[94] demonstrated that this sampling technique produces valid estimates of individual centrality in a social network that was representative of the population parameter. Furthermore, this sampling technique allowed the identification of a relatively bounded network. Also, a random sampling method would not provide a sufficient number of contacts to be located and interviewed in the allocated amount of time for data collection. On balance, this sampling strategy appropriately identified the target population and recruited available diagnosed syphilis cases and a set number of their contacts within the predetermined timeframe.

3.3.1 Maximizing response rate

Participation may be influenced by the subject's perception of confidentiality. Persons attending STI clinic settings may have behavioural and social features that make them especially vulnerable, and as such may not trust health officials. If subjects perceive confidentiality to be compromised, it is likely that those most at risk (e.g. the homeless, persons who trade sex for money and drugs, socially stigmatized populations such as MSM) will be less likely to participate. Ideally, developing trust and rapport over a long period of time would circumvent this bias. However, the STD clinic is a well-established confidential clinic, and trust and the approach utilized by the staff can mitigate this potential bias.[93, 95]

Participation may be influenced by mode of data ascertainment. Face-to face interviews were conducted to maximize participation as this method of data collection has been shown to decrease non-response.[96] Although monetary incentives were not provided, other strategies based on Dilman's social exchange theory [97] were incorporated. These included, showing positive regard to subjects (*reward*), reducing any inconvenience by having the researcher on site for the duration of the study period (*cost*), and giving the respondents reason to *trust* the interviewer.

3.3.2 Minimizing the potential for bias with self-report methods

Self-reports of sexual behaviour have been criticized for being inherently unreliable and invalid. Sensitive survey questions are intrinsically vulnerable to error for three central reasons; 1) participants may view the questions as an invasion of privacy, 2) fear of disclosure due to legal repercussions (e.g., for those who participate in illicit drug use or prostitution), and 3) the question requires that the participant admit she/he has participated in socially undesirable behaviour (e.g. sex with prostitutes).[98] In consequence, the threat to validity is threefold: 1) higher overall non-response rates 2) lower item-specific response rates and, 3) greater measurement error than surveys on other topics.[98] Once more, the approach utilized by the researcher and staff mitigated this potential bias.

To reduce reporting bias, techniques that improve recall of sexual behaviour, such as providing anchor dates for the six-month reporting period, and use of calendars [99] were utilized. The interviewer used direct questions without apology or tentativeness to reduce ambiguous responses.[99] As well, the survey question was designed to “place the burden of denial on the participant”.[99] Finally, face-to-face interviews allowed the interviewer to provide clear definitions, clarify and probe unclear or vague responses.[92]

Prior to data collection, to improve classification of venues named by participants, the researcher met with a key informant from the gay community who was likely to be familiar with places where men go to meet new sex partners. During data collection, all public venues named were verified for authenticity and location. To help classify street venues, such as sex strolls, the researcher went on a ride-a- along with the harm reduction team on the Calgary Safeworks street van. Mobile services provided by the van are part of the Harm Reduction program in Calgary that was developed to prevent the spread of HIV and hepatitis. The Safeworks street van targets populations involved in prostitution and those living with substance abuse with a goal of increasing knowledge about unsafe injection and sexual practices that may lead to hepatitis/HIV transmission.

3.3.3 Laboratory detection of syphilis and diagnosis

Syphilis diagnosis and stage was determined by the Calgary STD clinic medical director based on history, clinical examination, collection and analysis of a syphilis lesion specimen and/or interpretation of syphilis serology.[26]

Accurate laboratory findings are of particular importance to the diagnosis of syphilis. In response to the syphilis outbreak in Alberta, regional laboratories forward syphilis serology requests to the Provincial Laboratory for Public Health. The serologic tests used for syphilis detection are as follows: 1) Syphilis enzyme immunoassay (EIA), the screening test (Architect Syphilis TP, ABBOTT Laboratories, Illinois, U.S.A., 2007); 2) Rapid Plasma Reagin (RPR) to monitor therapy (BD Macro-Vue ™ RPR, Becton, Dickinson and Company, Maryland, U.S.A., 2008); and 3) Syphilis INNO-LIA, the confirmatory test for syphilis (Innogenetics NV, Ghent, Belgium, 2008).

The ARCHITECT Syphilis TP assay is a chemiluminescent microparticle immunoassay for the qualitative detection of IgG and/or IgM to *T. pallidum* in serum or plasma. This two-step highly automated assay is a screening test for syphilis. As outlined by the manufacturer, the sample, micoparticles coated with recombinant *T. pallidum* antigens (TpN47 TpN17, and TpN15) and assay diluent are combined. After washing the acridinium-labelled anti-human IgG and IgM conjugate is added in the second step. Following another wash, Pre-Trigger and Trigger Solutions are added to the reaction mixture. The resulting chemiluminescent reaction is measured as relative light units (RLU). A sample is considered *T. pallidum* antibody positive if the chemiluminescent signal in the sample is greater than or equal to the cut-off signal. Samples with a chemiluminescent signal less than the cut-off are considered negative. The ARCHITECT Syphilis TP assay has demonstrated sensitivity of 98.4-99.2% and specificity of 98.4-99.1% in the literature. [100, 101]

The Rapid Plasma Reagin (RPR) 18 mm circle card test is not used as a diagnostic test because it has been shown to be insensitive to primary and late syphilis.[102] Rather, the RPR is used for staging syphilis infection, monitoring efficacy of therapy (falling titres), and determining re-infection (rising titres).[103] To perform the laboratory test, the patient's serum is placed on the plastic-coated card and antigen is added. The RPR antigen suspension is a carbon particle cardiolipin antigen that detects reagin, an antibody-like substance present in serum or plasma. A mechanical rotator is used to mix the antigen and antibody. After rotation the cards are macroscopically read. The reagin binds to the test antigen causing flocculation (clumping). When a specimen contains antibody, black clumps against the white background of the plastic-coated card appear (reactive). If the specimen does not contain antibody an even light gray color is visible (nonreactive). All samples indicating reactivity are read quantitatively in terms of the highest dilution. Sensitivity and specificity of the RPR test are stage specific. The range of sensitivity reported in the literature is 77-100% in primary syphilis, 100% in secondary syphilis, 95-100 % in latent and 73% in late latent syphilis; the test has demonstrated a 93-99% specificity.[103]

The syphilis INNO-LIA line immunoassay is a confirmatory test for *T. pallidum* antibodies in serum or plasma. Three recombinant antigens (TpN47, TpN17, TpN15) and one synthetic peptide antigen (TmpA) derived from *T. pallidum* are coated as discrete lines on a nylon strip. In addition to these treponemal antigens, the test strip has four control lines. The test is based on the enzyme immunoassay principle. When a serum or plasma sample is incubated with the antigen coated strip *T. pallidum* antibodies, if present, will bind with antigen lines present on each strip. Addition of a substrate produces a dark brown color proportional to the amount of *T. pallidum* antibody present in the sample. Performing the test is a labour-intensive manual procedure. Results are interpreted by comparing the color intensity of antigen lines to control lines. A sample is considered *T. pallidum* antibody positive if two or more bands with minimum color intensity of 0.5 are visible. A sample is considered negative if all the bands have color intensity less than 0.5 or if only a single band has a maximum intensity of 0.5. Indeterminate results occur if one band has a minimum intensity of 1.[104] Evaluation of this assay in the literature has demonstrated high sensitivity and specificity, 100% and 99.3% respectively.[104]

In addition to the serologic tests used for syphilis detection, dark-field examination was also employed for direct visualization of *T. pallidum.* Direct visualization of *T. pallidum* from lesions of primary and secondary syphilis is a definitive diagnosis for syphilis.[103] Treponemes cannot be visualized with the standard light microscope. Dark-field microscopy is an illumination technique that changes the path of the light so it illuminates the specimen from the sides causing particles in the sample to be brightly lit against a dark background.[103] Exudate was obtained from the lesion, placed on a slide and read under the microscope immediately. Treponemes are identified by their morphology and distinctive corkscrew movement.[103] It is difficult to distinguish *T. pallidum* from spirochetes in the mouth thus dark-field microscopy is not reliable with oral lesions.[103] Although the sensitivity of this test has been reported to be around 80%,[103] sensitivity of dark-field examination is highly dependent on the training and experience of the user.

3.4 Network construction

Three distinct one-mode networks were constructed: 1) a sexual network of syphilis cases and their sex partners, where the variable that defined the network was a sexual relation; 2) a sexual affiliation network where the nodes were infected cases and their sex partners linked together by their patronage of the same social venue; and 3) the dual network where the nodes were venues and the variable that defined the network was the patronage of persons to those social venues. None of the participants self identified as bisexual, thus two mutually exclusive sexual networks were constructed; a sexual network of MSM and a sexual network of individuals who identified as heterosexual. Sexual affiliation networks were constructed in a parallel approach, as there was no common patronage of venues between persons who identified as heterosexual and those who identified as MSM.

3.4.1 Sexual network

A sexual relation was defined as any vaginal, anal or oral sexual contact. The sexual network was constructed by simply linking infected cases and all named sex partners in the last six months.

3.4.2 Duality of a sexual affiliation network

The term venue was used to define any event, private, public or virtual place that was attended in the last six months where a sexual partner was met. The network of individuals (syphilis cases and their partners) connected by a social venue and the network of venues connected by the patronage of those persons were constructed by employing the analytic method proposed by Breiger.[84] That is, a two-mode affiliation network '*A*' (where the rows in the matrix are infected persons and their partners, and the columns sex partner meeting venues) was transformed into two separate one-mode networks; a network of persons linked by a social venue '*P*' and a network of social venues linked by persons '*S*'. This was done by simply transposing the original two-mode matrix, applying matrix multiplication to find the product of the original and transposed matrix to construct the person-to-person network ($P = A\,(A^T)$) and calculating the product of the transposed and original matrix to construct the venue-to-venue network ($S = (A^T)\,A$) (**Figure 3-1**). The mathematical proof is not presented here but has been previously described in detail by Breiger.[84] Transforming a two-mode affiliation network into two separate one-mode networks allows the researcher to apply the standard social network analytical tools used for one-mode networks and permits one to perform a simultaneous dual analysis.[1]

3.4.3 Network size

The number of cases in the Calgary area during the study period determined the size of the networks. Structural analysis using a partial network design is less dependent on network size, rather that relevant individuals are included in the network (appropriate network boundary). Link-trace sampling was used to define network boundaries and no limits were placed on the amount of sexual partners or places named.

Step one: Transpose the matrix

	Sex partner meeting places		
	X	Y	Z
People			
A	1	0	1
B	0	1	0
C	0	1	1
D	0	1	0

Original matrix 'A'

	People			
	A	B	C	D
Places				
x	1	0	0	0
y	0	1	1	1
z	1	0	1	0

Transposed matrix 'A^T'

Step two: Matrix multiplication

$(A^T)A =$

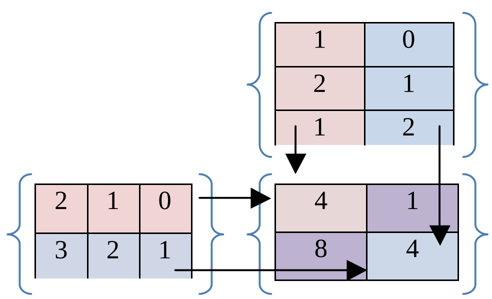
	Sex partner meeting places		
	x	y	z
x	1	0	1
y	0	3	1
z	1	1	2

$A(A^T) =$

	People			
	A	B	C	D
A	2	0	1	0
B	0	1	1	1
C	1	1	2	1
D	0	1	1	1

An analytic method proposed by Breiger:[84] a two-mode affiliation network '*A*' is transformed into two separate one-mode networks; a network of persons linked by a social venue '*P*' and a network of social venues linked by persons '*S*'.

Matrix multiplication example



$$\left\{\begin{matrix} 2\ 1\ 0 \\ 3\ 2\ 1 \end{matrix}\right\} \cdot \left\{\begin{matrix} 1\ 0 \\ 2\ 1 \\ 1\ 2 \end{matrix}\right\} = \left\{\begin{matrix} 2x1 + 1x2 + 0x1 & 2x0 + 1x1 + 0x2 \\ 3x1 + 2x2 + 1x1 & 3x0 + 2x1 + 1x2 \end{matrix}\right\} = \left\{\begin{matrix} 4 & 1 \\ 8 & 4 \end{matrix}\right\}$$

Figure 3-1: Duality of an affiliation network

3.5 Network analysis

There were two levels of analysis in this network study; global or group-level network analysis and point or node-level analysis. Group-level analysis was used to compare the network structure of persons connected through sexual contact with the network structure of persons connected through venues. Node-level analysis was used to determine what type of venue connected the most individuals. The primary outcome variables for group-level network analysis used to compare the network structure of persons linked together by sexual contact versus connected by a social venue were network density, connectedness, Freeman's degree centralization, size and frequency of components and clique structure. The primary outcome variables for point-level network analysis were Freeman's point degree and betweenness centrality.

3.5.1 Group-level network parameters

Density is one of the most widely used group level parameters in network analysis. It refers to the level of network cohesion.[1] A compliment to density is network connectedness. A graph is connected if all points are reachable from all other points in the graph (i.e. one component).[1] Densely connected sexual networks have implications for transmission of infection.

Degree centralization quantifies the extent to which centrality of the most central vertex or node varies from the centrality of all other nodes in the graph.[105] For example, a highly centralized network would take the shape of a star, where a single central node is connected to all other nodes in the graph, that are not connected to each other. This important group-level measure can provide important insights into the organization of the network around particular central nodes.

Components are simply connected subgraphs in a larger graph where all points are reachable from all others (by either direct or indirect ties) and no points have ties to points outside the component.[50] Component structure can provide insight into areas of high density, thus high infectivity.

Finally, cliques can be defined as a subgraph of three or more points in which all points are adjacent to each other.[1] Cliques can overlap, that is the same node can be connected to more than one clique. Analysis of clique structure can be insightful for identifying patterns of venue use.

See **Appendix D** for a detailed explanation and mathematical definition for density, Krackhardt connectedness [106] and Freeman's centralization measure.[105] Ties were treated as undirected, and dichotomized prior to the calculation of these group-level network parameters. Values for density, connectedness and centralization measures are proportions that range between 0 and 1, which are expressed as percentages in this report. All network parameters (network density, Freeman network centralization index, connectedness, cliques and centrality), were calculated using UCINET version 6.247 Software for Social Network Analysis.[107] UCINET was also used to draw network maps.

3.5.2 Node-level analysis

To determine what type of venue connected the most individuals, algebraic measures of network point degree and betweenness centrality were calculated for the venue networks. A classical measure of point centrality is degree centrality. Degree of a point is the number of other points it is adjacent to. Degree centrality is simply the vertex that has the most direct connections to other vertices in the network or graph.[105] In a network of sex partner meeting places the venue with the highest degree centrality is the one that is directly connected (by people) to the most other venues. A node that lies on the shortest path or geodesic between other nodes has betweenness centrality.[105] This centrality index can measure the extent to which places act as intermediaries for the spread of information through a network. Venues that are between other venues connect places (and therefore the people who visit them) that are otherwise not connected. Thus these venues may influence how information is disseminated through the network of venues. A detailed description and mathematical definition of these indices is located in **Appendix D** of this report.

Since one-mode ties derived from two-mode ties are always symmetric, the venue network is undirected (symmetric) by nature. The calculation of point betweenness centrality also requires the data to be binary. This is logical bearing in mind the definition of betweenness centrality. Point degree centrality however can be calculated with valued data. Dichotomizing ties in the venue network prior to the calculation of point degree centrality was intuitively unsatisfying. The valued tie indicated how many individuals connected two venues. This is important when considering a health intervention such as social marketing. Arguably a venue that is connected to three other venues by twenty people is more important than a venue connected to three other venues by three individuals. For valued data the non-normalized values of degree centrality should be used and are reported as sums of all degrees. Betweenness scores are normalized and are expressed as a decimal value ranging between 0 -1 in this report.

3.5.3 Core-periphery blockmodeling

Blockmodeling of social networks is a social network technique that aims to reduce an observed, often complex social structure into a simpler model of relationship patterns.[108] The basic idea of the core/periphery structure is that a network can be separated into exclusive groups; a highly dense cohesive core and one or more periphery positions that are connected to the core but not to each other (low density).[1, 109] For example, in the venue-to-venue matrix this model will identify a set of venues that have high density of ties between them because they share many individuals in common. UCINET uses two methods to find the core/periphery structure; the continuous model that estimates the degree of "coreness" of each node, and the discrete model.[109] The discrete model was used in this analysis. This method subdivides nodes into two classes, the core and the periphery. Five fit function algorithms are available in UCINET; this analysis use the "CORR" function which uses Pearson correlation to correlate the permuted observed data matrix to an ideal structure matrix consisting of ones in the core block and zeros in the peripheral block (**Figure 3-2**).[109] UCINET will give you an overall goodness-of-fit value of a given blockmodel. A high goodness-of-fit value implies good fit with the ideal structure. However, statistical testing for the significance of the core/periphery structures was not done thus the blockmodeling methods used in this report are primarily descriptive.

		1	2	3	4	5	6	7	8	9	10
	1		1	1	1	1	1	1	1	1	1
	2	1		1	1	1	1	1	1	1	1
Core	3	1	1		1	1	1	1	1	1	1
	4	1	1	1		1	1	1	1	1	1
	5	1	1	1	1		0	0	0	0	0
	6	1	1	1	1	0		0	0	0	0
	7	1	1	1	1	0	0		0	0	0
Periphery	8	1	1	1	1	0	0	0		0	0
	9	1	1	1	1	0	0	0	0		0
	10	1	1	1	1	0	0	0	0	0	

The idealized core periphery structure in a network where the core actors are densely connected to each other (consisting of ones in the core block) and the periphery actors are connected to the core but not to each other (zeros in the peripheral block).
Borgatti SP and MG Everett. Models of core/periphery structures. Social Networks 1999;21:375-95.[109]

Figure 3-2: Idealized core periphery structure

3.5.4 Hierarchal clustering

A notable constraint of the aforementioned model is the assignment of all nodes into only two discrete blocks: core and periphery. Thus, another approach used to model venue seeking behaviour was hierarchal clustering. Johnson's hierarchical clustering is a common social network analysis technique that partitions nodes in a network into clusters according to some empirical measure of similarity.[110] In the context of individuals connected by venues, it may be valuable to identify groups who patronize the same venues to seek sex partners. In the network of venues, this technique can identify clusters of venues based on the number of individuals patronizing the venue they have in common.

To identify clusters of individuals linked together by the same sex partner meeting place, clique analysis was performed on the network of people linked together by social venues. Then hierarchal clustering was performed to model patronage of venue patterns. The process of hierarchical clustering was also applied to the dual matrix, the matrix of venues, to ascertain the degree of similarity among venues (i.e. overlapping patronage). In this analysis, the complete linkage method (furthest neighbour) [50] was used to identify clusters. In the context of a connected venue network, this method starts with a single cluster of all venues, and then begins to partition venues into groups defined by the "smallest similarity" [50] (i.e. a cluster of venues are grouped together if only one person attended all the venues, the next step clusters venues together if they have two people in common and so on). The algorithm continues the iterative process until the most homogenous group is identified [50] (i.e. pairs of venues that have the most people in common).

Another common method is the single linkage or nearest neighbour method. This algorithm works in reverse to the complete linkage method; the closest points are merged together in a group first. However the disadvantage of the nearest neighbour method is that the algorithm is more likely to miss homogenous clusters.[50]

3.5.5 Visual representation of network data

There is no correct way to visually represent network data,[50] and graph layout does not affect the calculation of the network parameters used in this study. Nevertheless, spatial layout of graph diagrams and the use of visual techniques such as node color, shape or size can emphasize network properties and allow better understanding of the underlying social structure. Graphs of the network data were drawn in 2-dimentional space using NetDraw version 2.091 visualization software available with UCINET.[107] The sexual affiliation networks (person-to-person and venue-to-venue) were laid out using the NetDraw default spring-embedding algorithm. This algorithm uses an iterative process to position nodes based on geodesic distance (shortest path) and minimizes overlap of nodes to enable visualization of the structural characteristics of the network. The sexual networks were displayed using the same default. However, some nodes were moved to ensure network structure was not obscured. For example, if a node was displayed in such a way that it appeared to be falsely connected to another node it was moved to create separation and prevent visual distortion.

3.6 Statistical analysis

Network data are not random and violate the assumption of independence required by standard statistical tests. Furthermore, sampling distributions of most network parameters are unknown or lack normality. When parametric assumptions are in question or when they are clearly violated as is the case in this study, re-sampling methods such as permutation tests [111, 112] and bootstrapping are preferred.[113]

To determine if a venue attribute affected its position in the network, univariate comparisons were made using a two-sample permutation test for equality of means analogous to the simple two-sample t-test. The dependent variable of interest was the sociometric network location; mean Freeman degree and betweenness centrality. The independent variables included Internet compared to non-Internet sites in the MSM venue network and street places compared to non-street locations in the heterosexual venue network. UCINET performs a permutation t-test to compare the means of two groups with a default of 10,000 trials to create the permutation-based sampling distribution of the mean difference. However the algorithm by which the software performs this test has not been published. Thus the two-sample Fisher-Pitman permutation test (fptest) for equality of means was performed with exact p-values calculated,[114] using the STATA/IC version 10.1 statistical package.[115]

A paired-sample t-test based on a bootstrap approach outlined by Snijders and Borgatti [113] was used to compare the densities of the sexual network and the network of these same actors linked together by a social venue. Although theoretically this method can be used with most network statistics,[113] the statistical tools for testing differences in connectedness, centralization and number of cliques are not yet available in UCINET. All tests were two sided: p-values < 0.05 were considered significant. A description of the permutation test for equality of means and the paired-sample t-test based on the bootstrap approach are located in **Appendix E** of this report.

3.7 Scientific and ethical approval

The University of Calgary Conjoint Health Research Ethics Board (CHREB) approved this research project in January 2009. A subsequent request to the CHREB Chair to amendment the study protocol to include 1) additional recruitment sites and 2) additional anonymous health information extracted from the Alberta STD partner notification investigation form was submitted and approved in July 2009.

3.8 Informed consent

Each patient provided informed written consent after receiving a complete description of the study by the investigator. Due to the highly sensitive nature of the research topic, tear-off sheets of whom to contact for additional information, or questions concerning rights as a possible participant in the research study were developed and offered to all participants who declined a copy of the consent. To avoid inadvertent contact with potential participants, suspected infectious syphilis cases and their sexual contacts were ascertained and recruited for enrollment by nurses at the STD clinic. After completion of the clinic visit, the nurse would explain to each patient that a master’s student was undertaking a study on syphilis and sought verbal consent for the investigator to speak with him or her about the study. After approval was obtained to include offsite locations for patient recruitment, the consent process occurred in a parallel manner; patient contact was only made after verbal consent. Vulnerable patients such as the homeless, those working in the sex-trade and known drug users were assessed on a case-by-case basis to determine if mental illness, intoxication, or chronic substance abuse impeded the potential subjects' capacity to consent.[116]

3.9 Confidentiality

Collecting sensitive information such as STD disease status and data on intimate sexual relations raises a number of privacy issues. Protection of the physical security and confidentiality of the information was given the highest priority. To prevent unauthorized external or internal access to identifying information, data collected for this study were initially kept in the Alberta Health Services Calgary STD clinic medical records room. This locked area is only accessible to authorized healthcare personnel. Subsequently, persons were assigned non-linkable unique network identifiers and all personal identifying information was removed when data was entered into a personal computer. Once study data was computer entered and validated, the hard copies were permanently destroyed. Final disposition of identifying information collected for research purposes occurred at the STD clinic by means of confidential shredding. To avoid identification through research dissemination, any information that may permit the identity of subjects or social venues was suppressed before publication or release.

Chapter Four: Results

This chapter provides an account of participant recruitment, descriptive data on the study population, and reports the main results of network and statistical analyses. The chapter begins with descriptive data on the entire study population, and then reports results of the heterosexual and MSM network analyses separately. Results from analyses of the three one-mode heterosexual networks will be reported first, followed by the results of the MSM network analyses.

4.1 Participant selection

Figure 4-1 shows participant selection for network construction. Of the 70 individuals who were identified during the study period, 4 (6 %) were treated offsite prior to ethical approval for additional recruitment sites, 2 (3%) were unable to participate, 2 (3%) were not able to provide written consent, and 1 could not be located during the study period. Of the 61 remaining participants, 9 declined to participate for a response rate of 85%. Thus data were collected on 52 individuals to construct the sexual and sexual affiliation networks. An additional eight individuals were consented and interviewed for the study. However, these eight individuals did not meet inclusion criteria after follow-up syphilis serology; five were staged late latent syphilis, two were sexual contacts of late latent syphilis and one individual was a sexual contact of someone who was deemed to be a biological false positive.

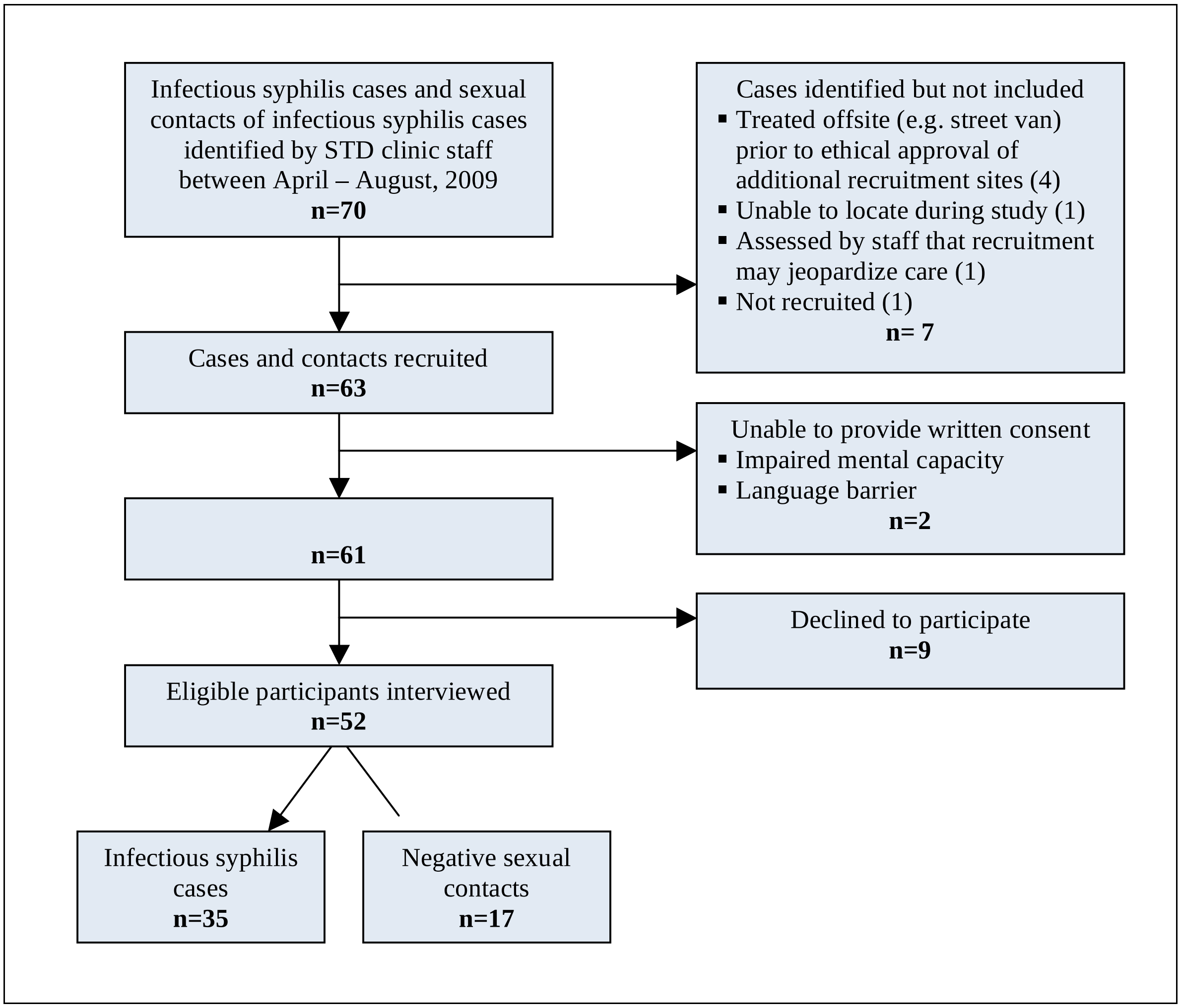


Figure 4-1: Participant selection for network construction in an outbreak of infectious syphilis in the Calgary, Alberta, April – August 2009

Non-participants did not differ importantly in terms of age, ethnicity or sexual orientation. However, 39% (n=7) of non-participants were female compared to 15% (n=8) of participants (**Table 4-1**). Of the 7 non-participant females, 4 (57%) were sex-trade workers.

Table 4-1: Comparison of study participants and non-participants

	Participants (n=52) N (%)	Non-participants (n=18) n (%)
Age (years)		
Median	36	32
Interquartile range	29-46	27-43
< 20	4 (8)	0 (0)
20-29	10 (19)	6 (33)
30-39	17 (33)	5 (28)
40-49	13 (25)	4 (22)
50 +	8 (15)	2 (11)
Sex		
Male	44 (85)	11 (61)
Female	8 (15)	7 (39)
Ethnicity		
White	42 (81)	15 (83)
Black	1 (2)	0 (0)
Aboriginal	5 (10)	2 (11)
Other	4 (8)	0 (0)
Sexual practices		
Heterosexual	27 (52)	13 (72)
MSM	25 (48)	5 (27)
HIV co-infected	12 (23)	2 (11)
Syphilis infection		
Primary syphilis	13 (25)	2 (11)
Secondary syphilis	9 (17)	6 (33)
Early Latent syphilis	13 (25)	9 (50)

Statistical comparison was avoided because participant data is not dependent.

4.2 Characteristics of network members

A total of 154 network members composed of 46 cases of infectious syphilis and 108 named sexual contacts were identified in the sexual and sexual affiliation networks. Since link-trace sampling was used to define network boundaries, if a named sexual contact tested positive for infectious syphilis, that individual became a case and their sexual partners traced. **Table 4-2** shows socio-demographic and infection characteristics of network members. The median age of cases was 36 years (age range 18 to 75 years); 78%

(n=36) of cases were men, 78% (n=36) were white, and 61% (n=28) identified as heterosexual. Of these syphilis cases, 30% (n=14) were staged primary, 26% (n=12) staged secondary, and 39% (n=18) were staged as early latent syphilis. Two individuals were presumed infectious cases, but the stage of syphilis could not be determined because medical follow-up occurred outside of the health region. Among the 46 cases, 6 MSM were re-infections.

Named sexual contacts ranged in age from 18 to 56 years. Of the 108 named contacts, 82% (n=89) were male, 65% (n=70) were white and 70% (n=76) were identified as MSM. Infection status could not be determined in a large number of named contacts due to untraceable anonymous and pseudo-anonymous sexual partnering.

4.3 Characteristics of venues

Overall, 77% (n=40) of participants reported visiting at least one venue in the last six months where sexual partnering occurred (**Table 4-3**). Given that no restrictions were placed on the type of venue named by participants, an inevitable ‘other’ category was derived.

Table 4-2: Socio-demographic and infection characteristics of network members in an outbreak of infectious syphilis in Calgary, Alberta, April – August, 2009

	Cases (n=46) n (%)	Named sexual contacts (n=108) n (%)
Age (years)		
Median	36	N/A
Interquartile range	27-46	
< 20	1 (2)	2 (2)
20-29	15 (33)	19 (18)
30-39	11 (24)	21 (19)
40-49	12 (26)	10 (9)
50 +	6 (13)	4 (4)
Sex		
Male	36 (78)	89 (82)
Female	10 (22)	19 (18)
Ethnicity		
White	36 (78)	70 (65)
Black	1 (2)	2 (2)
Aboriginal	6 (13)	5 (5)
Other	2 (4)	6 (2)
Sexual practices		
Heterosexual	28 (61)	32 (30)
MSM	18 (39)	76 (70)
HIV co-infected	10 (22)	0 (0)
Syphilis infection		
Primary syphilis	14 (30)	0 (0)
Secondary syphilis	12 (26)	0 (0)
Early Latent syphilis	18 (39)	0 (0)
Presumed infectious syphilis (stage unknown)	2 (4)	0 (0)
Indeterminant	0 (0)	2 (2)
Negative	0 (0)	15 (14)
Unknown	0 (0)	91 (84)
Re-infection	6 (13)	0 (0)

*If a named sexual contact tested positive for infectious syphilis, that individual became a case and their sexual partners traced. Figures for named sexual contacts may not sum to 100 due to anonymous contacts that could not be traced.

Table 4-3A shows 84% (n=21) of MSM participants reported visiting at least one venue in the last six months where sexual partnering occurred. MSM named 21 places where they met sex partners. The Internet (76%), bars/lounges (24%) and parks (12%) were the most commonly reported venues for having met a sex partner. Venues reported by MSM were located in Calgary, a community in southern Alberta, Edmonton and Vancouver. However, sexual encounters met through the Internet were linked to contacts in Vancouver, Toronto Ontario, San Francisco California and Spain.

Table 4-3: Places where study participants met a sex partner in the last 6 months

A. MSM participants			
Venues named (No. 21)		**Participants (n = 25)**	
	No.	Attended venue N (%)	Did not attend venue N (%)
Internet site	10	19 (76)	6 (24)
Bar/Lounge	3	6 (24)	19 (76)
Park	3	3 (12)	22 (88)
Bathhouse	2	2 (8)	23 (92)
Private Party	2	2 (8)	23 (92)
Other*	1	1 (4)	24 (96)
Visited at least one venue where sexual partnering occurred			
Yes			21(84)
No			4(16)

* 'Other' included a large public event.

B. Heterosexual participants			
Venues named (No. 32)		**Participants (n = 27)**	
	No.	Attended venue N (%)	Did not attend venue n (%)
Internet site	1	1 (4)	26 (96)
Bar/Pub	8	7 (26)	20 (74)
Sex stroll/Street	8	7 (26)	20 (74)
Private party	8	7 (26)	20 (74)
Other*	6	6 (22)	21 (78)
Visited at least one venue where sexual partnering occurred			
Yes			19(70)
No			8(30)

* 'Other' included a homeless shelter, mall, college, hostel, fast food venue & Aboriginal Reserve &. Unable to categorize one venue because one individual named the Northwest Territories but declined to specify a specific place.

Among heterosexual participants, 70% (n=19) reported visiting at least one venue in the last six months where sexual partnering occurred. Of the 32 venues reported by heterosexual individuals, bars (26%), street corners (26%) and private parties (26%) were the most frequently named places. The category 'other' (22%) included a homeless shelter, mall, college, youth hostel, fast food venue and Aboriginal reserve (**Table 4-3B**). One venue could not be categorized because one participant named the Northwest Territories but declined to report a specific place. The majority of venues utilized by heterosexual participants were located in Calgary, with the exception of five venues that were located in Edmonton Alberta, a community in north-eastern Alberta, a suburb of Vancouver British Columbia, the Northwest Territories, and New Delhi India.

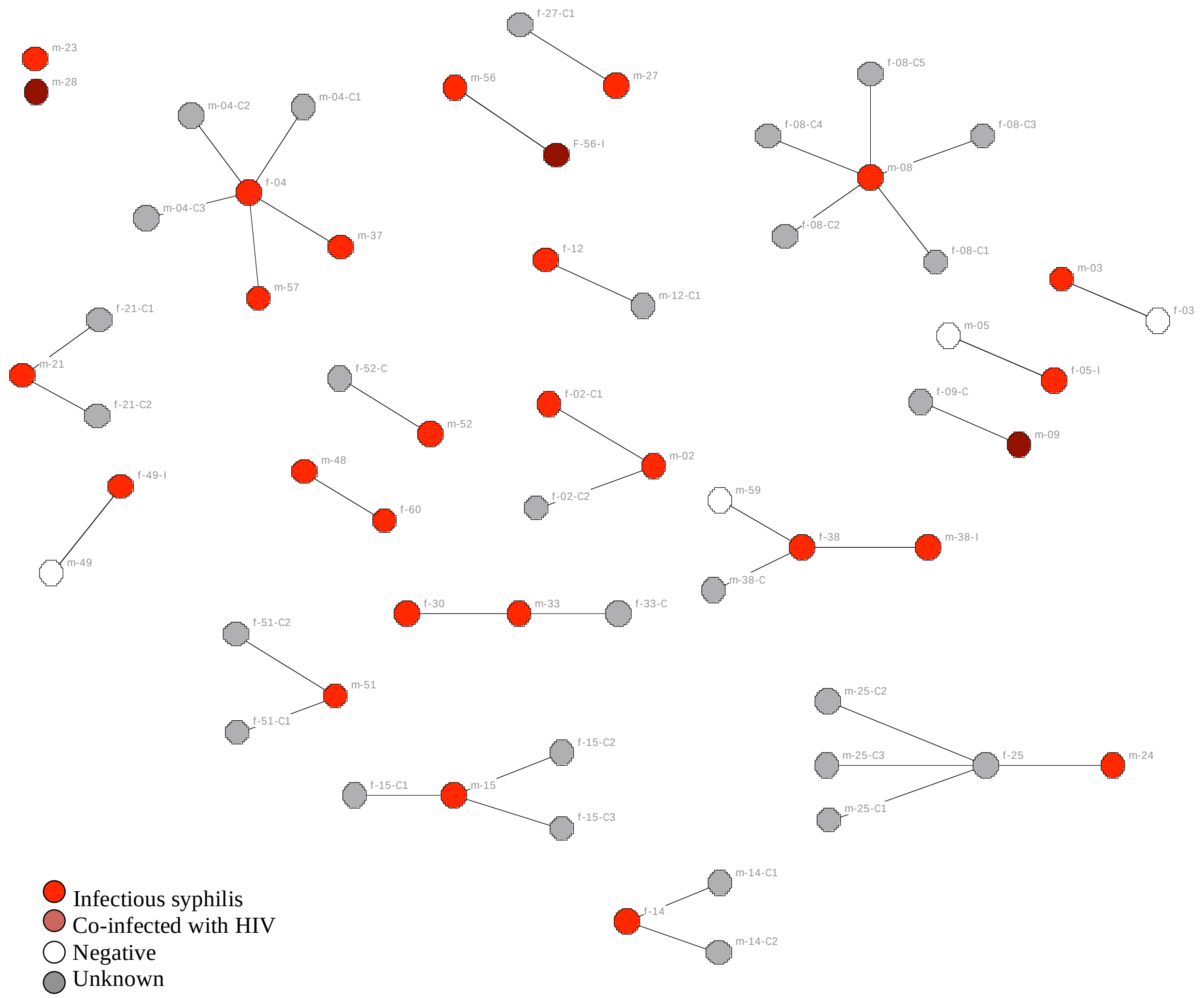
4.4 Graph representation of networks

In the sexual network diagrams, circles represent people and lines indicate sexual contact. In the one-mode sexual affiliation network of people, again persons are shown as circles but the link represents a common venue(s) patronized. In the dual sexual affiliation network of sex partner meeting places, venues are represented as squares and the lines connecting them a person(s).

4.5 Results of heterosexual network analyses

4.5.1 Comparison of the network structure of heterosexual persons linked by sexual contact versus a social venue

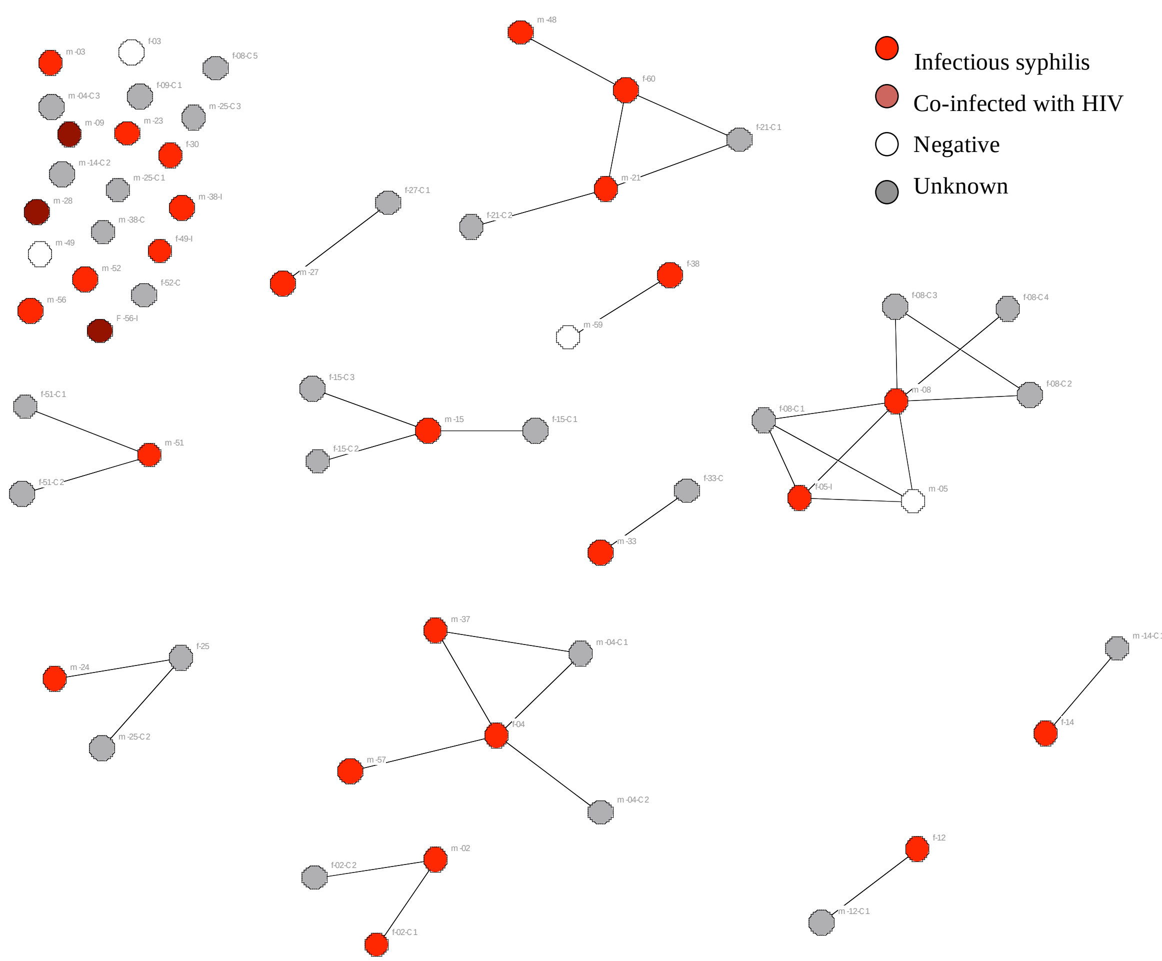
In all, 60 heterosexual network members, comprised of 28 cases of infectious syphilis and 32 named sexual contacts, were identified in the sexual network (**Figure 4-2**).



Individuals are represented by circles linked together by sexual contact

Figure 4-2: Heterosexual sexual network (n = 60)

Among the 28 infectious syphilis cases, 64% (n=18) were men and 11% (n=3) were co-infected with HIV. Of the 10 infectious cases in women, 50% (n=5) described themselves as sex trade workers. Among infectious cases in men, 22% (n= 4) reported having sex with a sex trade worker. Sexual network members were linked together by only 39 sexual ties resulting in a fragmented network containing 21 components. These same 60 individuals linked together by common patronage of a social venue, resulted in a comparable 34 ties (**Figure 4-3**).



In this network, the nodes are people linked together by common patronage of a venue(s). 32 venues link 60 persons.

Figure 4-3: **Heterosexual sexual affiliation network (n = 60)**

Arguably, the network structure did not change considerably when the link considered was a sexual contact compared to a social venue. **Table 4-4A** illustrates the similarity in the network-level measures of heterosexual persons connected through sexual contact compared with these same persons connected through sex partner meeting venues.

Density was not significantly different (0.3%: 95% CI, -0.5% - 1.1%). Difference in connectedness and centralization between the two networks was 0.8% and 2% respectively. Although permutation statistical tools are not yet available in UCINET for

Table 4-4: Network measures and characteristics of the sexual network compared with the sexual affiliation network among heterosexual persons

A. Network-level measures of persons connected through sexual contact compared with persons connected through sex partner meeting venues					
	Sexual network N = 60	Affiliation network n = 60	Difference	Bootstrap 95 % CI	*P* Value
Density	2.2%	1.9%	0.3%	-0.5% - 1.1%	0.47
Connectedness	4.3%	3.5%	0.8%	-	-
Centralization	6.5%	8.5%	2%	-	-
Largest clique	0	4	4	-	-

B. Comparison of network structure and infection characteristics relative to network components						
	Size of component	Frequency of component	Proportion of total network members (%)	Infectious syphilis N = 28	Previous syphilis infection	Co-infection with HIV n = 3
Sexual network N = 60	1	2	3%	2	0	1
	2	9	30%	11	0	2
	3	5	25%	7	0	0
	4	2	13%	3	0	0
	5	1	8%	1	0	0
	6	2	20%	4	0	0
Sexual affiliation network N = 60	1	20	33%	11	0	3
	2	5	17%	5	0	0
	3	3	15%	3	0	0
	4	1	7%	1	0	0
	5	2	17%	6	0	0
	7	1	12%	2	0	0

testing differences in connectedness and centralization, these network-level measures were not notably different in the affiliation network compared to the sexual network. The low density and connectedness scores noted in both the sexual and affiliation network reflect the lack of cohesion or disconnection among members in both networks. When the networks were examined to determine the extent to which the whole network had a centralized structure, low centralizations scores suggest that both networks were not compactly organized around focal nodes. In addition, areas of high cohesion were not identified in either network; the largest clique in the sexual affiliation network was a group of four persons connected by a sex stroll, compared to no cliques in the sexual network. Three additional cliques, linking three individuals each, were found in the sexual affiliation network; a group connected by a shopping mall, a bar, and a street corner located in front of an addictions treatment centre (**Table 4-5**).

Table 4-5: Clique membership in heterosexual affiliation network

Venue	Clique membership
Sex stroll (9) (n = 4)	m-05 f-05-I1 m-08 f-08-C1
Shopping centre (14) (n = 3)	m-08 f-08-C2 f-08-C3
Bar (7) (n = 3)	f-04 m-04-C1 m-37
Street corner (29) (n = 3)	m-21 f-21-C1 f-60

Cliques were formed if individuals were adjacent to each other in the network of heterosexuals connected by venues. For example, if at least three individuals visited the same place to seek a sex partner a clique was identified.

Table 4-4B shows a comparison of infection characteristics relative to network components of the sexual network and the affiliation network among heterosexual individuals. In the sexual network, dyads and triads occurred with the greatest frequency, accounting for 55% of total network members. In the sexual affiliation network, one half of all network members were either an isolate (33%) or belonged to a dyad (17%). Cases of infectious syphilis were dispersed among the components in both networks, with the largest amount of cases (39%) occurring among dyads in the sexual network and among isolates (39%) in the affiliation network.

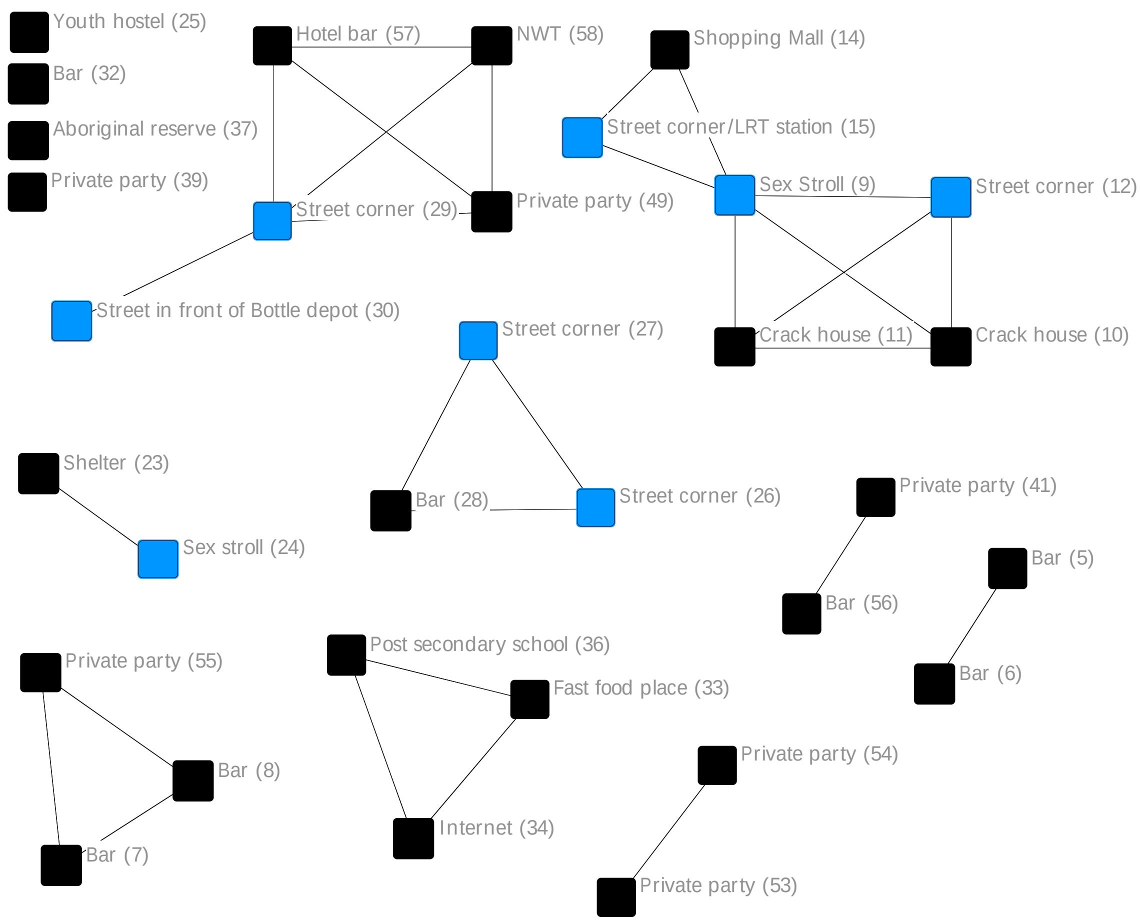
Visual inspection and the aforementioned network measures comparing the sexual network of heterosexual persons infected by syphilis with the sexual affiliation network of these same individuals, indicate that both networks are sufficiently fragmented to the extent that formation of a core periphery structure was precluded.

4.5.2 Dual analysis of the heterosexual venue network

Overlap of clique membership was virtually absent among heterosexual participants. Four cliques were identified in the heterosexual network connected by sex partner meeting places (**Table 4-5**). However, only one individual was in more than one clique. This individual, a male, belonged to a clique connected by a sex stroll and a clique connected by a shopping centre because he sought sex from sex trade workers at both places. Therefore, additional information would not be gained by performing core-periphery blockmodeling or hierarchal clustering.

4.5.2.1 Point degree and betweenness centrality of the heterosexual venue network

A sex stroll and a street corner located outside of an addictions treatment centre had the highest degree centrality in the network of venues frequented by heterosexual participants (**Figure 4-4**). These two venues were the only places in the network that had a betweenness centrality score above zero (**Table 4-6**). The venue with the highest degree centrality, a sex stroll, connected two crack houses, a street corner where drugs were exchanged for sex, a mall, and an additional street corner located near a downtown LRT station.



Squares representing street venues are illustrated in blue and those squares indicating non-street venues are black.

Figure 4-4: Network of sex partner meeting places (n=32) connected by heterosexual persons that frequent them

Table 4-6: Point degree and betweenness centrality of places in the network of sex partner meeting venues connected by patronage of heterosexual persons

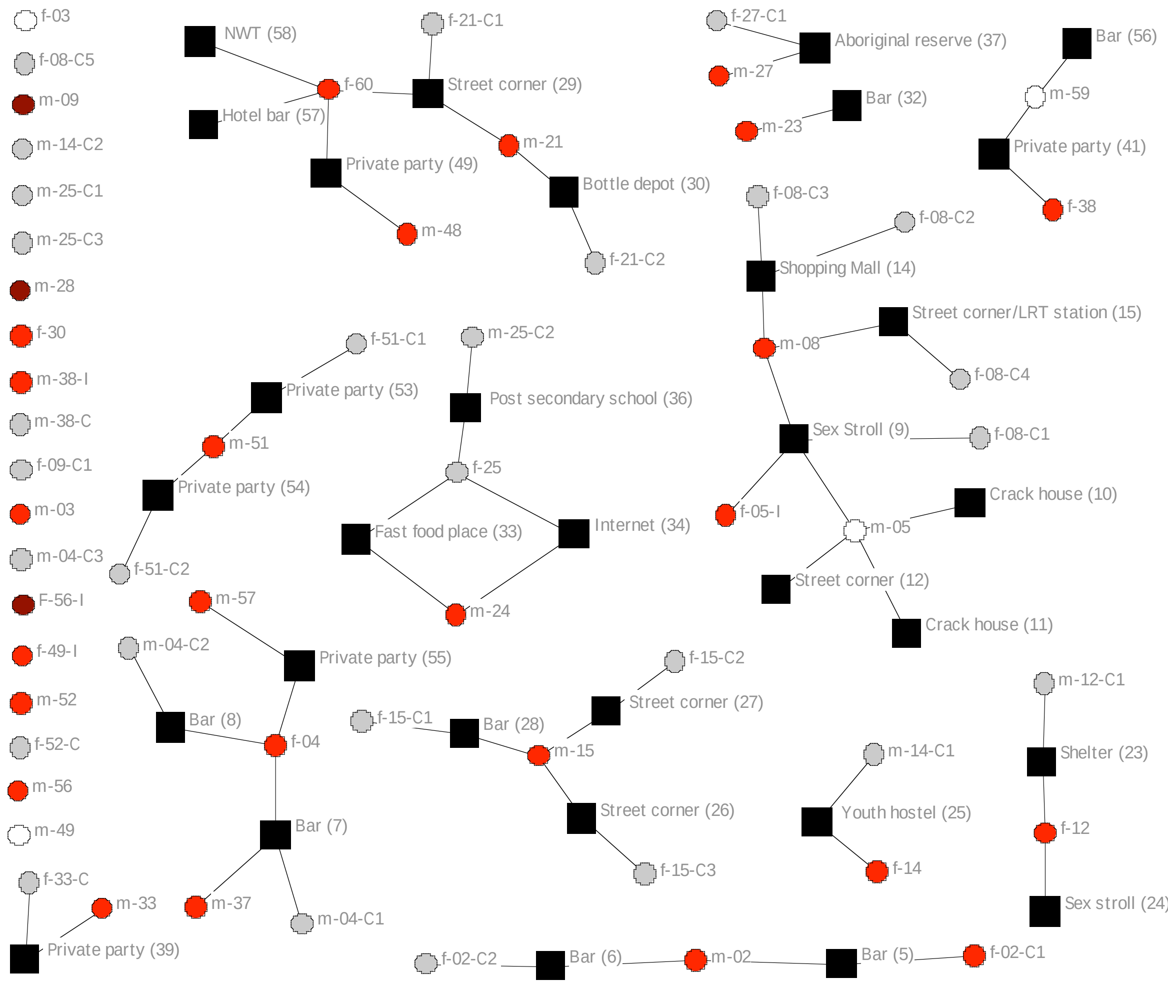
Sex partner meeting venues (n=32)	**Point centrality**	
	Degree	Normalized betweenness
Sex Stroll (9)	5	0.013
Street corner (29)	4	0.006
Crack house (10)	3	0
Crack house (11)	3	0
Street corner (12)	3	0
Hotel bar (57)	3	0
NWT (58)	3	0
Fast food place (33)	3	0
Internet (34)	3	0
Private party (49)	3	0
Bar (7)	2	0
Bar (8)	2	0
Shopping Mall (14)	2	0
Train station (15)	2	0
Street corner (26)	2	0
Street corner (27)	2	0
Bar (28)	2	0
Post secondary school (36)	2	0
Private party (55)	2	0
Bar (6)	1	0
Bar (56)	1	0
Bar (5)	1	0
Shelter (23)	1	0
Sex stroll (24)	1	0
Private party (41)	1	0
Private party (53)	1	0
Private party (54)	1	0
Street corner (30)	1	0
Bar (32)	0	0
Youth hostel (25)	0	0
Aboriginal reserve (37)	0	0
Private party (39)	0	0

Point degree centrality scores of venues calculated with valued data. Calculation of betweenness requires data to be binary. Betweenness centrality scores normalized.

Table 4-7 shows street venues had higher degree centrality than non-street venues (difference, 0.9; P=0.09), but this difference was not significant. Note that the network is relatively disconnected and the difference in degree centrality is modest. Furthermore, although the largest component connected seven individuals, no single venue connected more than two infectious syphilis cases (**Figure 4-5 and Figure 4-6**). A direct comparison of point betweenness centrality among street and non-street venues was not done as only two venues in the heterosexual venue network had a betweenness centrality greater than zero.

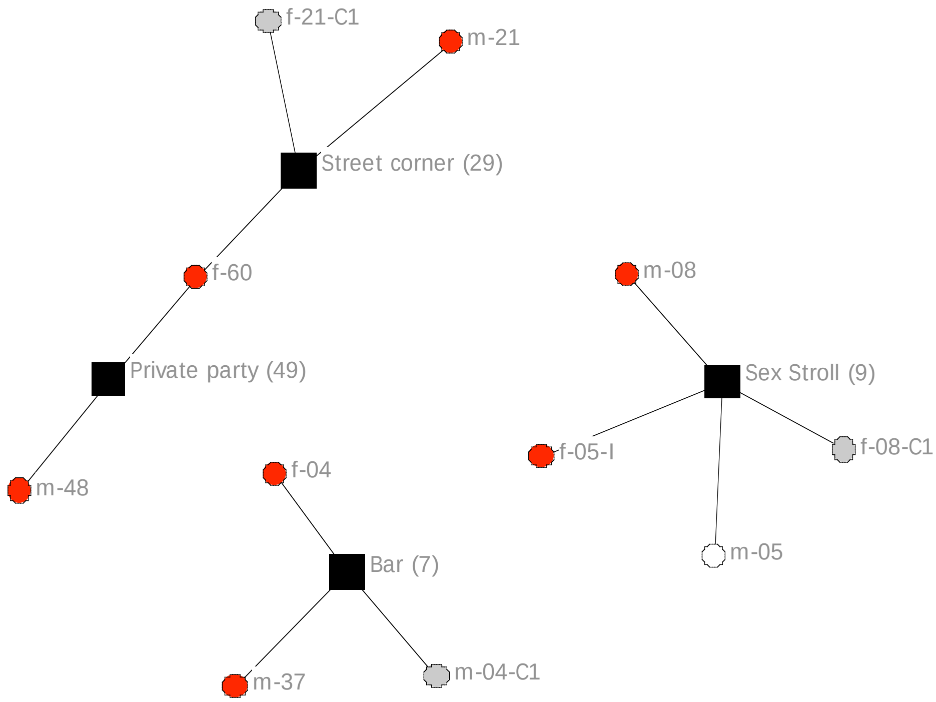
Table 4-7: Comparison of point degree centrality of street corner/sex stroll venues and non-street corner/sex stroll venues connected by patronage of heterosexual participants

Comparison of point degree centrality measures of street corner/sex stroll venues and non-street corner/sex stroll venues				
	Street venues n = 8	Non-street venues n = 23	Difference	*P* Value
Mean point degree centrality	2.5	1.6	0.9	0.09
Point betweenness centrality	Only two venues had betweenenss centrality, venue 9 and venue 29			-
Point degree centrality scores of venues calculated with valued data. To test for equality of means the two-sample Fisher-Pitman permutation test was used with exact p-values calculated.				



Circles represent people and sex partner meeting places are symbolized by squares in this two-mode sexual affiliation network consisting of 60 individuals and 32 venues

Figure 4-5: Two-mode sexual affiliation network among heterosexual persons



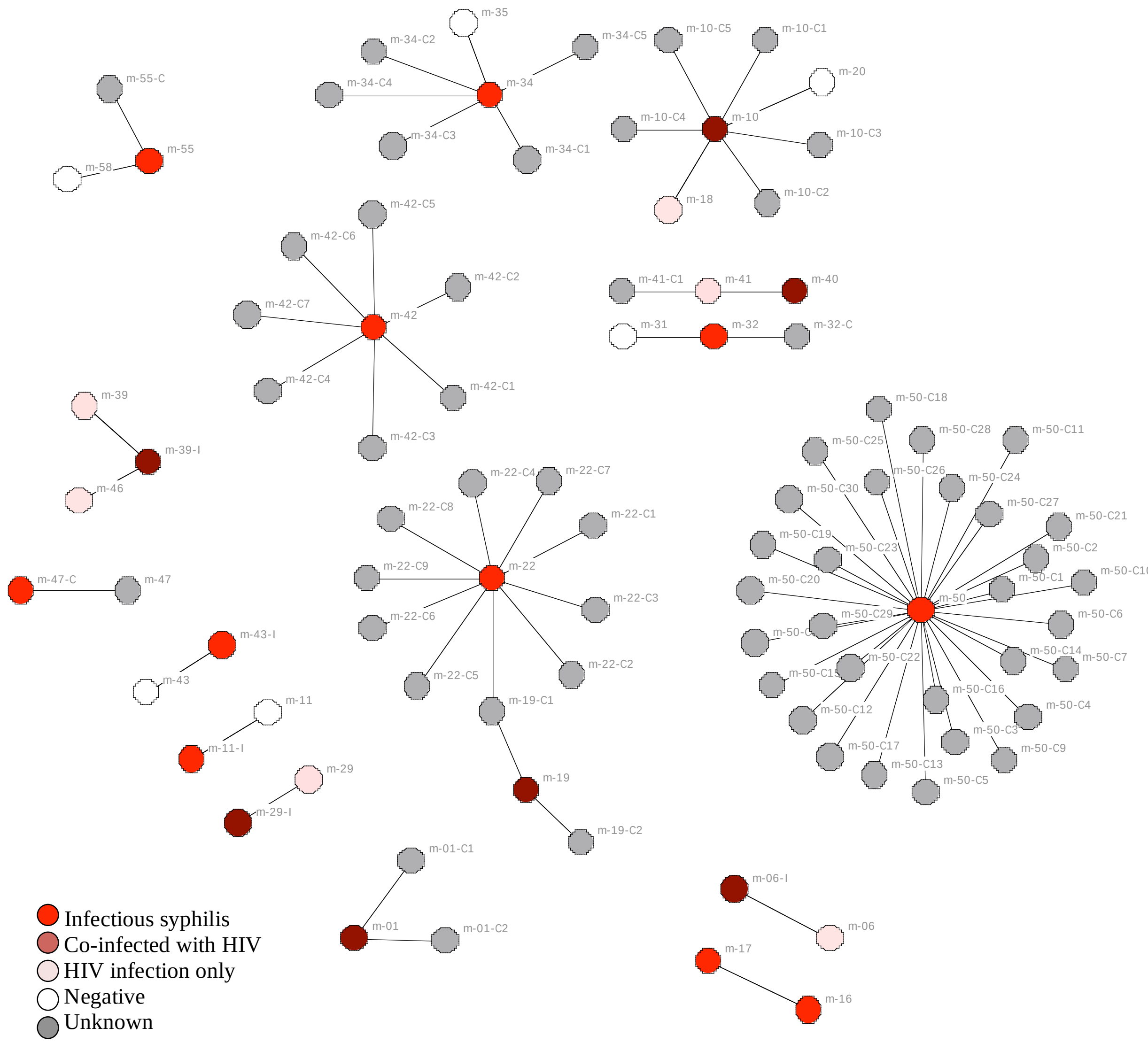
Venue (9) and venue (29) had the highest point degree centrality in the network of sex partner meeting places connected by individuals identifying as heterosexual. No single venue connected more than two infectious syphilis cases.

Figure 4-6: Venues with the highest degree centrality in the heterosexual sexual affiliation network; displayed as a two-mode network.

4.6 Results of MSM network analyses

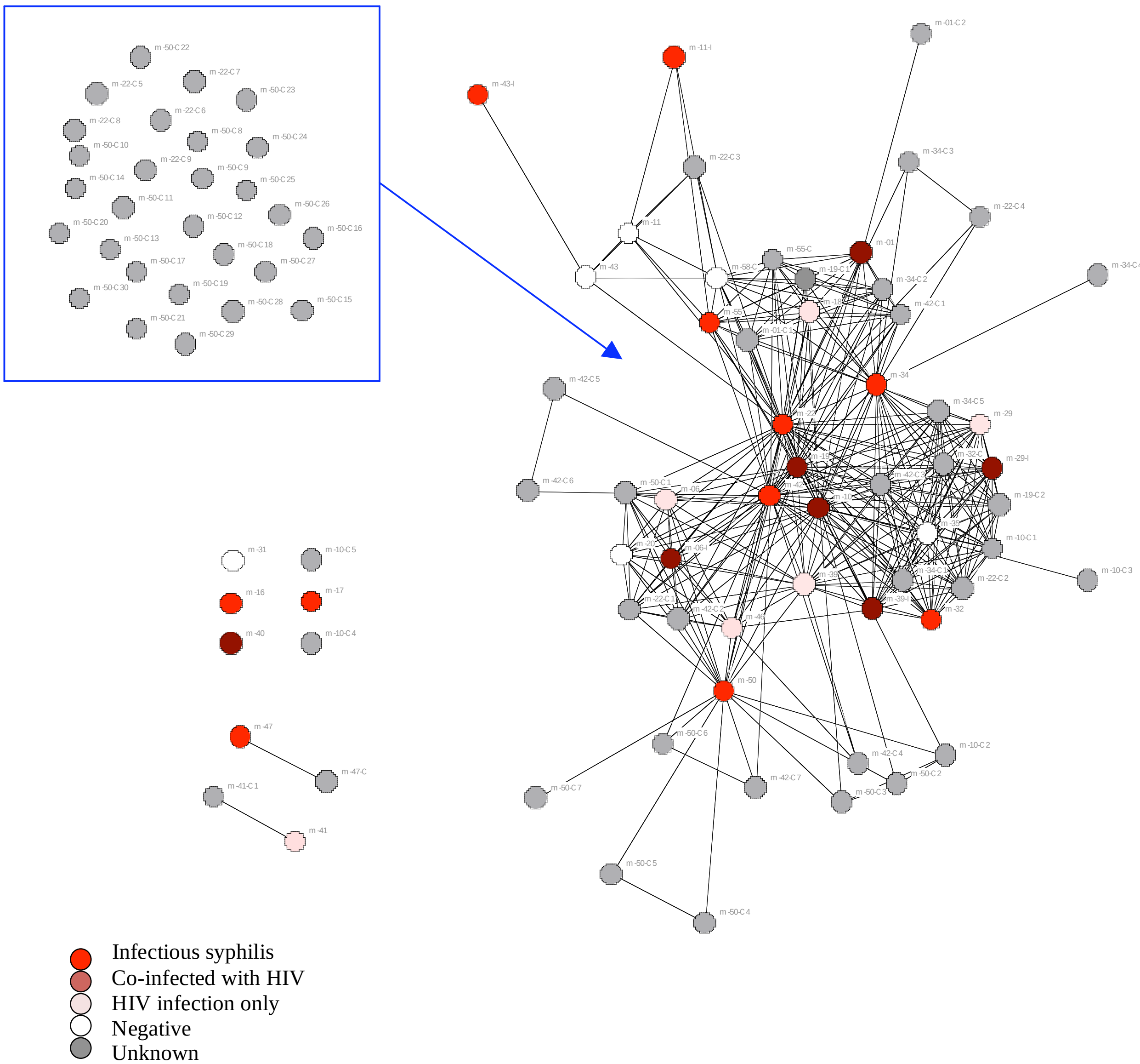
4.6.1 Comparison of the network structure of MSM linked by sexual contact versus a social venue

Overall, 94 network members, comprised of 18 cases of infectious syphilis and 76 named sexual contacts, were connected by 78 sexual ties in the sexual network (**Figure 4-7**). Among individuals diagnosed with infectious syphilis, 39% (n=7) were co-infected with HIV. In total, 14% (n=13) of network members were known to be HIV positive. Two sexual contacts of infectious syphilis cases, both of whom tested negative for syphilis, were newly diagnosed with HIV infection. The sexual network was relatively disconnected containing 16 components ranging in size from 2-31. As expected, the network was ‘scale-free’;[117] a few men reported many partners whereas the majority of men only listed one or two partners. A different relational pattern emerged in the sexual affiliation network. There was almost a five-fold increase in network ties (351 ties) when the link considered was a social venue versus a sexual contact (**Figure 4-8**). Examination of the network structure revealed six isolates, two dyads and one large densely connected subcomponent of 84 men.



Men are represented by circles linked together by sexual contact

Figure 4-7: MSM sexual network (n = 94)



In this network, the nodes are men linked together by common patronage of a venue(s). 21 venues link 94 men. The 28 nodes shown as isolates in the blue box are in fact connected to the large component.

Figure 4-8: MSM sexual affiliation network (n = 94)

It should be noted, that 28 men shown as isolates in the sexual affiliation network were in fact connected to the large component. Participants m-22 and m-50 reported using several Internet sites weekly for sex seeking. These two men reported meeting 28 men on five Internet sites in the last 6 months but were unable to identify which partner was met on each of the five sites. To avoid erroneous network measures, these nodes were removed from the sexual affiliation matrix prior to calculation of density and connectedness. However, an appropriate comparison of density requires that both networks have the same number of nodes. Thus, these nodes were also removed from the sexual network prior to calculation of density and statistical analysis. Arguably, this approach makes the assumption that removal of these isolates from the sexual network would not change the density of this network importantly. Therefore, density of the sexual network was initially calculated using all 94 nodes. This calculation resulted in a density measure of 1.8%, compared to 2.3% when calculated with only 66 nodes; which is not notably different. In further effort to avoid reporting a misleading p-value, the statistical analysis was repeated using all 94 points in both networks. The difference in density was 6% (95% CI, 4% -9%: $P < 0.001$). Such an approach, however, conveys an unjustifiably conservative interpretation of the difference in density between the two networks and is likely an underestimate of the true difference.

Table 4-8A shows the network-level measures of MSM connected through sexual contact compared with the network of these men connected through sex partner meeting venues. The network connected by venues was significantly more cohesive than the network connected by sexual contact. In the analysis that was restricted to 66 men, the affiliation network had 14% higher density than the sexual network (CI, 9.6% -18.5%: $P < 0.001$). When connectedness of the network was considered, 72% of all men were reachable from all other men in the affiliation network compared to only 15% in the sexual network. The normalized degree centralization score was 31% for the sexual network compared to 35% for the sexual affiliation network.

Table 4-8:Network measures and characteristics of the sexual network compared with the sexual affiliation network in MSM

A. Network-level measures of persons connected through sexual contact compared with those of persons connected through sex partner meeting venues

	Sexual network N = 94	Affiliation network n = 94	Difference	95 % CI	*P* Value
Density*	2.3%	16.4%	14.1%	9.6% -18.5%	< 0.001
Connectedness*	14.7%	71.8%	57.0%	-	-
Centralization	31.1%	34.64%	3.5%	-	-
Largest clique	0	18	18	-	-

* Two study participants, who reported using several Internet sites weekly to find sex partners, indicated that they met 28 men in the last 6 months on the Internet but were unable to identify how many partners were met at each specific site. Therefore these 28 men were removed from the sexual affiliation matrix prior to calculation of density & connectedness (n=66). To ensure an appropriate comparison of density, these men were also removed from the sexual network preceding density calculation and statistical testing.

B. Comparison of network structure and infection characteristics relative to network components

	Size of component	Frequency of component	Proportion of total network members (%)	Infectious syphilis n = 18	Previous syphilis infection n = 9	Co-infection with HIV n = 7
Sexual network N = 94	2	6	13%	7	1	2
	3	5	16%	5	6	3
	7	1	8%	1	0	0
	8	2	17%	2	2	1
	13	1	14%	2	0	1
	31	1	33%	1	0	0
Sexual affiliation network N = 94	1	6	6%	3	0	1
	2	2	4%	1	0	0
	84	1	89%	14	9	6

As previously discussed, the centralization measure provides information on whether the network is organized around its most central nodes, it does not however, indicate whether these central point(s) are clustered together or dispersed through the network. If the network's most central points are spread throughout the network, the measure of centralization is not particularly informative.[50] In the sexual network, the nodes with the highest point degree centrality (m-50, m-22, m-42, m-10, and m-34) are spread widely through the network (**Figure 4-7**).

On the other hand, the affiliation network (**Figure 4-8**) appeared to have a different network topology. However, high density obscured much of the underlying structure of the large connected subcomponent of this network. To further investigate the degree to which the large component of the affiliation network was structured around a central hub, an approach introduced in the unpublished work of Stokman and Snijders and outlined by Scott [50] was used. First, the nodes in the large subcomponent of the affiliation network were ordered by their point degree centrality. Then, the distribution of centrality scores was examined to discern the centre, margin, and periphery by identifying the 'break' in the distribution. The centre of the network contains its most central points; nodes with the highest point centrality. The network periphery contains nodes with the lowest centrality scores and the margin is the set of nodes that divide the centre from the periphery. **Table 4-9** indicates that there is a distinct cluster of six nodes in the centre of the network. As noted by Scott,[50] this approach is feasible, inasmuch as there is an unavoidable arbitrariness since it is for the analyst to decide on the boundaries between the core, margin and periphery. To circumvent this problem, core/periphery block modelling was also pursued to identify the structural core. This method identified the same six nodes in the core. Interestingly, among these six most central individuals in the sexual affiliation network, 5 men were syphilis positive, two of which were HIV co-infected and one syphilis re-infection; the 6th individual was infected with HIV.

Table 4-9: Structural centre of the connected subcomponent of the MSM sexual affiliation network; persons linked together by a social venue

	Network member (n = 56)*	Point degree centrality	
High centrality	m-42	39	Centre
↑	m-22	39	
	m-10	38	
	m-19	34	
	m-34	29	
	m-39	26	
	m-50	20	Margin
	m-39-I	18	
	m-19-C2, m-29, m-32, m-29-I, m-42-C3, m-34-C5, m-35 m-22-C2, m-34-C1, m-10-C1, m-58, m-32	17	
	m-55	15	
	m-46, m-01	14	
	m-19-C1, m-01-C1, m-34-C2, m-55-C, m-42-C1, m-18	13	
	m-42-C2, m-06-I, m-06, m-22, m-50, m-20-C	12	
	m-11	6	Periphery
	m-43	5	
	m-10-C2, m-22-C3, m-50-C3, m-50-C2	4	
↓	m-34-C3, m-50-C6, m-42-C4, m-11-I, m-22-C4, m-42-C7	3	
Low centrality	m-50-C5, m-42-C6, m-50-C4, m-42-C5	2	
	m-34-C4, m-43-I, m-10-C3, m-01-C2, m-50-C7	1	

* Note that this densely connected subcomponent contained 84 men. 28 men were removed from the analysis because it could not be determined exactly which individual was connected to each venue.

No cliques were identified in the sexual network compared to 13 cliques in the affiliation network. Clique analysis in the affiliation network allowed identification of groups of men connected by the same venue. The largest clique identified was a group of 18 men connected by a single Internet site. It is interesting to note in this regard that Internet sites also connected the next two largest cliques; a group of 14 and a group of 13 men (**Table 4-10)**.

Table 4-10: Clique membership in MSM sexual affiliation network

Venues that formed cliques	Clique membership
Internet site 16 (n=18) Clique 1.	m-10 m-10-C1 m-19 m-19-C2 m-22 m-22-C2 m-29 m-29-I m-32 m-32-C m-34 m-34-C1 m-34-C5 m-35 m-39 m-39-I m-42 m-42-C3
Internet site 1 (n=14) Clique 2.	m-01 m-01-C1 m-10 m-18 m-19 m-19-C1 m-22 m-34 m-34-C2 m-42 m-42-C1 m-55 m-55-C m-58
Internet sites 13 (n=13) Clique 3.	m-06 m-06-I m-10 m-20 m-19 m-22 m-22-C1 m-39 m-42 m-42-C2 m-46 m-50 m-50-C1
Internet sites 13, 16, 43 and park 47* (n=7) Clique 4.	m-10 m-19 m-22 m-39 m-39-I m-42 m-46
Gay bar 19 (n=5) Clique 5.	m-11 m-22 m-22-C3 m-43 m-58
Internet sites 1, 20 & Gay bar 19* (n=4) Clique 6.	m-11 m-22 m-55 m-58
Internet site 31 (n=4) Clique 7.	m-22 m-22-C4 m-34 m-34-C3
Internet site 17 (n=5) Clique 8.	m-10 m-10-C2 m-50 m-50-C2 m-50-C3
Internet site 20 (n=4) Clique 9.	m-11 m-11-I m-55 m-58
Internet site 43 (n=4) Clique 10.	m-39 m-42 m-42-C4 m-46
Bath house 45 (n=3) Clique 11.	m-42 m-42-C5 m-42-C6
Park 51 (n=4) Clique 12.	m-42 m-42-C7 m-50 m-50-C6
Park 50 (n=3) Clique 13.	m-50 m-50-C4 m-50-C5

Cliques were formed if individuals were adjacent to each other in the network of MSM connected by venues. For example, if at least three men visited the same place to seek a sex partner a clique was identified. *Two cliques involved three or more places instead of a single sex partner meeting venue. See **Appendix F** for description of these two cliques.

Lastly, a comparison of infection characteristics relative to network components of the sexual network and the affiliation network among MSM are shown (**Table 4-8B**). In the sexual network, cases of syphilis are scattered across the network, with two thirds of cases occurring in 11 different components, each connecting 2 or 3 men. In contrast, almost 80% of syphilis cases occurred in one component of 84 men in the affiliation network.

These network measures suggest that the network of men connected by sex partner meeting places is relatively cohesive and that this cohesion is structured around a central hub of six particular men, whereas the network of these same men connected by sexual contact is fragmented and absent of a single central core. Furthermore, the majority of syphilis cases are concentrated in a single component in the affiliation network, compared to widely spread syphilis infection throughout the sexual network. This large component connecting 84 men, albeit indirectly, would be an ideal target for intervention strategies. Rather than target the central individuals in the component, a second and simpler approach is to target the places connecting them.

4.6.2 From people to places; dual analysis of the MSM venue network

One should take care to note, that the large subcomponent of the affiliation network is not connected by one or two places. Rather, these 84 men are linked together by 19 venues. The highly dense network structure of this component suggests a rather complex pattern of seeking partners at venues. To elucidate patterns of venue patronage for the purpose of sex seeking, the dual matrix of venues was examined and core-periphery blockmodeling and hierarchal clustering was performed. Point degree and betweenness centrality of the venue network connected by MSM were also calculated to determine which venue connected the most men. **Figure 4-9** shows the network of venues connected by patronage of MSM.

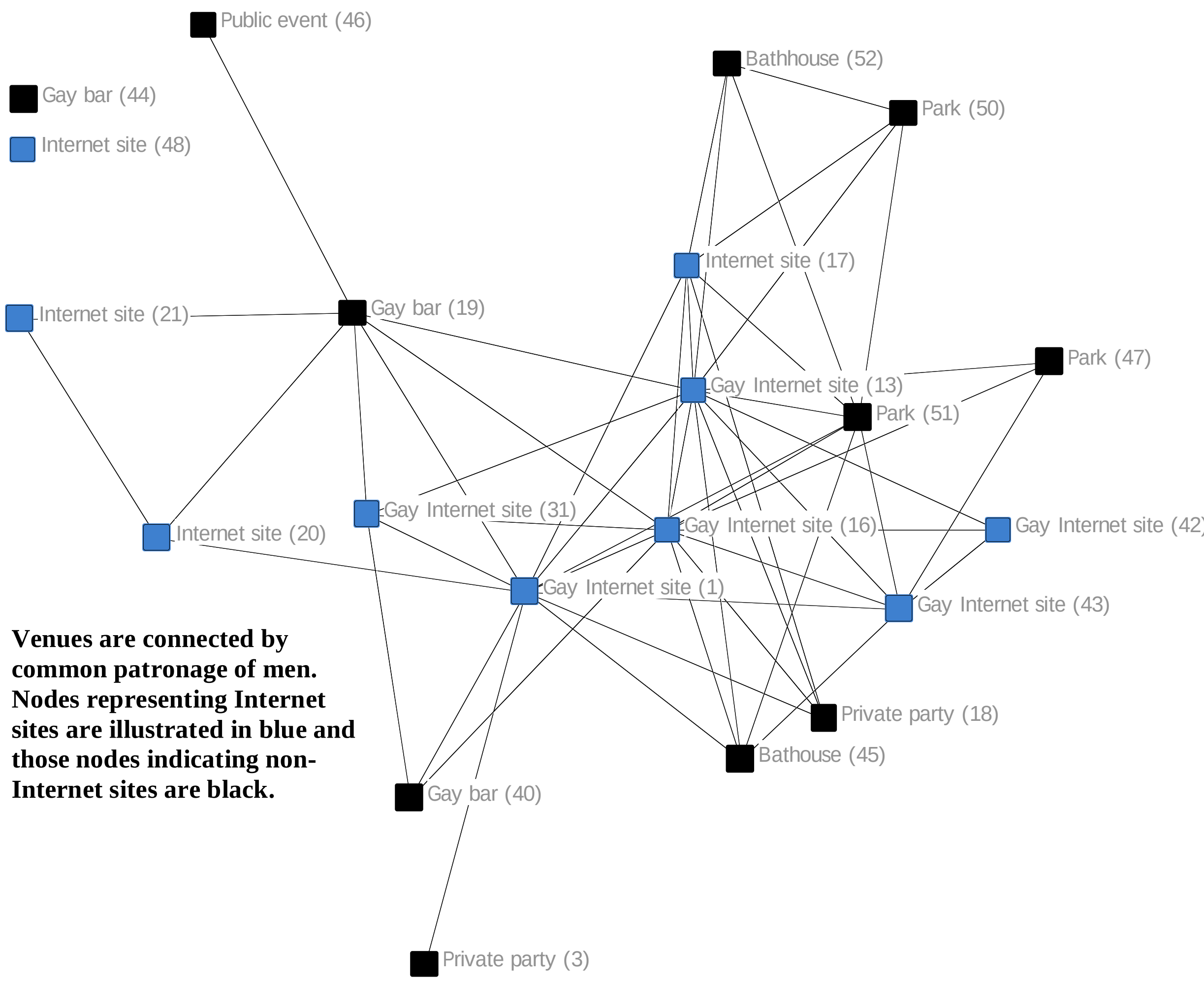


Figure 4-9: Network of sex partner meeting places (n=21) connected by the MSM that frequent them

4.6.2.1 Core-periphery blockmodeling of MSM venue network

Blockmodeling was performed to identify the set of venues that had high density of ties between them because of the patronage of individuals (**Table 4-11)**.

Table 4-11: Core/periphery model of MSM sex partner meeting venue network

Core/Periphery Class Memberships:

1. **Core:** Gay Internet site (1) Gay Internet site (13) Gay Internet site (16)
2. **Periphery**: Private party (3) Internet site (17) Private party (18) Gay bar (19) Internet site (20) Internet site (21) Gay Internet site (31) Gay bar (40) Gay Internet site (42) Gay Internet site (43) Gay bar (44) Bath house (45) Public event (46) Park (47) Internet site (48) Park (50)
3. Park (51) Bathhouse (52)

Blocked Adjacency Matrix

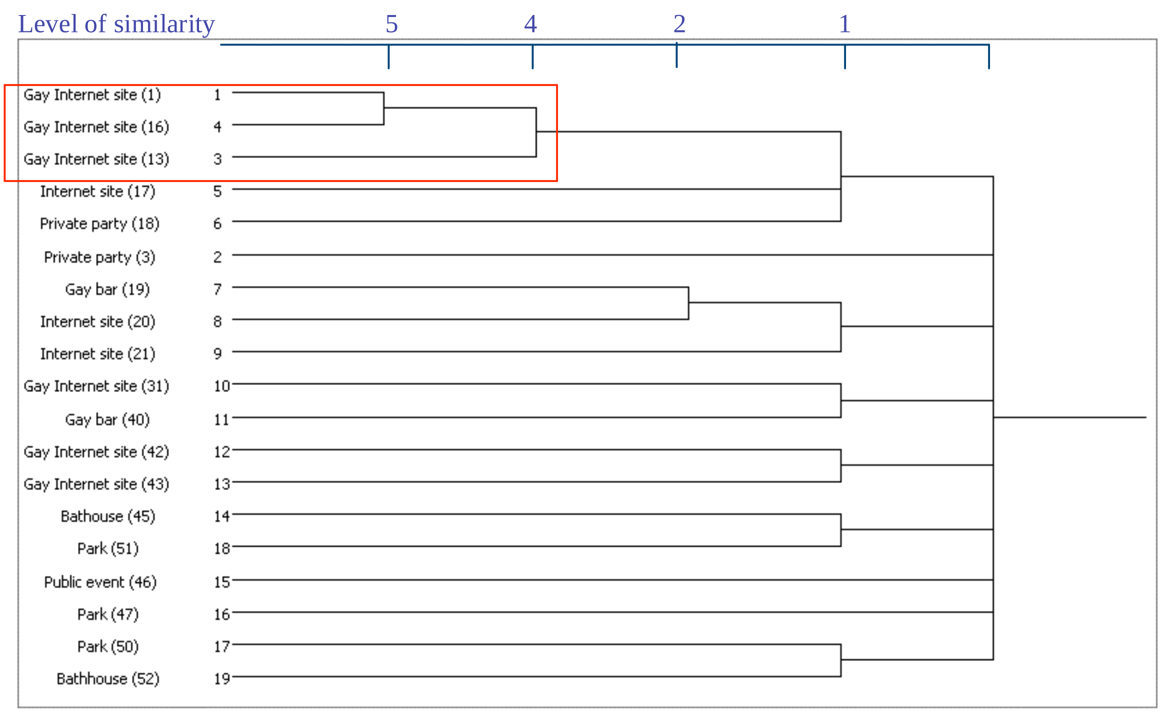
	1 Ga	4 Ga	3 Ga	2 Pr	5 In	6 Pr	7 Ga	8 In	9 In	10 Ga	11 Ga	12 Ga	13 Ga	14 Ga	15 Ba	16 Pu	17 Pa	18 In	19 Pa	20 Pa	21 Ba	
1 Gay Internet site (1)	14	5	4	1	1	1	2	2		2	1		1		1					1		
4 Gay Internet site (16)	5	18	5		1	1	1			2	1	1	2		1		1			1		CORE
3 Gay Internet site (13)	4	5	13		2	1	1			1		1	3		1		1		1	2	1	
2 Private party (3)	1			2																		
5 Internet site (17)	1	1	2		5	1													1	1	1	
6 Private party (18)	1	1	1		1	2																
7 Gay bar (19)	2	1	1				5	2	1	1						1						
8 Internet site (20)	2						2	4	2													
9 Internet site (21)							1	2	2													
10 Gay Internet site (31)	2	2	1				1			4	1											
11 Gay bar (40)	1	1								1	2											
12 Gay Internet site (42)		1	1									1	1									
13 Gay Internet site (43)	1	2	3									1	4		1		1			1		PERIPHERY
14 Gay bar (44)														2								
15 Bathhouse (45)	1	1	1										1		3					1		
16 Public event (46)							1									2						
17 Park (47)		1	1										1				2					
18 Internet site (48)																		2				
19 Park (50)			1		1														3	1	1	
20 Park (51)	1	1	2		1								1		1				1	4	1	
21 Bathhouse (52)			1		1														1	1	2	

Final fitness: 0.856

Blockmodeling identified a core/periphery structure with two exclusive groups; a cohesive core and the remaining venues on the periphery. Gay Internet site (1), Gay Internet site (13), and Gay Internet site (16) were identified as being members of the core.

4.6.2.2 Hierarchal clustering of MSM venue network

To examine more closely the pattern of venue patronage for the purpose of sex seeking, hierarchal clustering was performed. **Figure 4-10** illustrates the dendrogram from hierarchical modeling of the matrix of venues connected by MSM.



Level of similarity scale indicates common patronage of men. Complete linkage method used.

Figure 4-10: Dendrogram of hierarchal clustering of MSM venue network

Gay Internet site (1), Gay Internet site (16), and Gay Internet site (13) have a high degree of similarity because of overlapping patronage by individuals at these three sites. As expected, the hierarchal clustering of the dual matrix, the network of men connected by venues elucidated a comparable picture. This model is illustrated in **Appendix F**.

4.6.2.3 Point degree and betweenness centrality of MSM venue network

Algebraic measures of point degree and betweenness centrality were calculated to determine which sex partner meeting venue connected the most men. **Table 4-12** shows that venues (1), (13) and (16) have the highest point degree centrality. These three Internet venues connected the most individuals.

Table 4-12: Point degree and betweenness centrality of places in the network of MSM sex partner meeting venues

Sex partner meeting venues (n=21)	**Point centrality**	
	Degree	**Betweenness**
Gay Internet site (13)	24	.19
Gay Internet site (16)	22	.13
Gay Internet site (1)	22	.22
Gay Internet site (43)	10	.02
Park (51)	9	.03
Gay Bar (19)	9	.17
Internet site (17)	8	.02
Gay Internet site (31)	7	.008
Internet site (20)	6	.013
Bathhouse (45)	5	0
Park (50)	4	0
Private party (18)	4	0
Bathhouse (52)	4	0
Park (47)	3	0
Gay Internet site (42)	3	0
Internet site (21)	3	0
Gay Bar (40)	3	0
Private party (3)	1	0
Public event (46)	1	0
Internet site (48)	0	0
Gay bar (44)	0	0

Point degree centrality scores of venues calculated with valued data. Calculation of betweenness requires data to be binary. Betweenness centrality scores normalized.

When betweenness centrality was considered, venue (1) and venue (13) also had the highest point centrality. However, Venue (19), a gay bar, had the third highest betweenness centrality followed by venue (16). Interesting, the venue with the highest degree centrality and second highest betweenness centrality score, Internet venue 13, was directly connected to thirteen of the other twenty sex partner meeting places in the network. Overall, Internet venues had higher degree centrality than non-Internet venues (difference, 6.6: P=0.03) and higher betweenness centrality (difference, .04: P=0.16) (**Table 4-13**). However, the latter comparison necessitates a conservative interpretation considering a p-value > 0.05, thus random variation cannot be ruled out. As a technical aside, when the test was performed in UCINET the reported one-tailed and two-tailed p-value was identical to the Fisher-Pitman in STATA.

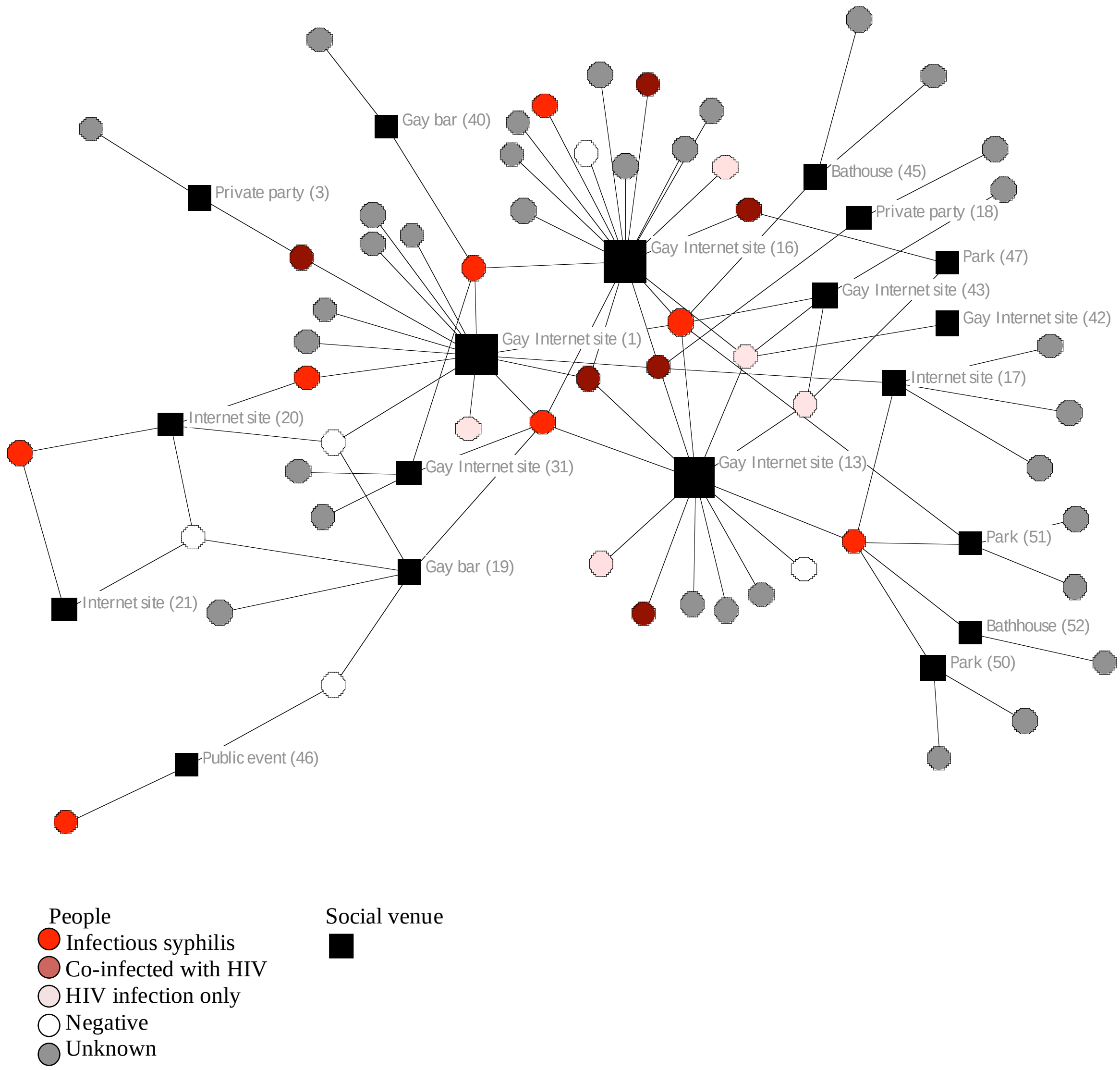
Table 4-13: Comparison of point degree centrality of Internet and non-Internet sex partner meeting venues, connected by patronage of MSM

Comparison of point degree centrality measures of Internet and non-Internet venues				
	Internet venues n = 10	Non-Internet venues n = 11	Difference	*P* Value
Mean point degree centrality	10.5	3.9	6.6	0.03
Mean point betweenness centrality	0.06	0.02	0.04	0.16

To test for equality of means the two-sample Fisher-Pitman permutation test was used with exact p-values calculated. Point degree centrality scores of venues calculated with valued data. Betweenness centrality scores are binary and normalized.

Another statistical analysis was performed to test the robustness of study findings. In the construction of the affiliation network, sexual contacts of cases were connected to a venue if the case reported meeting the contact at a specific venue. However, due to anonymous sexual partnering, many of these contacts could not be located for an interview. This problem may distort network topology inasmuch as an anonymous partner of one case may be the same anonymous partner of another case or the case itself. Thus another analysis restricted to interviewed participants was performed on the venue network connected by MSM. In the network of sex partner meeting venues, connected by interviewed participants only, Internet venues still had higher degree centrality than non-Internet venues (difference, 6: p=0.04).

Venues (1), (13) and (16) connected the most men in the MSM network of sex partner meeting venues. A cluster of 35 men were linked together by their patronage of these three Internet venues. Most importantly, these three sex partner meeting venues connected two thirds of all infectious syphilis cases in the network (**Figure 4-11 and Figure 4-12**).



Circles represent people and sex partner meeting places are symbolized by a square. This two-mode sexual affiliation network subcomponent consisted of 54 men and 19 venues.

Figure 4-11: Two-mode sexual affiliation network among MSM

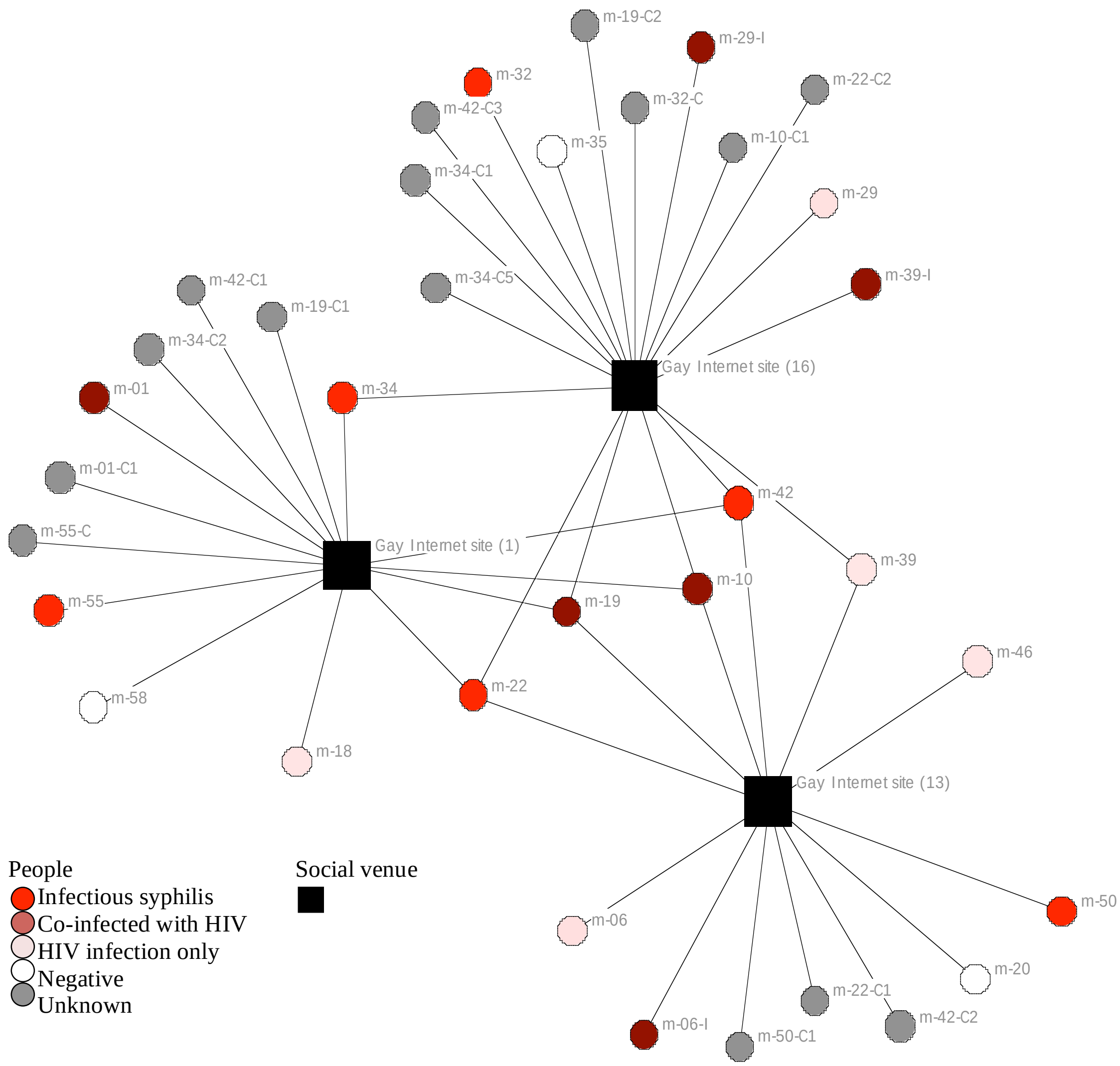


Figure 4-12: **Venues with the highest degree centrality in the MSM sexual affiliation network; displayed as a two-mode network**

In the sexual affiliation network, a cluster of 35 men were linked together by their patronage of three Internet venues. These three Internet venues had the highest degree centrality in the network of sex partner meeting venues and connected two thirds of all infectious syphilis cases.

Chapter Five: Discussion

In this chapter, an overall interpretation of results is provided with consideration given to other relevant research. Study limitations are examined including direction and magnitude of potential bias and statistical imprecision. Finally external validity of study findings and implications for practice and future research are discussed.

5.1 Synopsis of key findings; study objectives revisited

The primary research objective of this pilot survey network study was to explore the use of social network analysis as both an epidemiological and methodological tool to determine the relative importance of sex partner meeting places to the transmission of syphilis. Network analysis of a sexual affiliation network as an epidemiological tool allowed identification of key sex partner meeting venues that connected individuals who were infected with syphilis. Among MSM, a densely connected sexual affiliation network of 94 men, comprised of 18 cases of infectious syphilis and 76 named sexual contacts connected by 21 sex partner meeting venues was identified. The network structure of men linked together by sex partner meeting venues was significantly more cohesive than the network of these same men connected by sexual contact. Hierarchal modeling of venue seeking behaviour detected a cluster of 35 men linked together by their patronage of three Internet venues. These three Internet venues had considerable overlap of male patrons. That is, the same group of men went to all three sites. Thus an intervention at any one of these venues would reach men who patronize the other two. Furthermore, these three venues were directly connected to almost every venue in the network of sex partner meeting places. Analysis of the venue network showed that Internet venues had significantly higher degree centrality than non-Internet venues. Most importantly these three Internet venues connected two thirds of all infectious syphilis cases in the network.

A comparison of the heterosexual affiliation and sexual network revealed similar network topology. In the network of 32 venues connected by patronage of 28 heterosexual syphilis cases and their 32 contacts, street venues had higher degree centrality than non-street venues, but this difference was not statistically significant. In contrast to the MSM network, the venue network of heterosexual persons was relatively disconnected. Furthermore, no one venue connected more than two cases of syphilis.

5.2 Consideration of possible mechanisms and explanations for study findings

It is conceivable that MSM seeking multiple and/or anonymous partners do so by means of social venues such as the Internet and these settings are foci of STI proliferation. The plausibility of this assumption rests on the knowledge that MSM who use the Internet to seek sex partners are more likely to have high-risk sex-related behaviour,[72, 76, 77] thus they are at increased risk for syphilis acquisition. A plausible explanation for the observed densely connected venue network is that sex seeking may be largely concentrated at relatively few sites that are widely known in the MSM community. In addition, MSM that use the Internet to find sex partners also seek partners at other venues such as bathhouses, bars, and parks [72] causing overlap of venue patronage. The observed difference in density between the sexual and affiliation network suggests there have been methodological challenges in collection of sexual network data, not least a considerable naiveté around the issue of anonymity. The affiliation network may be an indication of the true structure of the underlying sexual network.[10]

On the other hand, the venue network among heterosexuals was relatively disconnected. While some subgroups of the population such as sex-trade workers, intravenous drug users, and the street involved, may use similar or the same venues for sex seeking; venues used to find partners in the general population may be more diverse. When an epidemic moves out of subgroup populations, central venues may be more difficult to elucidate. Only one third of known syphilis cases in the heterosexual network in this study were either a sex-trade worker or their clients compared to 65 % in the previous Calgary outbreak.[24]

Another possible explanation was the temporal constraint of this study, which may have prevented patterns of heterosexual venue use to emerge. The largest clique in the heterosexual affiliation network was a group of four persons connected by a sex stroll. One of these individuals was named as a sexual contact to a case of secondary syphilis but tested negative for the infection so his partners were not included in the network. However, this self-identified crack cocaine dealer reported having sex with 23 commercial sex trade workers in the last six months who worked this stroll. Had this person tested positive for syphilis, this clique would have contained 27 individuals. He was also connected to several other women through two separate crack houses and a street corner.

Among MSM, the network of men connected by venues was significantly more cohesive than the sexual network. A possible explanation is that people may have recalled places better than persons whom they had sexual contact with. First, sexual partnerships initiated through Internet sites were commonly anonymous and remained so for the duration of the sexual encounter. In fact, 43% of MSM network members in this study were identified as anonymous sexual partners. However, most individuals who were unable to provide any identifiable information on sexual contacts were able to provide detailed information on places where they met sex partners. For example, case m-50 was unable to provide identifying information for any of the estimated thirty partners he reported. However, he listed five venues, three of which he used regularly, to recruit sex partners.

Secondly, even when sexual partners are known, people forget a substantial number of them [35] and individuals with many new partners are likely to forget more.[35] Furthermore, reporter error is strongly biased toward the routine and long-term patterns.[118] Participants who utilized venues regularly to “cruise” for sex were largely unable to provide names of casual contacts or even specific dates of when they met a sex partner. However, many of these participants could provide detailed accounts of their sex seeking behaviour such as the specific time of day they sought sex, how many times per week they cruised for sex, and on average the weekly or monthly number of partners successfully met at the venue(s) for the purpose of sex. Thus, inquiring about venues may have resulted in less missing edges and nodes than inquiring about partners.

Akin to MSM, heterosexual participants would frequently provide venue information when they were unable to offer identifiable information on contacts. However, one third of network members in the affiliation network were isolates (could not be connected to anyone else through a venue). Given that 70% of heterosexuals named at least one venue where sexual partnering occurred, the aforementioned reasons (temporal constraint and heterosexual epidemic may be moving outside subgroup populations) explains the lack of cohesion in the affiliation network of people.

5.3 Comparison of study findings with relevant findings from other published research

The findings of this study provide empirical evidence to support the notion that analysis of a sexual affiliation network could provide valuable information needed to target venues for STI prevention and control recently hypothesized by Frost.[10] Furthermore, this report confirms the value of inquiring about sex partner meeting venues to identify transmission patterns of STIs established in several other published reports [58, 68, 83, 89] and substantiates the utility of network analysis to quantify the importance of venues in an outbreak of a STI previously demonstrated by De et al.[68]

5.3.1 Prevalence of venue use for sex seeking

Reported prevalence of individuals who use venues to search for sex partners is variable and differs according to venue type and the population under study. It should be noted, however, that even among subgroup comparisons (i.e. same population and same venue) it is difficult to compare findings due to methodological differences in sampling. For example, findings from reports that recruit participants through the Internet will overestimate prevalence of individuals who look for partners online. Nevertheless, this study found that venue use for the purpose of seeking sex among MSM was consistent with estimates reported in some studies,[60, 64] but was higher than estimates reported by others.[61, 62, 66] Though there is a relative paucity of studies that measured the utilization of social venues for seeking sex partners among heterosexuals, the proportion of heterosexual participants that reported using at least one venue in this study was larger than estimates reported in two previous studies.[70, 89] It should be noted that the study by Mcfarlane et al.[70] was a cross-sectional study of participants presenting to public health for HIV testing and the authors collected data on Internet use only. On the other hand, STI attendees in the current study are a reasonably homogenous group, and generally speaking may have somewhat liberal sexual attitudes. Also, most of these reports inquired about public venues only, while other studies focused exclusively on one or two venues such as the Internet. Thus, a higher proportion of venue use than previously reported was expected given that this study placed no restrictions on the type of venue named and permitted participants to name private places. Lastly, on preliminary examination one might expect prevalence to be higher in the present study because of the nature of snowball sampling (a case nominates his partners). However, prevalence of venue use among the original cases was about the same.

5.3.2 Venues use among heterosexual participants

In this report, street venues, bars, and private parties were the most frequently named places where sexual partnering occurred among heterosexual participants; each accounting for about a quarter of the places named. However, venues used by sex-trade workers or their clients to seek sex for drugs or money accounted for about 40% of all venues named. In a previous outbreak in Calgary, transmission was also traced to sex-trade venues.[24] In another study not restricted to MSM, the most common sex partner meeting places among syphilis cases was street venues; private residences accounted for 20% of geocodable venues named.[89] When studies were expanded to other STIs, a case-control study of a gonorrhoea outbreak found that 33% of cases and 12% of controls attended a bar.[87]

5.3.3 Online partner seeking among MSM

In 1999, an outbreak of syphilis in San Francisco among MSM was associated with meeting partners online.[69] Since that time, the Internet has emerged as an important venue for soliciting sex partners in MSM populations. In a previous outbreak in Calgary during the early 2000s, the Internet was also implicated in the transmission of syphilis infection.[24] A striking finding in the current study was that three quarters of MSM participants reported using the Internet to find sex partners. Among MSM participants who used venues for sexual partnering, only two reported non-Internet sites exclusively.

This is in contrast to a 2006 meta-analysis of 14 studies. In their report, Liau et al. [77] indicated that the percentage of MSM that go online to seek sex partners ranged from 23.3% to 98.5% depending on the methodology used in study recruitment. However, based on studies that recruited participants offline, 40% of MSM used the Internet for sex seeking.[77]

Of MSM participants interviewed in this report, one third were known to be HIV positive at the time of the interview. Studies have shown that MSM who are HIV positive are more likely to go online to seek sex partners than HIV negative/unknown MSM.[77] Almost 90 % of MSM known to be HIV positive interviewed in the current study reported using the Internet for partner finding. Therefore, prima facie, it was reasonable to expect higher Internet venue usage in this sample. However, in the previous Calgary outbreak, similar HIV co-infection among MSM was reported and sexual contact was more frequently initiated in bars and/or bathhouses.[24] Thus HIV status alone is not a plausible explanation for the differences in the observed prevalence. It is likely that the results in this investigation reflect the fact that the use of the Internet for finding sex partners appears to be increasing over time [67, 73] and those that use the Internet to find sex partners also seek partners at bathhouses, bars, and parks.[72]

5.4 Study strengths and limitations

5.4.1 Study strengths

To my knowledge, this is the first empirical study to analyze a sexual affiliation network of persons infected with syphilis. This study can serve as a starting point in discussions of the role of sexual affiliation networks in the proliferation of STIs and can inform further research. A notable strength of this study was the considerable willingness of subjects to participate in the study and report venues where sex partnering occurred. The Calgary STD clinic it is a well-established clinic that has a long-standing relationship with the community, founded on trust and a commitment to confidential services. Trust in the clinic and the approach utilized by the staff to recruit subjects likely contributed to the high response rate.

Boundary specification on which relation to consider in this study was clearly defined conceptually and operationally reducing the potential for measurement error. Unlike the methodological challenges of defining some social relations such as friendship,[119] the definition of sexual contact and venue use was unambiguous. Furthermore, face-to face interviews by one interviewer allowed full explanation and probing of both relations collected.

Finally, the study may have had some direct impact on STI control by identifying transmission patterns that informed staging and treatment decisions. For example, case m-37 could not remember any sexual contacts in the last six months. On a subsequent interview when asked about places, he remembered a bar where he had picked up a woman. He could not initially remember her name but did remember her nickname. Three months earlier a study participant who went by the same nickname stated she had picked up a man at this same bar. Based on the time frame reported by both participants it was determined that case m-37 was likely infected by the earlier case. Also, this study identified epidemiologic important sex partner meeting places ideal for target intervention.

5.4.2 Study limitations

Several limitations of this study warrant caution. Understanding causality and threats to study validity is the cornerstone of epidemiologic research. The drive for determinants of adverse health outcomes requires the recognition that both systematic and random error is present in every epidemiologic study and network studies are no exception. Generally the goal of epidemiologic studies is to determine the estimate of effect of an exposure variable(s) on an outcome parameter, from a randomly selected sample drawn from the source population of interest. Interpretation of epidemiologic estimates in this context requires the assessment and control of bias, including selection, misclassification and confounding.

The key difference between traditional epidemiologic research and network research is a shift from attributes of individuals to the pattern of relationships and interactions between them. This shift requires the collection of data on relationships as well as individuals, which poses unique challenges to the assessment of the validity of network research. In network research, missing nodes or edges have the potential to seriously distort network indices such as centrality and density measures, adversely affecting internal study validity. Most often, missing nodes or edges are due to boundary specification, respondent inaccuracy, non-response or study design.[120] This network study was vulnerable to recall bias (misclassification bias), non-response/missing data, boundary-specification error and temporal limitation.

5.4.2.1 Misclassification bias

In epidemiology misclassification bias results from measurement error of subjects, a value or an attribute.[121] In social network research, measurement error occurs when there is an erroneous classification between a pair of nodes that is different than the true underlying structure.[122] Although strategies were implemented in the design stage to increase memory recall, the fact is most people don't name all of their sexual partners;[35] a challenge that cannot be ignored. The impact of forgetting on the structural properties of friendship networks has been examined and the results suggest that forgetting of friends may underestimate the overall network density, degree centralization, and number of cliques.[123] However, more research is necessary to determine whether forgetting sexual partners distorts the measurement of structural properties in sexual networks; specifically with respect to link-trace sampling which may be particularly vulnerable to bias. The findings of the current study suggest it is plausible that memory recall may have been better for naming venues, strengthening the value of collecting data on affiliation networks.

There are inherent limitations associated with retrospective self-report methods in general. Due to the sensitive and private nature of sexual behaviour and the social and moral issues surrounding this topic, social desirability bias is an important concern. Inquiring about sex partner meeting places required that the participant admit she/he has participated in socially undesirable behaviour (e.g. sex with prostitutes). Behaviours perceived as socially unacceptable may have been underreported. There is evidence that participants may refuse to answer, substantially underreport, or simply report "no" when the sexual behaviour is not considered socially acceptable.[91, 98, 124] Thus, social desirability bias may lead to an underreporting of stigmatized behaviour, such as use of a sex-trade venue. This potential bias may have attenuated the difference in centrality seen between street and non-street venues.

5.4.2.2 Non-response and missing data

All studies are vulnerable to departure from simple random error even when response rates are high, as in the current study. Bias could occur if the relationship between network inclusion and venue-seeking behaviour is different for those who participate than for those who should be theoretically eligible for the study. It is possible that sex-trade workers were under represented in this study. As shown in Chapter four (**Table 4-1**), 40% of non-participants were female compared to 15 % of participants. Of the 7 non-participant females, 4 (57%) were sex-trade workers. Non-participation was due in part to individuals being treated offsite (e.g. street van) prior to ethical approval of additional recruitment sites. These individuals may have been more likely to name street venues for meeting sex partners. This would potentially result in an underestimate of the true difference in centrality between street venues and non-street venues in the heterosexual venue network, strengthening study findings. However the magnitude of the attenuated difference would be relatively small given only four individuals were not included. Furthermore, although baseline characteristics were available on non-participant syphilis cases, data on sexual contacts of these cases was unattainable. Thus it was not possible to determine whether systematic differences existed between those contacts who responded and those who did not.

In general centrality measures are reasonably stable in the face of missing data [125, 126] and degree and betweenness centrality are equally robust.[125] In fact with small amounts of data loss, Borgatti et al.[125] found that correlation (of centrality) between actual and simulated networks with missing data was greater than 90%.[125] In addition, the type of error (loss of a node or edge) had similar effects on the stability of centrality.[125] The latter study created random networks to test the robustness of centrality. Another study that used real whole networks taken from the literature, found the same high correlation between the simulated network (edges and nodes deleted at random) and the whole network, even with large amounts of data loss.[126] However, one should take care to note that contact-tracing sampling, such as the sampling approach used in the current study is more complex than the network sampling used in both the aforementioned studies. More research is needed to test effect of non-response on network measures in this type of study design.

Anonymous partnering may have resulted in an underestimate of the true density of the sexual networks. To check the validity of this assumption, a simulation network was created to test the effect of missing data on network structure. Under the premise that an anonymous partner of one case may be the same anonymous partners of another case or the case itself, 15 anonymous contacts were removed from the MSM sexual network and density recalculated. This resulted in a 40 % increase in density. However, the extent to which the problem of anonymous partnering distorted the network topology in this study is not known. Furthermore, the effect of anonymous sexual partnering on network density may not be the same in different settings.

5.4.2.3 Boundary specification

The relations that defined the networks were clearly defined; a study strength. However, there are limitations to a link-trace network survey design used in this study inasmuch as non-inclusion of some individuals and venues was unavoidable resulting in missing nodes and edges. Additionally, the study sample was bound geographically. Named sexual partners located outside of Calgary were not interviewed, and thus the sexual and sexual affiliation networks may be incomplete. Nevertheless, this method was the best method available to permit the identification of the target population.

5.4.2.4 Limitation of study power

The temporal limitation may have constrained network size. This study lacked statistical power to do a direct comparison of point betweenness centrality among Internet and non-Internet sites in the MSM venue network as just nine venues had a betweenness score above zero, only two of which were non-Internet sites. Similarly, only two venues in the heterosexual venue network had a betweenness centrality greater than zero.

5.4.3 Methodological issues

Network studies have several obvious inherent methodological limitations. The fact is samples (in complete or partial network research) are not independent and certainly cannot claim to be random samples. In consequence, generalizability of study results is limited. The sexual and affiliation network topology among syphilis cases and their partners shown in this study may not be representative of sexual and affiliation networks in other populations of syphilis cases. However, the explicit allowance of the responses of dyads to be dependent is the strength of social network research. The social network approach in this study did yield some interesting findings that could not have been obtained with a random sampling approach. Furthermore, the results of this study do suggest that the analysis of a sexual affiliation network can provide insight into to the transmission of syphilis. It is reasonable to assume that analysis of sexual affiliation networks in other populations of syphilis would also produce rich data about transmission patterns.

Although important advances have been made in statistical methods so the standard assumptions of independence and random sampling is not required, like re-sampling techniques such as permutation tests and bootstrap methods, these techniques have largely been developed in complete networks.[51] There is little empirical evidence on whether partial sexual networks are a representation of the 'real' complete network.

Complete networks require that the entire population under study is enrolled and that data on the relation of interest is obtained on every person.[51] Arguably, even when the researcher uses a complete network design, the fact is most (maybe all) networks are incomplete, missing edges or nodes. Furthermore, complete enumeration of the entire sexual network of all infectious syphilis cases is impossible as many syphilis cases in the population are unknown to health officials because the individual has not presented for testing. In addition, in this study (and in public health) only those individuals with infection have their partners traced.

Lastly, sexual affiliation networks do not provide definitive evidence of direct sexual connections, but rather an indirect source of information on underlying sexual networks.[10] Though most participants were able to estimate a date when they met a sex partner at a venue (e.g. “shortly after Christmas” or “second week in March”), many participants were unable to provide exact dates unless it was recent (last 2-4 weeks) or it was a specific event or memorable calendar date (e.g. New Years eve). Even when participants could provide exact dates, unequivocal sexual connections were difficult to elucidate. For example, two different syphilis positive males reported meeting another male for sex on the same weekend at the same park. It is likely that these two men had sex with each other. However, because the encounter was anonymous, identifying information was difficult to ascertain. Thus there is no way to know for certain that these two men are sexually connected.

Similarly, a female index case diagnosed with secondary syphilis reported regularly having sex for money on a specific street during the last six months. During the study period, another syphilis case enrolled in the study, a male, reported having sex with a sex-trade worker from the same street venue. Again, it was difficult to know with confidence that the initial index case transmitted syphilis to the male participant. Nevertheless, information on locations where syphilis may have been acquired did elucidate important epidemiologic information on the dynamics of syphilis transmission that was not ascertainable by the identity of sex partners alone.

5.5 Implications for practice and further research

5.5.1 STI prevention and control

This analysis highlights the difficulties in practice, not least of which is considerable challenge around the issue of partner notification and case finding. Approximately one half of heterosexual contacts and two thirds of MSM contacts in the sexual networks could not be located for testing, most often because casual anonymous partnering prevented the collection of sufficient identifying information. The findings in this report underscore the importance of inquiring about places where individuals meet their sex partners and the potential of analyzing sexual affiliation networks in practice to: 1) identify sexual partnership formation patterns to prioritize contact tracing; 2) increase the number of sexual partners elicited and brought to treatment; 3) identify venues for prevention and targeted intervention, expanding reach of the population at risk and 4) reduce stigmatization that may be associated with identifying individuals.

Information on sexual affiliations can identify sexual partnership formation patterns and increase the yield of contact tracing. Simply asking the question about places where individuals meet sex partners has benefit. Previous studies have shown that inquiring about places where individuals meet partners increased yield of sex partners elicited [127, 128] and the number of infected individuals brought to treatment.[128] Sexual partnerships initiated through the sex-trade and the Internet were frequently anonymous, making it tremendously difficult to trace direct contacts. However, data on venues where partners were recruited was a rich source of information.

An interesting case example is that of f-60. This participant, a self-identified sex-trade worker, reported no sexual partners on two separate interviews with two different staff members; she was later named by a male participant and is shown as a dyad in the heterosexual sexual network (**Figure 4-2**). However, when asked to list places where sexual partnering occurred, this participant named four venues, two venues where she had sex for money on a regular basis; an area known for crack cocaine use in Calgary and a bar in Edmonton. When asked if she could estimate how many sexual contacts she had in the last six months at these venues, she stated “too many to count”. Traditional partner notification methods were unable to identify any contacts or newly diagnosed cases from this index case. Furthermore, sexual analyses may have rendered f-60 inconsequential to the transmission of syphilis in the network. Information on sexual affiliations provided valuable data suggesting this participant may be a ‘core transmitter. Furthermore, these venues where sex partners were recruited may be relatively important to the current epidemic and could be used to help focus outreach and screening efforts.

Analysis of sexual affiliation networks can identify venues for STD prevention and control. Several important subtleties must be considered when determining the optimal venue for targeted prevention and intervention programs. Most MSM participants reported visiting multiple venues. The social venue most frequently named by MSM participants in this study was not the venue with the highest degree or betweenness centrality in the venue network. Inquiring about places alone may miss identifying the most optimal place for STI prevention and control. The venue with the highest degree centrality has the most direct connections to other sex partner meeting places and the people who frequent them. Betweenness centrality may be particularly important when considering a public health intervention (such as dissemination of health information) involving a social venue. Venues that are between other venues in the venue network connect venues (and therefore the people who frequent them) that are otherwise not connected. Thus these venues may influence the spread of information through the network of venues. For these reasons, sexual affiliation network analysis may help inform the PLACE intervention model [78] previously discussed in this report.

Targeting places where MSM meet sex partners for preventive interventions, such as STI counselling and on-site testing, has proven to be feasible, acceptable to both venue patrons and venue owners and operators,[129-133] and effective.[130,131] One study in the United Kingdom found that of the thirty gay venues invited to participate in an on-site syphilis screening program, 77% agreed.[131] Interventions on-site, such as health messaging and condom availability, have the benefit of reaching individuals at the time when condom use is negotiated.[134]

Nevertheless, many owners and operators of public venues fear that on-site syphilis prevention and health promotion activities may have a negative impact on their business and/or cause loss of customers.[135] To enhance venue participation, health care providers need to develop strong collaborative partnerships with both community-based organizations and with venue owners and managers.[131-133] Furthermore, the involvement of venue employees in the promotion of the health program and including venue staff in health promotion activities (e.g. testing), is likely to enhance acceptability.[131] Health officials need to find a balance between maintaining a low profile presence and promoting the health program and also commit to working with venue managers and staff to monitor, and be responsive to, negative feedback or complaints.[133]

The findings of this analysis suggest it may be essential to increase use of the Internet for purposes of public health initiatives to reach those at risk, particularly in MSM populations. Meeting partners online has been associated with previous STDs,[70, 71] recent HIV infection,[63] high-risk sexual behaviour such as fisting,[72] UAI,[76, 77] multiple [70, 71, 76] and anonymous sexual partners,[73] and more partners known to be HIV positive.[70, 74, 75] Many researchers have found the use of the Internet for prevention and education efforts is both possible [24, 69] and acceptable among MSM.[136] Internet-based interventions such as banner ads for syphilis prevention can result in a high number of click-throughs and facilitated chats by health providers in chat-room sessions on gay Internet sites can reach a substantial number of visitors per session.[137] Lastly, identification of venues, such as the Internet, removes stigmatization associated with identifying individuals or groups (often marginalized) at risk for transmission of STIs. However, more research is needed to firmly establish the efficacy of online interventions for STI/HIV prevention.[137, 138]

Data on the effectiveness of place-based STI/HIV health interventions in heterosexual venues such as bars is limited. However, community based mobile screening and treatment clinics targeted at places where sex and drugs are sold, have shown promising results for the control of syphilis. [83, 139, 140]

5.5.2 Recommendations for partner notification

On a practical note, lessons learned during data collection may have functional utility to partner notification/contact tracing. First, re-interviewing proved to be fruitful. While almost all participants agreed to be re-interviewed, the STD clinic staff were only able to identify ten individuals for re-interview. Opportunities for re-interview included follow-up treatment and serological testing. Of the ten participants that were re-interviewed, six individuals gave identifying information on partners that could not be ascertained during the first interview, including phone number and/or full name. These interviews resulted in an additional seven sexual contacts; four were brought to treatment, two were identified as recently diagnosed and treated, and one could not be located during the study period. Brewer [35] also found re-interviewing increased recall of partners.

Second, the opportunity for a single investigator to interview most of the cases and contacts during the study period for partner and venue information had obvious epidemiologic advantages. Knowledge from interviews of previous cases and contacts sometimes informed later interviews; analogous to solving a crossword puzzle where the puzzle pieces are cases and contacts and clues the information each one provided. The aforementioned examples are case in point.

Third, access to a computer during the partner interview may be valuable. For example, one case named five sexual partners but was only able to give useful identifying information on one partner because she stated she communicated with her partners through an online social networking site. The patient agreed to log on to the site during the interview to provide information on her remaining partners. While online the individual decided to notify her partners. One of her partners replied to her message during the interview and we were able to provide him with the address and directions to the clinic.

Finally, partner notification online may increase contact tracing yield. Offering assistance to patients to set up a new profile name on Internet sites they frequent, and assisting them to compose a message may have limited effectiveness. However working with Internet providers to provide direct healthcare/user interaction has proven successful (Dr. Ronald Read, personal communication).

Incorporating social network analysis into routine contact tracing/partner notification public health practices can be effective in increasing the yield of syphilis cases brought to treatment.[141] However a number of challenges have been identified including, the need for additional resources and specialized training to utilize SNA software, specialized software to extract data from provincial STI data management programs into SNA software programs, and considerable time may be required to develop useful network graphs.[141] In a resource-strapped public health environment with competing priorities these challenges are not trivial.

5.5.3 Future research

Further research is required to establish the best methods to collect data on venue use for the purpose of sexual partnering. Two comprehensive reviews of the empirical literature concluded that sexual behaviour research lacks a gold standard for validating self-report of sexual behaviour.[91, 99] Important steps have been made in identifying places where people meet new sex partners.[78] However, further research that compares different techniques for measuring sexual affiliations and replication of these studies over different age, ethnic, and high-risk groups can improve methodological precision.

Future sexual affiliation projects should consider the collection of frequency and pattern of venue patronage data in addition to the number of partners met at a particular venue. Frequency and pattern of venue use (e.g. time of day/day of week) could help inform public health efforts and reduce memory recall errors. Furthermore, this study suggests that recall of venues where individuals meet their partners maybe subject to less recall error than partner data, however empirical research is needed to test this hypothesis.

In addition, evaluations should be performed to establish whether public health initiatives/screening opportunities targeted at venues identified through social network analysis result in case finding, reach at-risk populations missed by conventional screening, have behavioural impact, and ultimately effect STI/HIV transmission. Further studies are needed to evaluate the efficacy of Internet-based interventions for STI/HIV prevention. Also, future research should examine the effectiveness of place-based interventions in heterosexual venues in North American populations and should aim to evaluate practices that increase the acceptability of place-based interventions to venue owners and clientele.

Finally, further methodological studies are needed to address bias/systematic error in network research with strategies for assessment and control. The application of social network methodology is ubiquitous and some well-known principles of network analysis such as centrality and density appear deceptively straightforward. However, many factors can distort these measures severely effecting study validity. More empirical robustness studies, that use contact tracing/link-trace network data, are necessary to examine the effect of missing data on network measures such as centrality, density, and centralization.

5.6 Conclusion

Alberta is facing a significant burden of syphilis infection. In public health, we have had limited success in reaching vulnerable populations most at risk. To meet this challenge, we need to expand prevention initiatives, increase screening opportunities, and embark on a number of targeted intervention strategies. In this pilot survey network study, social network analysis of a sexual affiliation network allowed identification of key sex partner meeting venues that connected individuals who were infected with syphilis in a sustained infectious syphilis outbreak in the Calgary Health Region in Alberta, Canada. These venues could provide opportunity to reach hidden populations at risk and provide public health officials with an epidemiologic target for primary and secondary prevention strategies to prevent further dissemination of disease. The present study provides evidence that models of disease transmission should consider social venues. Inquiring about venues where syphilis may have been acquired offered considerable insight into the dynamics of transmission that was not ascertainable by inquiring about sex partners alone.

References

1. Wasserman S, Faust K. Social Network Analysis: Methods and Applications. New York: Cambridge University Press; 1994.

2. Klovdahl AS. Social networks and the spread of infectious diseases: the AIDS example. Soc Sci Med 1985;21:1203-16.

3. Gupta S, Anderson RM, May RM. Networks of sexual contacts: implications for the pattern of spread of HIV. AIDS 1989;3:807-17.

4. Rothenberg RB, Potterat JJ, Woodhouse DE, Muth SQ, Darrow WW, Klovdahl AS. Social network dynamics and HIV transmission. AIDS 1998;12:1529-36.

5. Potterat JJ, Rothenberg RB, Muth SQ. Network structural dynamics and infectious disease propagation. Int J STD AIDS 1999;10:182-5.

6. Bell DC, Atkinson JS, Carlson JW. Centrality measures for disease transmission networks. Soc Networks 1999;21:1-21.

7. Liljeros F, Edling CR, Amaral LAN. Sexual networks: implications for the transmission of sexually transmitted infections. Microbes Infect 2003;5:189-96.

8. Doherty IA, Padian NS, Marlow C, Aral SO. Determinants and consequences of sexual networks as they affect the spread of sexually transmitted infections. J Infect Dis 2005;191:s42-54.

9. Friedman SR, Neaigus A, Jose B, et al. Sociometric risk networks and risk for HIV infection. Am J Public Health 1997;87:1289-96.

10. Frost SDW. Using sexual affiliation networks to describe the sexual structure of a population. Sex Transm Infect 2007;83:i37-42.

11. Singh AE, Romanowski B. Syphilis: Review with Emphasis on Clinical, Epidemiologic, and Some Biologic Features. Clin Microbiol Rev 1999;12:187-209.

12. Fleming DT, Wasserheit JN. From epidemiological synergy to public health policy and practice: the contribution of other sexually transmitted diseases to sexual transmission of HIV infection. Sex Transm Infect 1999;75:3-17.

13. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement. Epidemiology 2007;18:800-4.

14. Vandenbroucke JP, von Elm E, Altman DG, et al. Strengthening the reporting of observational studies in epidemiology (STROBE): explanation and elaboration. Epidemiology 2007;18:805-35.

15. Eatough G. Fracastoro's Syphilis. Liverpool, Great Britian: Francis Cairns; 1984.

16. Clark EG, Danbolt N. The Oslo study of the natural history of untreated syphilis; an epidemiologic investigation based on a restudy of the Boeck-Bruusgaard material; a review and appraisal. J Chron Dis 1955;2:311-44.

17. Garnett GP, Aral SO, Hoyle DV, Cates Jr W, Anderson RM. The natural history of syphilis: Implications for the transmission dynamics and control of infection. Sex Transm Dis 1997;24:185-200.

18. Fiumara NJ. Syphilis in newborn children. Clin Obstet and Gynecol 1975;18:183-9.

19. Public Health Agency of Canada. Reported cases and rates of infectious syphilis by province/territory and sex. Available at http://www.phac-aspc.gc.ca/std-mts/sti-its_tab/syphilis_pts1993-08-eng.php. Accessed January 30, 2010.

20. Alberta Health and Wellness. Blood borne pathogens and sexually transmitted infections action plan. June, 2008. Available at http://www.health.alberta.ca/documents/BBP-STI-plan-2008.pdf. Accessed April 29, 2009.

21. Alberta Health and Wellness. Sexually Transmitted Infections, preliminary data January to December 2008. Presentation to Alberta Advisory Committee on HIV and STI February 23, 2009.

22. Public Health Agency of Canada. Reported cases and rates of infectious syphilis 2008-2009. Available at http://www.phac-aspc.gc.ca/std-mts/stdcases-casmts/cases-cas-09-eng.php. Accessed January 29, 2010.

23. Public Health Agency of Canada. National goals for the prevention and control of sexually transmitted diseases in Canada. CCDR 1997; 23S6:2-9.

24. Jayaraman GC, Read RR, Singh A. Characteristics of Individuals With Male-to-Male and Heterosexually Acquired Infectious Syphilis During an Outbreak in Calgary, Alberta, Canada. Sex Transm Dis 2003;30:315-9.

25. Mahoney JF, Arnold RC, Harris AD. Penicillin treatment of early syphilis: a preliminary report. Am J Public Health 1943;33:1387-91.

26. Public Health Agency of Canada. Canadian Guidelines on Sexually Transmitted Infection 2006 edition. Ottawa, ON: Public Health Agency of Canada; 2006.

27. Ghanem KG, Erbelding EJ, Cheng WW, Rompalo AM. Doxycycline compared with benzathine penicillin for the treatment of early syphilis. Clin Infect Dis 2006;42:e45-9.

28. Wong T, Singh AE, De P. Primary syphilis: serological treatment response to doxycycline/tetracycline versus benzathine penicillin. Am J Med 2008;121:903-8.

29. Province of Alberta. Communicable Diseases Regulation. In: Public Health Act, Alberta Regulation 238/1985. Edmonton: Alberta Queen's Printer; 2009.

30. Public Health Agency of Canada. Syphilis chapter (revised January 2010). Canadian Guidelines on Sexually Transmitted Infections. Ottawa, ON: Public Health Agency of Canada.

31. Gunn RA, Montes JM, Toomey KE, et al. Syphilis in San Diego County 1983-1992: Crack cocaine, prostitution, and the limitations of partner notification. Sex Transm Dis 1995;22:60-6.

32. Peterman TA, Toomey KE, Dicker LW, Zaidi AA, Wroten JE, Carolina J. Partner notification for syphilis: A randomized, controlled trial of three approaches. Sex Transm Dis 1997;24:511-8.

33. Andrus JK, Fleming DW, Harger DR, et al. Partner notification: can it control epidemic syphilis? Ann Intern Med 1990;112:539-43.

34. Kohl KS, Farley TA, Ewell J, Scioneaux J. Usefulness of partner notification for syphilis control. Sex Transm Dis 1999;26:201-7.

35. Brewer DD, Garrett SB, Kulasingam S. Forgetting as a cause of incomplete reporting of sexual and drug injection partners. Sex Transm Dis 1999;26:166-76.

36. Brewer DD. Case-finding effectiveness of partner notification and cluster investigation for sexually transmitted diseases/HIV. Sex Transm Dis 2005;32:78-83.

37. Hogben M, Paffel J, Broussard D, et al. Syphilis partner notification with men who have sex with men: A review and commentary. Sex Transm Dis 2005;32:S43-7.

38. Macdonald G. The analysis of equilibrium in malaria. Tropical diseases bulletin 1952;49:813-29.

39. May RM, Anderson RM. Transmission dynamics of HIV infection. Nature 1987;326:137-42.

40. Anderson RM. Transmission dynamics of sexually transmitted infections. In: Holmes KK, Sparling PF, Mardh PA et. Sexually transmitted diseases. Third ed. New York: McGraw-Hill; 1999:25-37.

41. Wasserheit JN, Aral SO. The dynamic topology of sexually transmitted disease epidemics: implications for prevention strategies. J Infect Dis 1996;174:S201-13.

42. Rothenberg R, Narramore J. Commentary: The relevance of social network concepts to sexually transmitted disease Control. Sex Transm Dis 1996;23:24-9.

43. Rothenberg R, Kimbrough L, Lewis-Hardy R, et al. Social network methods for endemic foci of syphilis: a pilot project. Sex Transm Dis 2000;27:12-8.

44. Yorke JA, Hethcote HW, Nold A. Dynamics and control of the transmission of gonorrhea. Sex Transm Dis 1978;5:51-6.

45. Thomas JC, Tucker MJ. The development and use of the concept of a sexually transmitted disease core. J Infect Dis 1996;174:S134-43.

46. Rothenberg RB. The geography of gonorrhea: empirical demonstrations of core group transmission. Am J Epidemiol 1983;117:688-94.

47. Jennings JM, Curriero FC, Celentano D, Ellen JM. Geographic identification of high gonorrhea transmission areas in Baltimore, Maryland. Am J Epidemiol 2005;161:73-80.

48. Bush KR, Henderson EA, Dunn J, Read RR, Singh A. Mapping the core: Chlamydia and gonorrhea infections in Calgary, Alberta. Sex Transm Dis 2008;35:291-7.

49. Tanfer K. Sex and disease. Playing the odds in the 1990s. Sex Transm Dis 1994;21:S65-72.

50. Scott J. Social Network Analysis: A Handbook. Second ed. London: Sage publications; 2000.

51. Morris M. Network Epidemiology: A Handbook for Survey Design and Data Collection. New York: Oxford University Press; 2004.

52. Luke DA, Harris JK. Network analysis in public health: history, methods, and applications. Annu Rev Public Health 2007;28:69-93.

53. Borgatti SP, Everett MG. Network analysis of 2-mode data. Soc Networks 1997;19:243-69.

54. Rothenberg RB, Sterk C, Toomey KE, et al. Using social network and ethnographic tools to evaluate syphilis transmission. Sex Transm Dis 1998;25:154-60.

55. Seña AC, Muth SQ, Heffelfinger JD, O'Dowd JO, Foust E, Leone P. Factors and the sociosexual network associated with a syphilis outbreak in rural North Carolina. Sex Transm Dis 2007;34:280-7.

56. Stigum H, Magnus P, Bakketeig LS. Effect of changing partnership formation rates on the spread of sexually transmitted diseases and human immunodeficiency virus. Am J Epidemiol 1997;145:644-52.

57. Humblet O, Paul C, Dickson N. Core group evolution over time: high-risk sexual behavior in a birth cohort between sexual debut and age 26. Sex Transm Dis 2003;30:818-24.

58. Potterat JJ, Rothenberg RB, Woodhouse DE, Muth JB, Pratts CI, Fogle (II) JS. Gonorrhea as a social disease. Sex Transm Dis 1985;12:25-32.

59. Wylie JL, Jolly A. Patterns of chlamydia and gonorrhea infection in sexual networks in Manitoba, Canada. Sex Transm Dis 2001;28:14-24.

60. Paz-Bailey G, Meyers A, Blank S, et al. A case-control study of syphilis among men who have sex with men in New York City: association with HIV infection. Sex Transm Dis 2004;31:581-7.

61. Binson D, Woods WJ, Pollack L, Paul J, Stall R, Catania JA. Differential HIV risk in bathhouses and public cruising areas. Am J Public Health 2001;91:1482-6.

62. Aynalem G, Smith L, Bemis C, Taylor M, Hawkins K, Kerndt P. Commercial sex venues: a closer look at their impact on the syphilis and HIV epidemics among men who have sex with men. Sex Transm Infect 2006;82:439-43.

63. Thiede H, Jenkins RA, Carey JW, et al. Determinants of recent HIV infection among Seattle-area men who have sex with men. Am J Public Health 2009;99:S157-64.

64. Imrie J, Lambert N, Mercer CH, et al. Refocusing health promotion for syphilis prevention: results of a case-control study of men who have sex with men on England's south coast. Sex Transm Infect 2006;82:80-3.

65. Grov C, Parsons JT, Bimbi DS. Sexual risk behavior and venues for meeting sex partners: an intercept survey of gay and bisexual men in LA and NYC. AIDS Behav 2007;11:915-26.

66. Niccolai LM, Stephens N, Jenkins H, Richardson W, Muth SQ, Rothenberg R. Early syphilis among men in Connecticut: epidemiologic and spatial patterns. Sex Transm Dis 2007;34:183-7.

67. Simms I, Fenton KA, Ashton M, et al. The re-emergence of syphilis in the United Kingdom: the new epidemic phases. Sex Transm Dis 2005;32:220-6.

68. De P, Singh AE, Wong T, Yacoub W, Jolly AM. Sexual network analysis of a gonorrhoea outbreak. Sex Transm Infect 2004;80:280-5.

69. Klausner JD, Wolf W, Fischer-Ponce L, Zolt I, Katz MH. Tracing a syphilis outbreak through cyberspace. JAMA 2000;284:447-9.

70. McFarlane M, Bull SS, Rietmeijer CA. The Internet as a newly emerging risk environment for sexually transmitted diseases. JAMA 2000;284:443-6.

71. McFarlane M, Bull SS, Rietmeijer CA. Young adults on the Internet: risk behaviors for sexually transmitted diseases and HIV1. J Adolesc Health 2002;31:11-6.

72. Mettey A, Crosby R, DiClemente RJ, Holtgrave DR. Associations between internet sex seeking and STI associated risk behaviours among men who have sex with men. Sex Transm Infect 2003;79:466-8.

73. Taylor M, Aynalem G, Smith L, Bemis C, Kenney K, Kerndt P. Correlates of Internet use to meet sex partners among men who have sex with men diagnosed with early syphilis in Los Angeles County. Sex Transm Dis 2004;31:552-6.

74. Kim AA, Kent C, McFarland W, Klausner JD. Cruising on the Internet highway. J Acquir Immune Defic Syndr 2001;28:89-93.

75. Bolding G, Davis M, Hart G, Sherr L, Elford J. Gay men who look for sex on the Internet: is there more HIV/STI risk with online partners? AIDS 2005;19:961-8.

76. Benotsch EG, Kalichman S, Cage M. Men who have met sex partners via the Internet: prevalence, predictors, and implications for HIV prevention. Arch Sex Behav 2002;31:177-83.

77. Liau A, Millett G, Marks G. Meta-analytic examination of online sex-seeking and sexual risk behavior among men who have sex with men. Sex Transm Dis 2006;33:576-84.

78. Weir SS, Boerma T. From people to places: overview of the PLACE method and lessons learned. Measure Evaluation Bull 2002;4:1-6.

79. Weir SS, Morroni C, Coetzee N, Spencer J, Boerma JT. A pilot study of a rapid assessment method to identify places for AIDS prevention in Cape Town, South Africa. Sex Transm Infect 2002;78:i106-13.

80. Figueroa JP, Dolan CB, Dale D, Hileman SB, Weir S. An assessment of sites where persons go to meet sexual partners in St. James, Jamaica, using the PLACE method. Sex Transm Dis 2007;34:410-5.

81. Weir SS, Tate JE, Zhusupov B, Boerma JT. Where the action is: monitoring local trends in sexual behaviour. Sex Transm Infect 2004;80:ii63-8.

82. Khan M, Brown L, Nagot N, Salouka S, Weir SS. HIV-related sexual behavior in urban, rural and border areas of Burkina Faso. AIDS Behav 2006;10:607-17.

83. Michaud JM, Ellen J, Johnson SM, Rompalo A. Responding to a community outbreak of syphilis by targeting sex partner meeting location: an example of a risk-space intervention. Sex Transm Dis 2003;30:533-8.

84. Breiger RL. The duality of persons and groups. Social Forces 1974;53:181-90.

85. Klovdahl AS, Graviss EA, Yaganehdoost A, et al. Networks and tuberculosis: an undetected community outbreak involving public places. Soc Sci Med 2001;52:681-94.

86. Klovdahl AS, Graviss EA, Musser JM. Infectious disease control: combining molecular biologic and network methods. In: Levy JA, Pescosolido BA, eds. Social Networks and Health Vol 8, Advances in Medical Sociology. New York: Elsevier Science Ltd.; 2002:73-99.

87. De P, Singh AE, Wong T, Yacoub W. Outbreak of *Neisseria gonorrhoeae* in northern Alberta, Canada. Sex Transm Dis 2003;30:497-501.

88. Wylie JL, Shah L, Jolly AM. Demographic, risk behaviour and personal network variables associated with prevalent hepatitis C, hepatitis B, and HIV infection in injection drug users in Winnipeg, Canada BMC Public Health 2006;6:229-48.

89. Michaud JM, Johnson SM, Ellen J. Comparison of sex partner meeting venues and residences of syphilis cases in Baltimore. Sex Transm Dis 2004;31:239-42.

90. Schroder KEE, Carey MP, Vanable PA. Methodological challenges in research on sexual risk behavior: II. Accuracy of self-reports. Annals of Behavioral Medicine 2003;26:104-23.

91. Catania JA, Gibson DR, Chitwood DD, Coates TJ. Methodological problems in AIDS behavioral research: influences on measurement error and participation bias in studies of sexual behavior. Psychol Bull 1990;108:339-62.

92. Fenton KA, Johnson AM, McManus S, Erens B. Measuring sexual behaviour: methodological challenges in survey research. Sex Transm Infect; 2001:84-92.

93. Bell DC, Montoya ID, Atkinson JS. Partner concordance in reports of joint risk behaviors. J Acquir Immune Defic Syndr 2000;25:173-181.

94. Johnson JC, Boster JS, Holbert D. Estimating relational attributes from snowball samples through simulation. Soc Networks 1989;11:135-58.

95. Potterat JJ, Woodhouse DE, Muth SQ, et al. Network dynamism: history and lessons of the Colorado Springs study. In: Network Epidemiology: A Handbook for Survey Design and Data Collection. New York: Oxford University Press; 2004:87-114.

96. Hox JJ, De Leeuw ED. A comparison of nonresponse in mail, telephone, and face-to-face surveys. Applying multilevel modeling to meta-analysis. Quality and Quantity 1994;28:329-44.

97. Dillman DA. Mail and internet surveys: The tailored design method. 2000.

98. Tourangeau R, Yan T. Sensitive questions in surveys. Psychol Bull 2007;133:25.

99. Weinhardt LS, Forsyth AD, Carey MP, Jaworski BC, Durant LE. Reliability and validity of self-report measures of HIV-related sexual behavior: Progress since 1990 and recommendations for research and practice. Arch Sex Behav 1998;27:155-80.

100. Young H, Pryde J, Duncan L, Dave J. The Architect Syphilis assay for antibodies to *Treponema pallidum*: an automated screening assay with high sensitivity in primary syphilis. Sex Transm Infect 2009;85:19-23.

101. Marangoni A, Moroni A, Accardo S, Cevenini R. Laboratory diagnosis of syphilis with automated immunoassays. J Clin Lab Anal 2009;23:1-6.

102. Singh AE, Wong T, De P. Characteristics of primary and late latent syphilis cases which were initially non-reactive with the rapid plasma reagin as the screening test. Int J STD AIDS 2008;19:464-8.

103. Larsen SA, Steiner BM, Rudolph AH. Laboratory diagnosis and interpretation of tests for syphilis. Clin Microbiol Rev 1995;8:1-21.

104. Hagedorn HJ, Kraminer-Hagedorn A, De Bosschere K, Hulstaert F, Pottel H, Zrein M. Evaluation of INNO-LIA syphilis assay as a confirmatory test for syphilis. J Clin Microbiol 2002;40:973-8.

105. Freeman LC. Centrality in social networks: conceptual clarification. Soc Networks 1979;1:215-39.

106. Krackhardt D. Graph theoretical dimensions of informal organizations. In: Carley KM, Prietula MJ, eds. Computational Organization Theory. Hillsdale, New Jersey: Lawrence Erlbaum Associates 1994:89-111.

107. Borgatti SP, Everett MG, Freeman LC. Ucinet for Windows version 6.247: Software for Social Network Analysis. Harvard, MA: Analytic Technologies; 2002.

108. Borgatti Martin G, Stephen P. Regular blockmodels of multiway, multimode matrices. Soc Networks 1992;14:91-120.

109. Borgatti SP, Everett MG. Models of core/periphery structures. Soc Networks 1999;21:375-95.

110. Johnson SC. Hierarchical clustering schemes. Psychometrika 1967;32:241-54.

111. Ludbrook J, Dudley H. Why permutation tests are superior to t and F tests in biomedical research. The American Statistician 1998;52:127-32.

112. Ludbrook J. Advantages of permutation (randomization) tests in clinical and experimental pharmacology and physiology. Clinical and Experimental Pharmacology and Physiology 1994;21:673-86.

113. Snijders TAB, Borgatti SP. Non-parametric standard errors and tests for network statistics. Connections 1999;22:161-70.

114. Kaiser J, Lacy MG. A general-purpose method for two-group randomization tests. Stata Journal 2009;9:70-85.

115. StataCorp. Stata Statistical Software for Macintosh: Release 10.1: College Station, TX: Stata Corporation; 2009.

116. Woodhouse DE, Potterat JJ, Rothenberg RB, et al. Ethical and legal issues in social network research: the real and the ideal. In: Needle RH, Coyle SL, Genser

SG, et al, eds. Social networks, drug abuse and HIVtransmission. Rockville, MD: National Institute on Drug Abuse,1995:131–43. (NIDA research monograph 151).

117. Barabasi AL, Bonabeau E. Scale-free networks. Scient Am 2003;288:60-9.

118. Freeman LC, Romney AK, Freeman SC. Cognitive structure and informant accuracy. American Anthropologist 1987;89:310-25.

119. Fischer CS. What do we mean by 'friend'? An inductive study. Soc Networks 1982;3:287-306.

120. Kossinets G. Effects of missing data in social networks. Soc Networks 2006;28:247-68.

121. Last JM. A Dictionary of Epidemiology. Fourth ed. New York: Oxford University Press; 2001.

122. Holland PW, Leinhardt S. The structural implications of measurement error in sociometry. Journal of Mathematical Sociology 1973;3:85-111.

123. Brewer DD, Webster CM. Forgetting of friends and its effects on measuring friendship networks. Soc Networks 2000;21:361-73.

124. Allen S, Meinzen-Derr J, Kautzman M, et al. Sexual behavior of HIV discordant couples after HIV counseling and testing. AIDS 2003;17:733-40.

125. Borgatti SP, Carley KM, Krackhardt D. On the robustness of centrality measures under conditions of imperfect data. Soc Networks 2006;28:124-36.

126. Costenbader E, Valente TW. The stability of centrality measures when networks are sampled. Soc Networks 2003;25:283-307.

127. Brewer DD, Garrett SB. Evaluation of interviewing techniques to enhance recall of sexual and drug injection partners. Sex Transm Dis 2001;28:666-77.

128. Brewer DD, Potterat JJ, Muth SQ, et al. Randomized trial of supplementary interviewing techniques to enhance recall of sexual partners in contact interviews. Sex Transm Dis 2005;32:189-93.

129. Woods WJ, Binson DK, Mayne TJ, Gore LR, Rebchook GM. HIV/sexually transmitted disease education and prevention in US bathhouse and sex club environments. AIDS 2000;14:625-6.

130. Huebner DM, Binson D, Woods WJ, Dilworth SE, Neilands TB, Grinstead O. Bathhouse-based voluntary counseling and testing is feasible and shows preliminary evidence of effectiveness. J AIDS 2006;43:239-46.

131. Lambert NL, Fisher M, Imrie J, et al. Community based syphilis screening: feasibility, acceptability, and effectiveness in case finding. Sex Transm Infect 2005;81:213-6.

132. Blank S, Gallagher K, Washburn K, Rogers M. Reaching out to boys at bars: utilizing community partnerships to employ a wellness strategy for syphilis control among men who have sex with men in New York City. Sex Transm Dis 2005;32:S65-72.

133. Mullens AB, Staunton S, Debattista J, Hamernik E, Gill D. Sex on premises venue (SOPV) health promotion project in response to sustained increases in HIV notifications. Sexual Health 2009;6:41-4.

134. Weir SS, Pailman C, Mahlalela X, Coetzee N, Meidany F, Boerma JT. From people to places: focusing AIDS prevention efforts where it matters most. AIDS 2003;17:895-903.

135. Vega MY, Roland EL. Social marketing techniques for public health communication: a review of syphilis awareness campaigns in 8 US cities. Sex Transm Dis 2005;32:S30-6.

136. Bolding G, Davis M, Sherr L, Hart G, Elford J. Use of gay Internet sites and views about online health promotion among men who have sex with men. AIDS Care 2004;16:993-1001.

137. Klausner JD, Levine DK, Kent CK. Internet-based site-specific interventions for syphilis prevention among gay and bisexual men. AIDS Care 2004;16:964-70.

138. Bull SS, Lloyd L, Rietmeijer C, McFarlane M. Recruitment and retention of an online sample for an HIV prevention intervention targeting men who have sex with men: The Smart Sex Quest Project. AIDS Care 2004;16:931-43.

139. Hibbs JR, Gunn RA. Public health intervention in a cocaine-related syphilis outbreak. Am J Public Health 1991;81:1259-62.

140. Kahn RH, Moseley KE, Thilges JN, Johnson G, Farley TA. Community-based screening and treatment for STDs: results from a mobile clinic initiative. Sex Transm Dis 2003;30:654-8.

141. Ogilvie G, Knowles L, Wong E, et al. Incorporating a social networking approach to enhance contact tracing in a heterosexual outbreak of syphilis. Sex Transm Infect 2005;81:124-7.

142. Rothenberg RB, Potterat JJ, Woodhouse DE, Darrow WW, Muth SQ, Klovdahl AS. Choosing a centrality measure: epidemiologic correlates in the Colorado Springs study of social networks. Soc Networks 1995;17:273-97.

143. Manly BFJ. Randomization, bootstrap and Monte Carlo methods in biology. Third ed. Boca Raton, Florida: Chapman & Hall/CRC; 2006.

144. Efron B. Bootstrap methods: Another look at the jackknife. The Annals of Statistics 1979;7:1-26.

Appendix A: Consent

FACULTY OF MEDICINE | UNIVERSITY OF CALGARY

TITLE OF RESEARCH PROJECT:

The Use of Social Network Analysis to Quantify the Importance of Social Venues in an Infectious Syphilis Outbreak in Calgary, Alberta: A pilot study.

SPONSOR:

Alberta Health Services: Calgary Health Region

RESEARCH TEAM:

Dr. Elizabeth A. Henderson, Ms. Rhonda L. Fur, Dr. Ronald R. Read, Dr. Jenny Godley, Ms. Katherine Bush & Ms. Colleen Roy

This consent form is only part of the process of informed consent. It should give you the basic idea of what the research is about and what your participation will involve. If you would like more detail about something mentioned here, or information not included here, please ask. Take the time to read this carefully and to understand any accompanying information. You will receive a copy of this form. The University of Calgary Conjoint Health Research Ethics Board has approved this research study

WHAT WOULD I HAVE TO DO?

Alberta Health and Wellness requires the collection of data on the Syphilis History and Syphilis Contact Notification form for routine care. This information may be routinely disclosed for the purposes of providing health services or infectious disease control. In addition to this routine use of data, we seek your permission for members of the research team to review your form and to get more detail from you on sex partner meeting places. The purpose for seeking this information is to develop understanding of the role social meeting places play in a persistent infectious syphilis outbreak in the Calgary Health region. The information we get from this study may help us to provide better screening opportunities in the future for patients with Syphilis. The question on meeting places will take an additional 5 minutes to complete. In all other respects you will receive routine care.

DO I HAVE TO PARTICIPATE?

Participation in the study aspect is voluntary and if you do not wish to participate, you may refuse without jeopardizing your health care. Once the interview on meeting places has begun, if you decide not to continue, please indicate this to the interviewer and no further information will be collected.

RISKS, BENEFITS AND PRIVACY:

There are no additional risks or benefits to participants in the research over and above what apply in the mandatory collection of this data.

Data collected for the purposes of the research project will be kept in a locked file cabinet accessible only to the research team. After participants are given unique identifiers, personal identifying information will be permanently destroyed. Also, any information that may permit the identity of individuals or social venues will be concealed in any reporting of results to protect anonymity.

SIGNATURES

Your signature on this form indicates that you 1) have understood to your satisfaction the information regarding your participation in the research project, and 2) agree to participate as a research subject.

In no way does this waive your legal rights nor release the investigators, or involved institutions from their legal and professional responsibilities. You are free to withdraw from the study at any time without jeopardizing your health care.

Participant's Name	Signature and Date
Investigator/Delegate's Name	Signature and Date
Witness' Name	Signature and Date

QUESTIONS/CONCERNS

If you have further questions or want clarification regarding this research and/or your participation, please contact:

Ms. Rhonda Fur (403) 955-6700 or Dr. Henderson (403) 944-4373

If you have any questions concerning your rights as a possible participant in this research, please contact the Director of the Office of Medical Bioethics, University of Calgary, at 403- 220-7990.

A signed copy of this consent form has been given to you to keep for your records and reference.

Appendix B: Alberta syphilis history & contact form

ALBERTA HEALTH & WELLNESS - SYPHILIS HISTORY

Name: ____________________ (include maiden name and alias)

STD Clinic File#: ____________ AH File#: ____________

Date of Birth: YYYY MMM DD Gender: ☐F ☐M Marital Status: ☐

Address:
Street: ____________________
City / Town: ____________________
Province: ____________ Postal Code: ____________
Telephone: ( ) ____________ Cell Phone: ( ) ____________
Other locating or contact information: ____________________

Ethnicity: ☐Caucasian ☐Black ☐Oriental ☐Other Asiatic ☐First Nations ☐Metis ☐Inuit ☐Other ________

Lives on Reserve: ☐Yes ☐No Name of Reserve: ____________

Date of Immigration: YYYY MMM DD Country of Birth: ____________

Location of Immigration Medical: ____________________

Family Doctor: ____________________

Reason for this visit: (X all that apply) ☐Contact ☐Symptoms ☐Prenatal ☐STD Screening ☐Sexual Assault ☐Annual Checkup ☐Blood Work Follow-up ☐Immigration Follow-up ☐Treatment for Syphilis

PREVIOUS HISTORY: Previous Diagnosis of Syhilis: ☐Yes ☐No Other Treponemal Infections: (i.e., yaws, pinta, etc.) ☐Yes ☐No

Describe previous history: (i.e., sores(chancres), rashes, previous serology result, past treatment with injections or pills, other STI, etc.)

If YES for previous syphilis, was the stage of infection known: ☐Not Known ☐Primary ☐Secondary ☐Early Latent ☐Late Latent ☐CNS ☐Congenital ☐Other ____________

PREVIOUS Tx: ☐Yes ☐No Drug & Dose (if known): ____________ Drug is unknown: ☐Pills ☐Injection(s)

Location of Treament: ____________ (i.e.,clinic, city/town, province, country) Date: ____________ (approximate date, if acutual date is unknown)

CURRENT HISTORY: Describe clinical findings reported by the patient and/or the physician/clinic:
(i.e., sores (chancres), rashes, fever, discharge, dysuria, other STI, etc.)

If Pregnant: EDD: YYYY MMM DD or LMP: YYYY MMM DD

(X all that apply) ☐Sex with females only ☐Sex with males only ☐Sex with both males & females ☐Sex Trade Worker ☐Sex with Sex Trade Worker ☐Injection Drug User (IDU) ☐Sex with IDU

Laboratory tests:
HIV: ☐Positive ☐Negative ☐Pending Test Date: YYYY MMM DD
HSV: ☐Positive ☐Negative ☐Pending Test Date: YYYY MMM DD
DFA: ________ ☐Positive ☐Negative Test Date: YYYY MMM DD

CSF: Date: YYYY MMM DD
VDRL: ________ Protein: ________
WBC: ________ Glucose: ________
RBC: ________

CURRENT TREATMENT:
Stage of Infection: ☐Primary ☐Secondary ☐Early Latent ☐Late Latent ☐CNS ☐Congenital ☐Other ____________
Syphilis Staging Verified by: ☐Dr. A. Singh ☐Dr. R. Read ☐Dr. B. Romanowski ____________
Treated with: Incude: Date(s) of Treatment, Drug, Dose, Route, Frequency

Treated by: Name: ____________ Location: ____________
(See Reverse for Partner Information. If a mother is presumed Late Latent, children should be tested.)

Completed by: ____________________ Date: ____________

10/6/2006 1

ALBERTA HEALTH & WELLNESS - SYPHILIS - CONTACT INFORMATION

Contact One Information:

Name (include alias):
Last First Middle

Gender: Male Female
Date of Birth: YYYY MMM DD
Age:
Marital Status:

Ethnicity: Caucasian Black Oriental Other Asiatic First Nations Metis Inuit Other

Current Address:
Street:
City / Town:
Province: Postal Code:
Phone: ( ) Cell Phone: ( )
Other locating / contacting information:

Relationship to Patient: (X all that Apply)
Steady Partner
Working in Sex Trade
Ex-Partner
Sex for Money
Casual Known
Sex for Cigarettes or Alcohol
Casual Unknown
Sex for Drugs

Date of last sexual contact:

Date of Syphilis Serology: YYYY MMM DD
Result of Syphilis Serology: RPR TPPA FTA

Treatment:

Contact Two Information:

Name (include alias):
Last First Middle

Gender: Male Female
Date of Birth: YYYY MMM DD
Age:
Marital Status:

Ethnicity: Caucasian Black Oriental Other Asiatic First Nations Metis Inuit Other

Current Address:
Street:
City / Town:
Province: Postal Code:
Phone: ( ) Cell Phone: ( )
Other locating / contacting information:

Relationship to Patient: (X all that Apply)
Steady Partner
Working in Sex Trade
Ex-Partner
Sex for Money
Casual Known
Sex for Cigarettes or Alcohol
Casual Unknown
Sex for Drugs

Date of last sexual contact:

Date of Syphilis Serology: YYYY MMM DD
Result of Syphilis Serology: RPR TPPA FTA

Treatment:

If the index case is female and the presumptive diagnosis is late latent syphilis, children should be tested.

Child One - Name
Last First Middle
Gender: Male Female
Date of Birth: YYYY MMM DD
Age:
Location:
Date of Syphilis Serology: YYYY MMM DD
Result of Syphilis Serology: RPR TPPA FTA

Child Two - Name
Last First Middle
Gender: Male Female
Date of Birth: YYYY MMM DD
Age:
Location:
Date of Syphilis Serology: YYYY MMM DD
Result of Syphilis Serology: RPR TPPA FTA

Child Three - Name
Last First Middle
Gender: Male Female
Date of Birth: YYYY MMM DD
Age:
Location:
Date of Syphilis Serology: YYYY MMM DD
Result of Syphilis Serology: RPR TPPA FTA

Please attach additional pages for contact information as required.

Appendix C: Venue interview question

ID # ________________ Date ________________

(1) Please list all places you attended in the past 12 months where sexual partnering may have occurred?

A place may include any event, private, public or virtual place such as: a private club; a public club or bar, bathhouse, restaurant, café, park, bookstore, street corner, c-train; or an Internet site, chat room etc.)

** (Use prompts to facilitate the collection of sufficient information to allow characterization of the place).*

Place/Social Venue	**Location or identifying landmarks/features**	**Characterization of social venue**	**Approximate Date**	**Time of day venue attended** (morning/afternoon/ night)
1. E.g. Nightclub & Lounge	Corner of 2^{nd} St. and 13 Av SW, Calgary	Heterosexual public nightclub/bar	Last month	Night
2.				
3.				
4.				
5.				

Complete a separate questionnaire if additional venues are identified.

Appendix D: Mathematical formulas for network parameters

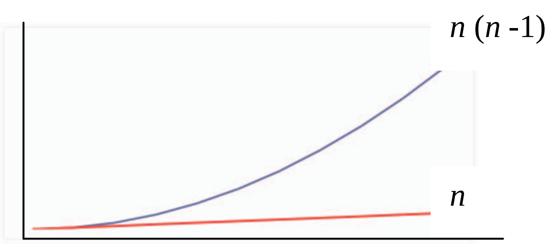
D.1. Group-level network parameters

D.1.1. Density

Density is one of the most widely used group level indices. It refers to the level of cohesion of the entire network.[1, 50]

$$\mathcal{L}/n\,(n-1)/2 \text{ (undirected formula)}$$ [50]

Where $\mathcal{L}$ is simply the number of ties in the network, n the number of nodes or points and $n\,(n-1)/2$ the maximum number of lines a graph can contain (each point can be connected to all other points except itself). Density is relative to network size and a fair comparison of density requires the networks are the same size. The following graph illustrates the limitations of density in large graphs and the how comparing networks of different sizes can be misleading.



The rate at which the number of lines increases is more rapid than number of nodes

The sexual network was a dichotomized matrix (sexual connection = 1, 0 otherwise), however because all ties were considered undirected in this study, the network was symmetrized prior to the calculation of density. The one-mode sexual affiliation networks were undirected (symmetric) by nature, but required dichotomizing prior to the calculation of density.

D.1.2. Krackhardt connectedness

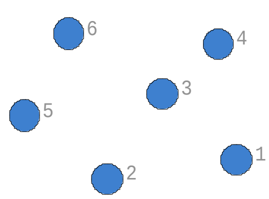
Another measure of group level cohesion is connectedness. A graph is connected if all points are reachable from all other points in the graph (i.e. one component).[1] Connected sexual networks have implications for transmission of infection.

$$1 - \left[\frac{\sum_{i>j} c_{ij}}{n\,(n-1)/2} \right]$$

Krackhardt connectedness undirected formula [106]

- c_{ij} = 1 if point i cannot reach point j by a path of any length
- c_{ij} = 0 if point i can reach point j by a path of any length

Example, if all nodes in a network were isolates connectedness would equal zero



$$1 - \left[\frac{\Sigma\ 5+4+3+2+1}{6(6-1)/2} \right] = 0$$

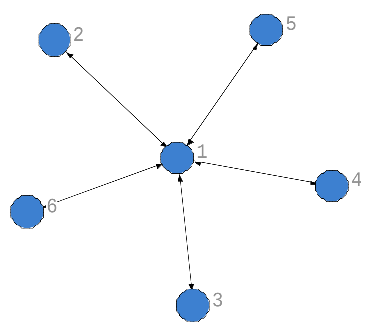
D.1.3. Freeman's degree centralization

This index quantifies the extent to which centrality of the most central point or node varies from the centrality of all other nodes in the graph.[105] For example, a highly centralized network would take the shape of a star, where a single central node is connected to all other nodes in the graph, that are not connected to each other. Freeman's normalized degree centralization [105] can be expressed as:

$$C_X = \frac{\sum_{i=1}^{n} [C_X(p^*) - C_X(p_i)]}{\max \sum_{i=1}^{n} [C_X(p^*) - C_X(p_i)]}$$

$N^2 - 3n + 2$

- C_x (p_i) = one of the point centralities (degree in the current study)
- C_x (p^*) = largest value of C_x (p_i) for any point in the network
- max = the maximum possible sum of differences in point centrality for a graph of n points



$$\frac{\sum (5\text{-}1) + (5\text{-}1) + (5\text{-}1) + (5\text{-}1) + (5\text{-}1) + (5\text{-}5)}{N^2 - 3n + 2} = 20/20 = 1\ (100\%)$$

The sexual affiliation network was dichotomized prior to the calculation of the latter two network statistics (connectedness and centralization). Although degree centrality was calculated with valued data, degree centralization was calculated with binary data. Centralization and connectedness were normalized based on the theoretic maximum (resulting in a score of 0-1).

D.2. Node-level network centrality

One of the fundamental applications of graph theory in social network analysis is the identification of the vertex that holds the most central position in the network.[1, 50] Consideration has been given to which network measure is epidemiologically important to the transmission of STI/HIV. Centrality has been described as a "surrogate for disease transmission potential".[95] Both simulation and empirical studies have demonstrated that centrally located individuals in STI networks influence disease propagation.[6, 142] Degree and betweenness point centrality have been used in the literature to quantify the relative importance of individuals and places in outbreak investigations of infectious disease.[85]

D.2.1. Degree centrality

Degree centrality is the vertex that has the most direct connections to other vertices in the network or graph.[105] In a sexual network this would be the person with the most sexual partners and in a venue network, the venue that is connected (by people) to the most other venues. Expressed formally, the degree centrality [1] for a particular node is:

$$C_D = d(n_i) = X_{i+} = \sum_j X_{ij}$$

where the degree of node *i* is simply the sum of direct connections to other nodes in the network.

D.2.2. Freeman's betweenness centrality

A node that lies on the shortest path or geodesic between other nodes has betweenness centrality.[105] In a sexual network this centrality index can measure the extent to which persons act as intermediaries for transmission of infection in a network. That is, the transmission of disease between individual *j* and individual *k*, who are not directly connected, may be dependent on other individuals in the network that lie on the path 'between' *j* and *k*. An individual with the uppermost betweenness centrality has the highest frequency of geodesics (shortest path between two persons) between other individuals. Venues that are between other venues in the venue network connect venues (and therefore the people who visit them) that are otherwise not connected. Thus these venues may influence the spread of information through the network of venues.

Freeman's betweenness centrality [105] can be expressed as:

$$C_B(n_i) = \sum_{j<k} g_{jk}(n_i) / g_{jk}$$

where $g_{jk}(n_i)$ is the frequency of geodesics linking two individuals (*j*, *k*) that contain individual *i*. $g_{jk}(n_i)/g_{jk}$ is the proportion of geodesics involving individual *i* for all possible shortest paths between *j* and *k*. Therefore $C_B(n_i)$ is simply the sum of these proportions for all pairs of individuals not including individual *i*. This equation is usually normalized by:

$$C'_B(n_i) = C_B(n_i) / [(g-1)(g-2)/2]$$

given that the maximum value possible for C_B is (g-1)(g-2)/2. Thus C'_B for a given node *i* will take on a value between 0 and 1.

Appendix E: Re-sampling methods for test of significance in network data

E.1. Permutation test for equality of means

The mean point degree centrality of network venues was higher than that of non-Internet venues in the network of MSM sex partner-meeting places. However, one needs to consider if it was likely this could have occurred by chance. If there is truly no difference in the mean centrality of Internet and non-Internet venues then randomly interchanging the Internet label on values of centrality in the network shouldn't matter. Thus, the null hypothesis is that the difference in mean centrality of Internet versus non-Internet venues is no different than what may occur from randomly exchanging the Internet and non-Internet labels on data points within the observed data set. To test this hypothesis a permutation test for equality of means was performed. The general approach to the test is as follows. First, all centrality scores are pooled. Scores are then randomly assigned to the Internet or non-Internet category, based on the number of each type of venue in the network. All possible arrangements (permutations) of separating centrality measures into Internet and non-Internet groups are obtained. Then the mean difference is calculated for each permutation, creating an empirical distribution of the mean difference between the two means under the null hypothesis. The p-value is derived from this permutation-based sampling distribution of the difference in the two means rather than from the theoretical t-distribution. The exact two-sided p-value of the test is calculated as the proportion of permutations where the absolute difference was the same or more extreme than the difference observed.[111, 112, 143]

Example of two-group randomization test

Internet (n=10)	**Non-Internet venues (n=11)**	**Mean difference**
	Observed data	
24 22 22 10 8 7 6 3 3 0	9 9 5 4 4 4 3 3 1 1 0	6.591
	Permuted data	
3 3 0 22 5 9 22 4 0 4	3 1 10 8 7 24 9 3 1 4 6	0.291
3 9 3 0 10 4 0 3 6 4	22 5 24 1 3 8 7 9 1 4 22	5.436
9 24 1 10 3 9 4 8 3 7	5 4 3 1 22 22 6 3 0 4 0	1.436
Permuted (10 +11)!/(10!11!) times to calculate all possible combinations (without regard to order) [114] of 21 centrality scores to the two Internet and non-Internet groups		

Mean difference is calculated for each permutation, creating a frequency distribution of the mean difference under the null hypothesis

E.2. Paired-sample t-test based on bootstrap approach

A more accurate estimate of the standard error based on the bootstrap approach, invented by Bradley Efron,[144] was achieved by performing the paired-sample t-test in UCINET to test the difference in density between the sexual and affiliation networks. Snijders and Borgatti [113] developed procedures for calculating standard errors for density based on re-sampling of vertices with a dyad-based bootstrap approach for ties. Systematically outlined in the report by Snijders and Borgatti, the general concept of the bootstrap approach with network data is that the observed network is treated as the population with many random samples drawn with replacement from the observed vertices/nodes.

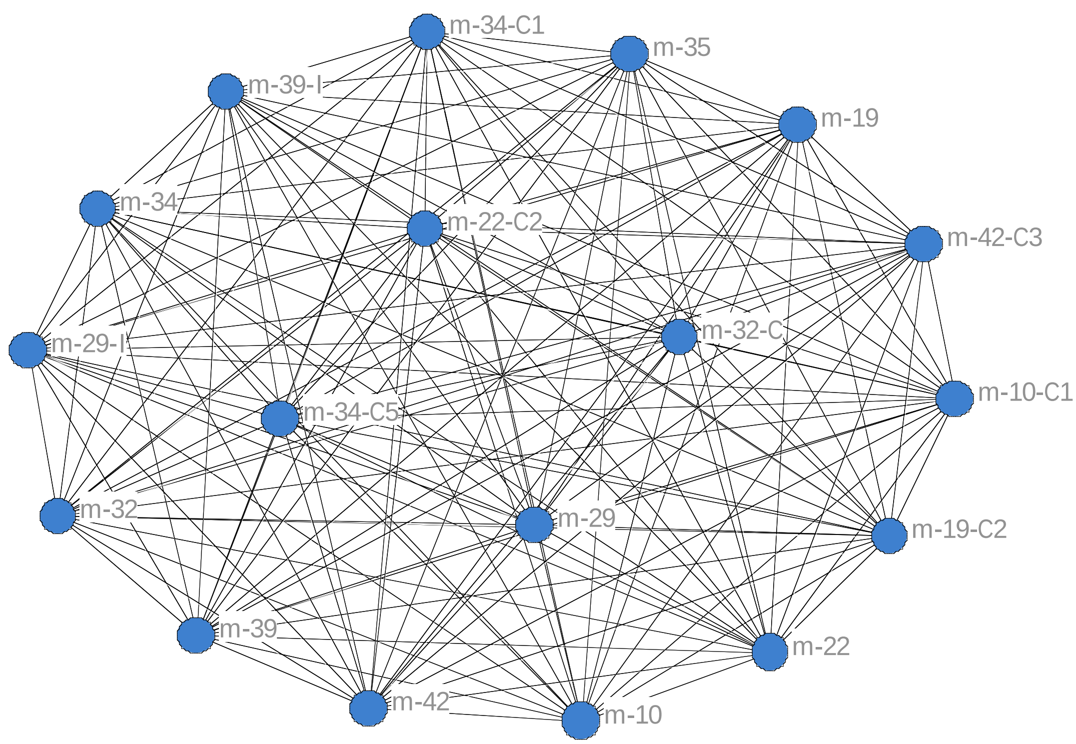
Sampling with replacement means that after a vertex is randomly drawn from the original network it is put back before drawing the next vertex. As a result any vertex can be drawn more than once or not at all. An artificial network of the same size as the original network is constructed with each randomly drawn sample of vertices. The null hypothesis in this study is that the network density is the same regardless of whether the relation was a sexual contact or an affiliation. Since the comparison is on the same set of actors, a t-test analogous to the conventional paired-sample t-test was used with standard errors derived from bootstrap methods. For each bootstrap sample drawn by the aforementioned method, two separate networks, one for each relation was constructed. The density for each network was determined and the difference calculated. This was repeated 10,000 times creating a bootstrap distribution of the difference in network density. The two-sided p-value is the proportion of bootstrap samples where the absolute difference was the same or more extreme than the difference observed. The standard deviation of the 10,000 values of the difference in density that make up the bootstrap distribution become the bootstrap SE used to derive confidence intervals.[113] Although the methods developed by Snijders and Borgattii [113] can be used with most network statistics, these statistical tools are not yet available in UCINET for testing differences in connectedness and centralization.

Appendix F: Clique membership of MSM

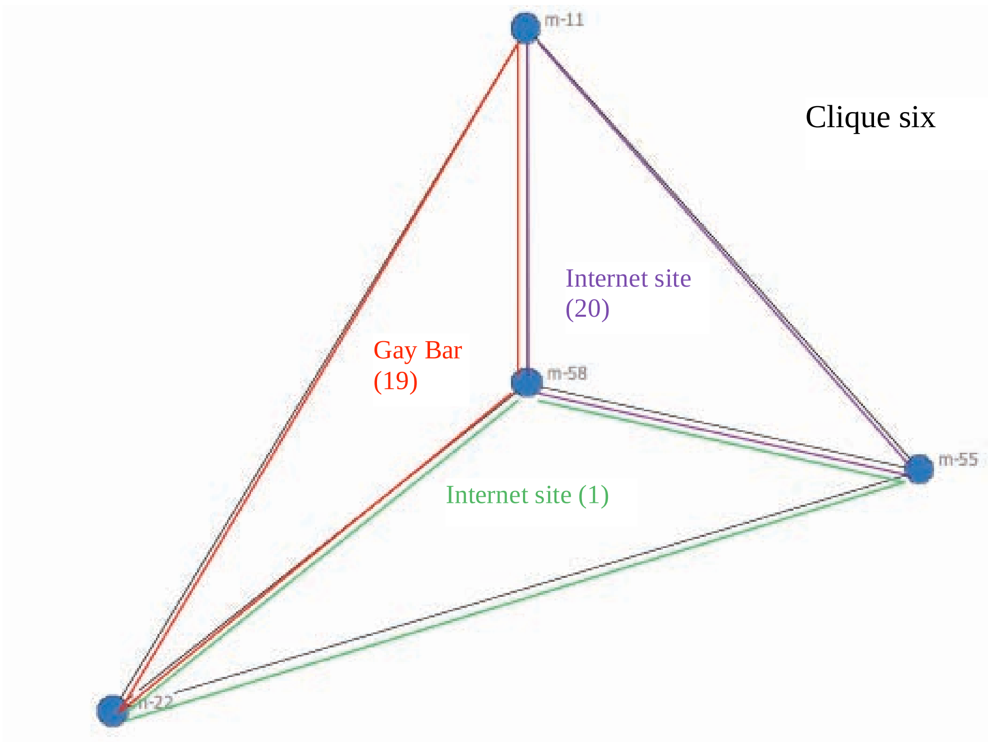
F.1. Clique formation

Cliques were formed if individuals were adjacent to each other in the network of MSM connected by venues. As illustrated in the results chapter of this report, eleven of the thirteen cliques were formed because at least three men visited the same place to seek a sex partner. For example, the largest clique was a group of 18 men connected by Internet site (16).

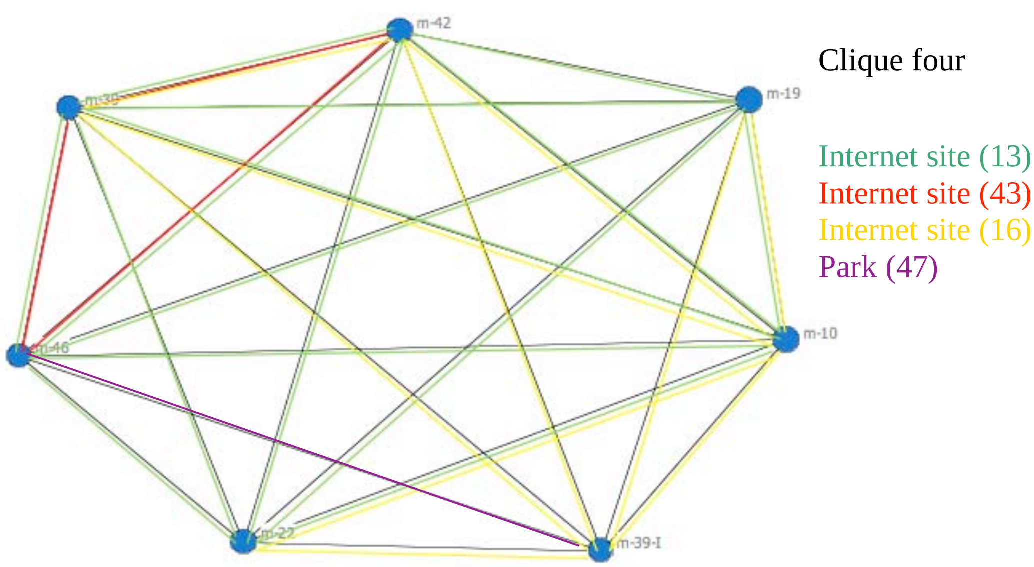
Clique one (n=18)



Two cliques involved multiple places instead of a single sex partner meeting venue. These four men form a clique because they are all adjacent to each other. M-11, m-55, and m-22 went to two of the three above venues; m-58 went to all three venues.



These seven men are connected by four venues.

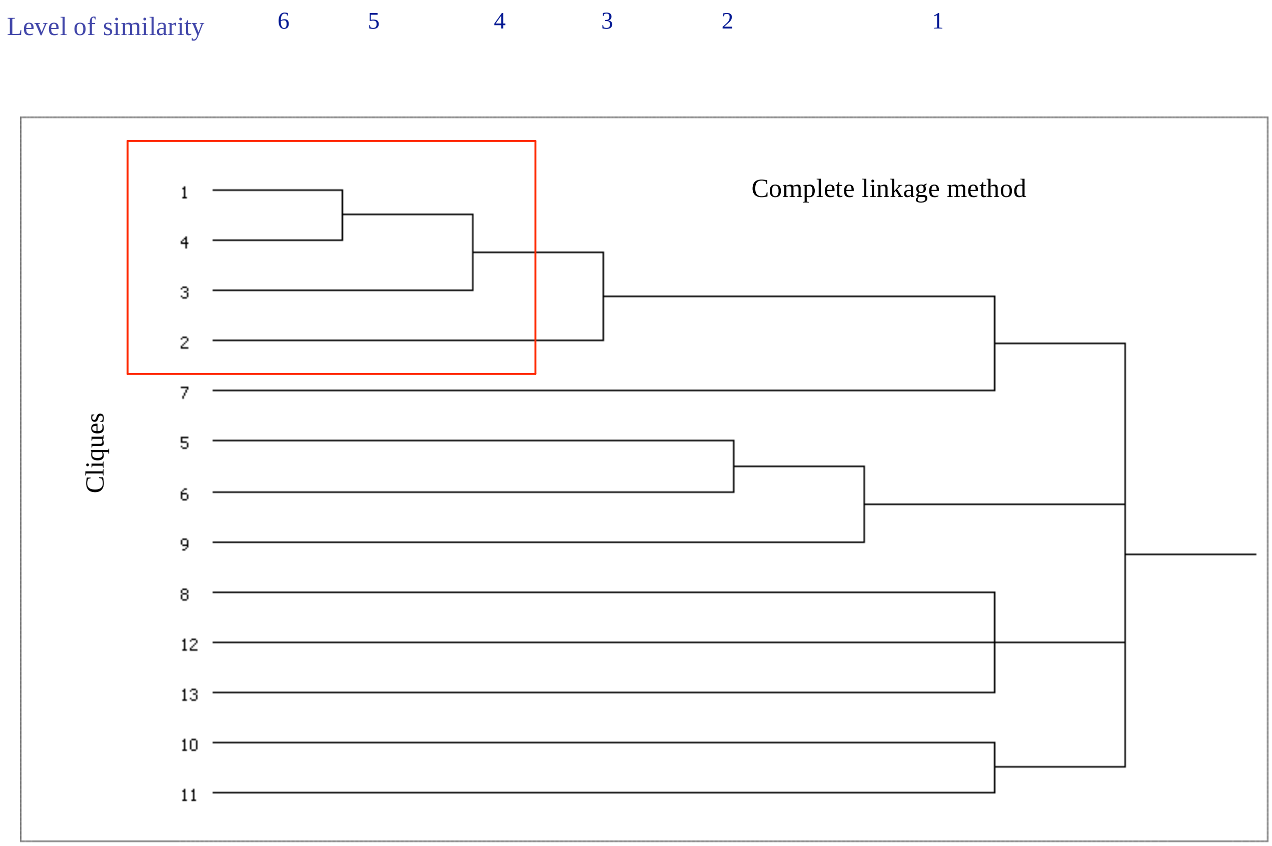


F.2. Hierarchal clustering of clique overlap

Hierarchal modelling of clique overlap in the sexual affiliation network (men connected by sex partner meeting places) was also performed. A group of individuals, cliques one through four, were identified as being members of a single cluster because of considerable overlap of clique membership (i.e. attended the same four venues). The following chart indicates the membership in these four cliques.

Venues that formed cliques	Clique membership
Internet site 16 (n=18) *Clique 1.*	m-10 m-10-C1 m-19 m-19-C2 m-22 m-22-C2 m-29 m-29-I m-32 m-32-C m-34 m-34-C1 m-34-C5 m-35 m-39 m-39-I m-42 m-42-C3
Internet site 1 (n=14) *Clique 2.*	m-01 m-01-C1 m-10 m-18 m-19 m-19-C1 m-22 m-34 m-34-C2 m-42 m-42-C1 m-55 m-55-C m-58
Internet sites 13 (n=13) *Clique 3.*	m-06 m-06-I m-10 m-20 m-19 m-22 m-22-C1 m-39 m-42 m-42-C2 m-46 m-50 m-50-C1
Internet sites 13, 16, 43 and park 47 (n=7) *Clique 4.*	m-10 m-19 m-22 m-39 m-39-I m-42 m-46

The following dendrogram indicates the similarity between these four cliques because of the overlap of men. The level of similarity is the overlap of men. For example six men were in clique one and clique four.



Dendrogram of hierarchal clustering of clique overlap of MSM connected by sex partner meeting places