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Linda Pelude

AUTEUR DE LA THÈSE / AUTHOR OF THESIS

M.Sc. (Epidemiology)

GRADE / DEGREE

Department of Epidemiology and Community Medicine

FACULTÉ, ÉCOLE, DÉPARTEMENT / FACULTY, SCHOOL, DEPARTMENT

Networks among Injection Drug Users:
Random or Scale-Free?

TITRE DE LA THÈSE / TITLE OF THESIS

Ann Jolly

DIRECTEUR (DIRECTRICE) DE LA THÈSE / THESIS SUPERVISOR

George Wells

CO-DIRECTEUR (CO-DIRECTRICE) DE LA THÈSE / THESIS CO-SUPERVISOR

EXAMINATEURS (EXAMINATRICES) DE LA THÈSE / THESIS EXAMINERS

Timothy Ramsay

Shi WuWen

Gary W. Slater

Le Doyen de la Faculté des études supérieures et postdoctorales / Dean of the Faculty of Graduate and Postdoctoral Studies

Networks among Injection Drug Users: Random or Scale-Free?

Linda Pelude

Thesis submitted to the Faculty of Graduate and Postdoctoral Studies in partial fulfillment of the requirements for the MSc Degree in Epidemiology

Epidemiology and Community Medicine
Faculty of Medicine
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Abstract

The primary goal of this research was to identify whether the structure of the network of individuals who inject drugs and share drug injection equipment in Winnipeg, Canada may be scale-free. Recently, sexual networks have been found to be scale-free in a wide range of populations which has important implications in terms of the spread of disease. Epidemic thresholds do not exist in a scale-free network and as a result even weakly infectious viruses can spread easily through a network of contacts. By analogy, identifying the structure of contacts formed by individuals in other infectious disease networks may also help to define transmission dynamics which can be used to develop more effective interventions.

In a series of three papers the scientific literature from a variety of disciplines including physics, epidemiology, mathematical, biological and computer sciences relating to scale free networks is reviewed and integrated; methods used to identify scale-free networks are tested and compared among individuals who inject drugs in Winnipeg, Canada using data from two network studies (a pilot study and a main study); and potential new interventions that could be implemented to help reduce the transmission of HIV and HCV among individuals who inject drugs by the existing needle exchange program are recommended based on the results.

Keywords: Scale-free networks, injection drug use, epidemiology, network analysis

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I couldn't have done it without all of you!

Contribution of Authors

Linda Pelude conceived and designed the analysis for this research. This was a secondary analysis of social network data collected from injection drug users in Winnipeg, Manitoba by Dr. Ann Jolly and her co-investigator Dr. John Wylie for completely different purposes. Initial data entry was done in Winnipeg. However, Linda cleaned and prepared the data for entry and analysis in three programs: SPSS, Curve Expert and Mathcad. All the analysis was primarily conducted by Linda with assistance from her primary supervisor Dr. A. Jolly and her co-supervisor Dr. George Wells. Linda drafted and finalized all the manuscripts.

Dr. Ann Jolly assisted with understanding network theory and methodology, statistical analysis, editing of the manuscripts and overall supervision of the thesis.

Dr. George Wells assisted with understanding the statistical methodology used, assisted with statistical analysis and editing of the manuscripts.

Dr. Fredrick Liljeros (Stockhom University, Stockhom, Sweden) wrote the bootstrapping program used to generate the 95% confidence intervals for the maximum likelihood estimation of the exponent for the network of injection drug users. In addition he assisted with the editing of the second and third manuscripts.

Dr. John Wylie (University of Manitoba, Winnipeg, Manitoba) assisted with the editing of all the manuscripts.

Dr. Lynne Leonard assisted with supervision in relation to injection drug use, HIV and HCV and assisted with the editing of all the manuscripts.

Table of Contents

List of Tables

List of Figures

Chapter One

Chapter Two

Chapter Three

Introduction

Among individuals who inject drugs (IDUs), using previously used needles or other injection equipment such as water, filters or cookers has been shown to carry the greatest probability of transmitting human immunodeficiency virus (HIV) and hepatitis C virus (HCV).[1-16] Epidemiological research has focused on identifying those factors associated with individual injection risk practices while epidemiologic models assume that the population of susceptible individuals are randomly mixed, one where all individuals who inject drugs are equally likely to be infected by contact with an individual who is HIV or HCV positive.[17-18] As a result, many intervention programs that aim to reduce the transmission of HIV and HCV among IDUs have been designed and implemented to modify the factors associated with individual injection risk practices or based on standard epidemiologic modeling that assumes a completely homogenous population.

However, where the spread of disease is also dependent on social networks and their contact patterns which are rarely homogenous among people who inject drugs, interventions that focus solely on modifying individual risk practices or that assume homogenous populations may have limited impact. Network analysis and the identification of the underlying structure of a network provide additional information that can help to determine the spread of disease in a community. Network analysis goes beyond the level of the individual by examining the relationships between people.[19-22]

A network is the structure or relations that form between individuals, objects or groups (e.g., family members, organizations, countries, cells or computers). Network analysis examines the way individuals or groups are connected while the structure of a network is assessed by examining the distribution of the frequency of contacts among individuals.[17, 22]

The distribution of the frequency of contacts in a network has been shown to follow distinct patterns. For example, there are 1) random networks; where links between individuals are created randomly but generally each individual has the same number of contacts (i.e., each individual in the network is connected to three other individuals); 2) regular networks, where links created between individuals follow precise rules, (i.e., each individual has exactly the same number of contacts and 3) small-world networks, where links are created through a combination of randomness and rules.[23] Recently,

some small world networks have been found to be scale-free.[24] Individuals in a scale-free network do not have a typical or average number of contacts. Rather, the majority of individuals have a small number of contacts while a small number of individuals have a large number of contacts.[17, 23, 25]

The structure of a network has been shown to have an effect on the spread of disease. Recent results indicate that the spread of disease in a scale-free network deviates significantly from that of random or regular networks.[26] Infection in a random network spreads to the whole network only if the spreading rate exceeds a critical value or threshold.

It has been suggested that in a scale-free network there is no critical threshold or the threshold is much lower than that seen in a random network.[27] This absence or lowered critical threshold could radically alter many of the standard assumptions used in epidemic modeling.[28] The loss or reduction of a critical threshold implies that even weakly infectious viruses can spread easily and epidemics could arise and propagate faster.[26]

Many public health interventions aimed at preventing or reducing the spread of infection attempt to reduce the epidemic threshold.[29] However, Dezsö and Barabási [26] have shown that interventions directed to random individuals in a scale-free network are ineffective as they are unable to alter the basic properties of the threshold-free diffusion process. They go on to suggest that interventions targeting the small number of individuals with a large number of contacts in a scale-free network could restore the epidemic threshold.[26] In other words, targeting preventive efforts to individuals with the most contacts may be a better way of preventing or limiting the spread of disease rather than targeting everyone.[30]

Combining individual and network methods may help to discover previously unidentified injection related risk factors and consequently new interventions could be implemented that may assist in reducing the transmission of blood-borne pathogens among people who inject drugs.

The overall objective of this thesis is to identify the structure of drug injection equipment sharing networks and how it may contribute to the transmission of HIV and HCV among people who inject drugs.

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1.1 Rationale

Determining the structure of the drug injection equipment sharing networks among IDUs will provide new information regarding the transmission of HIV and HCV among individuals who inject drugs. Specifically, identifying whether the network of IDUs who share drug injection equipment is scale free may have significant epidemiological implications. Scale free networks are characterized by the large variation in the distribution of the frequency of contacts between individuals. Epidemics arise and propagate faster in scale-free networks. Random treatments or interventions have little impact on the spread of disease in a scale-free network. As a result, fundamentally different interventions would be required to reduce the transmission of HIV and HCV through sharing drug injection equipment depending on the structure of these networks.

1.2 Objectives

The overall objective of this thesis is to determine how the structure of IDUs' drug injection equipment sharing networks contribute to the transmission of HIV/HCV among IDUs. Specific objectives include:

- To determine the structure of drug injecting and injection equipment sharing networks of IDUs
- To identify risk factors associated with drug injecting and injection equipment sharing networks of IDUs
- To compare the ordinary least squares (OLS) and maximum likelihood estimation (MLE) methods used to generate a value for the exponent
- To recommend potential new interventions to reduce the transmission of HIV/HCV among IDUs based on the structure of the network identified,

1.3 Ethics

The study design was approved by the Health Research Ethics Board of the University of Manitoba and the Winnipeg Regional Health Authority Research Review Committee. The analysis specific to this paper was also approved by the Ottawa Hospital Research Ethics Board.

1.3 Chapter Summaries

Chapter One: Epidemic thresholds: Do they really exist for all infectious disease networks?

The primary goal of this research was to identify the structure of the network of individuals who inject drugs and share injection equipment in Winnipeg, Canada. Specifically, to determine whether the network may be scale free. Empirical evidence is presented in relation to sexual contact networks which have been found to be scale-free in a wide range of populations. These results have important implications in terms of the spread of disease. Epidemic thresholds do not exist or, if present, are considerably lower in a scale free network compared to a random network and as a result even weakly infectious viruses can spread easily through a network of contacts.

As the first in a series of three manuscripts, the scientific literature relating to scale free networks from a variety of disciplines including physics, epidemiology, mathematics, biology and computer science is reviewed and integrated.

As the probability of transmission of HIV and HCV is greater when sharing needles and other injection equipment compared to sexual contact, the application of the techniques described in this paper to networks formed by individuals who inject drugs may reveal a previously unidentified risk factor that may help to explain the sustained transmission of HIV and HCV among IDUs.

Chapter Two: Changing perspectives: an alternative approach to help reduce the spread of disease among networks of individuals who inject drugs.

This chapter consists of the second of three manuscripts relating to this research which investigates the structure of the network of individuals who inject drugs and share injection equipment in Winnipeg, Canada. This second paper explores whether the methods used to identify the scale-free structure of sexual contact networks may be applied to networks of individuals who inject drugs. Two methods, ordinary least squares (OLS) and maximum likelihood estimation (MLE), reviewed in chapter one, were used to examine the structure of injection drug using networks through which disease may be transmitted and the two methods were compared.

Chapter Three: Scale free networks among injection drug users in Winnipeg Canada.

This chapter consists of the third and final manuscript relating to this research which investigates the structure of the network of individuals who inject drugs and share injection equipment in Winnipeg, Canada. In this paper, the emphasis is on corroborating and comparing the methods used to identify network structure in the previous chapter. In addition, factors associated with the structure of drug injecting networks are presented and interventions that may assist to reduce the transmission of HIV and HCV among injection drug users are recommended based on the results presented in this paper. This analysis focuses on a specific group of interest, individuals who have gone on binges of injection drug use.

2. Chapter One

Epidemic thresholds: Do they really exist for all infectious disease networks?

This chapter consists of the first of three manuscripts relating to this research which investigates the structure of the network of individuals who inject drugs in Winnipeg, Canada by using techniques previously used to identify the contact patterns of sexual networks in Sweden, Britain, Zimbabwe and Burkina Faso.

This first manuscript reviews and integrates the literature related to determining the structure of a network from a variety of disciplines including physics, epidemiology, mathematics, biology and computer science. In addition, the literature relating to the ability of standard epidemiological models to fully capture the heterogeneity of contact patterns in relation to the transmission of disease was reviewed.

Empirical evidence is presented in relation to sexual contact networks which have been found to be scale-free in a wide range of populations. These results have important epidemiologic implications in terms of the spread of disease. Epidemic thresholds do not exist or are much lower in a scale-free network compared to a random network and as a result even weakly infectious viruses can spread easily through a network of contacts.

As the probability of transmission of HIV and HCV is greater when sharing needles and other injection equipment compared to sexual contact, the application of the techniques described in this first manuscript to networks formed by individuals who inject drugs may reveal a previously unidentified risk factor that may help to explain the sustained transmission of HIV and HCV among IDUs.

Epidemic thresholds: Do they really exist for all infectious disease networks?

L. Pelude[1], J. Wylie[2,3], G. Wells[1], L. Leonard[1] and A. Jolly,[1,4]

[1] University of Ottawa, Ottawa, ON,

[2] Cadham Provincial Laboratory, Manitoba Health, Winnipeg, MB

[3] University of Manitoba, Winnipeg, MB,

[4] Division of Modeling and Projections, Centre for Infectious Disease Prevention and Control, Public Health Agency of Canada, Ottawa, ON

Keywords: Scale-free networks, injection drug use, epidemiologic modeling,

Abstract

Sexual contact networks have been found to be scale-free in a variety of populations. These findings have important implications in relation to the spread of disease. In a scale-free network, epidemic thresholds are non-existent or if present are much lower than that seen in a randomly mixed network. As a result, even pathogens with low transmissibility may spread easily through this type of network.

The literature relating to scale-free networks is scattered throughout a variety of disciplines including physics, epidemiology, mathematics, biology and computer sciences. This paper reviews and integrates the background, methods and empirical evidence relating to scale-free networks and the spread of disease.

In addition, the potential application of the techniques described in this paper to networks formed by individuals who inject drugs (IDUs) is discussed. Identifying the structure of injection drug using networks may reveal a previously unidentified injection related risk factor which may help to explain and consequently reduce the transmission of HIV and HCV among IDUs.

Background

Epidemiologic models attempt to describe when an epidemic can occur in a population based on a critical threshold parameter known as R_0, also known as the basic reproductive number.[1-2] This number (R_0) *is* the product of three quantities (βcD) and tells us the average number of new individuals that would be infected by one infected person in a completely susceptible population.[2-4] β is the average probability that the

pathogen is transmitted for each exposure, c is the average contact rate between susceptible and infected individuals and D is the average annualized duration of infectiousness.[3,5-6] If $R_0 < 1$, this reflects declining incidence and the population of infected individuals cannot grow.[2,6-7] If $R_0 = 1$, a state of equilibrium exists with no change in the number of susceptible or infected individuals and the disease is considered endemic.[6] If $R_0 > 1$ there will be an epidemic as the virus spreads exponentially in the population.[3,6] The larger the value of R_0, the more difficult it is to control the epidemic. R_0 values have been computed for a range of pathogens and some estimated values of R_0 include smallpox 5-7, measles 12-18, SARS 2-4, Rubella 3.7-6.4; HIV (among IDUs) 2.8-21.7, HIV (among MSM) 0.38 – 22.[5, 8-12]

The standard model used to determine R_0 assumes a completely homogenous population, one where each individual is assumed to have similar numbers of contacts and equal probability that two individuals will meet. However, this model does not sufficiently capture the dynamics of the spread of infectious disease as susceptible and infected individuals, networks and populations differ in characteristics that are epidemiologically relevant.[2,13] In relation to the transmission of STIs it is not reasonable to assume that sexual contacts are random and that there is homogeneity in the distribution of sexual contacts.[4,14] Heterogeneity in the number of sexual contacts has been incorporated into the standard model for R_0.[4, 14-15] In this model $R_0 = p_o (1 + \sigma^2/\mu)$, p_o is the average number of infections produced by one infected individual in a completely susceptible population, σ^2 is the variance in the number of contacts and μ is the mean number of contacts in the population.[4, 14-15] This equation shows that the larger the variance in the number of contacts in a population relative to the mean, the larger R_0 becomes.[4, 14] Using this model it is clear that less infectious pathogens would be able to generate an epidemic depending on the variation in the number of contacts in a given population.

For example, Jolly et al., [16] calculated R_0 numbers for gonorrhea and chlamydia using individual and sex partner data from the notifiable disease and health insurance registries in Manitoba, Canada. Results showed that groups with a larger variance in the number of sex partners had R_0 numbers greater than 1. [16] The variance in the number of sex partners of one group infected with chlamydia was reported as 0.73 resulting in an average R_0 of 0.7 while in another group the variance in the number of sex partners was reported as 1.94 resulting in an average R_0 of 1.09.[16]

Although this model is more realistic as it incorporates heterogeneity into the equation, it continues to assume random mixing with respect to how contacts are formed and that the number of contacts per individual follows a normal distribution. As is the case with most social interactions, sexual contact, for the most part, is not a random act. Factors such as how sexual or social contacts are formed; the duration of contacts, and simultaneous contacts are not addressed by this equation. In addition, recent empirical work has shown that the distribution of the number of sexual partners is not normal;[17-19] it is highly right skewed with the majority of individuals having one or two contacts, while a few may report hundreds or more.[18, 19] Using the mean number of contacts as part of the equation to estimate R_0 will usually underestimate R_0.[13]

More recently researchers have incorporated two other analytical methods, social network analysis (SNA) and examining the distribution of the number of contacts to further our understanding of how epidemics of STIs may occur. SNA is a research method that goes beyond the level of the individual by examining the linkages or relationships between people.[20-22] A network is the structure or relations that form between individuals, objects or groups (e.g., family members, organizations, countries, cells or computers). Network analysis examines the way groups are connected or the relationships between individuals without reference to the individual attributes.[23]

Specifically, a sexual contact network consists of a set of nodes (representing individuals) and their edges (representing the individual's sexual contacts); this is also called a graph in network theory.[4, 14] The number of edges a node has defines its degree and the collection of nodal degrees is the degree distribution of the network.[4, 14] For example, if an individual (node) reports three sexual contacts (edges) the nodal degree would be three.

Examining the distribution of contacts in a sexual network involves a fairly new approach introduced by physicists studying complex networks. Empirical observation in various disciplines has shown that the spread of information, signals or disease is influenced by the type of network formed.[14, 24-26]

Networks can be classified according to the distribution of their connections (degree distribution). The degree distribution describes the frequency with which nodes or individuals with a certain number of connections or contacts occur in a network.[18] There are 1) random networks; where connections between nodes are created randomly but generally each node has the same number of connections (i.e., each individual in the network is connected to three other individuals); 2) regular networks, where connections

created between nodes follow precise rules, (i.e., each individual has exactly the same number of connections. For example, each individual is connected to three other individuals) and 3) small-world networks, where connections are created through a combination of randomness and rules.[26]

Recently, some small world networks have been found to be scale-free.[25] Scale-free network nodes do not have a typical or average number of connections. Rather, the majority of nodes have a small number of connections while a small number of nodes have a large number of connections.[14, 26] As a result, the standard deviation around the mean is extremely large and mathematically, the degree of distribution in a scale-free network is described by a power law; the probability of having x partners $P(x)$ is directly proportional to x to the minus alpha (α) $P(x) = Cx^{-\alpha}$.[14, 18, 27]

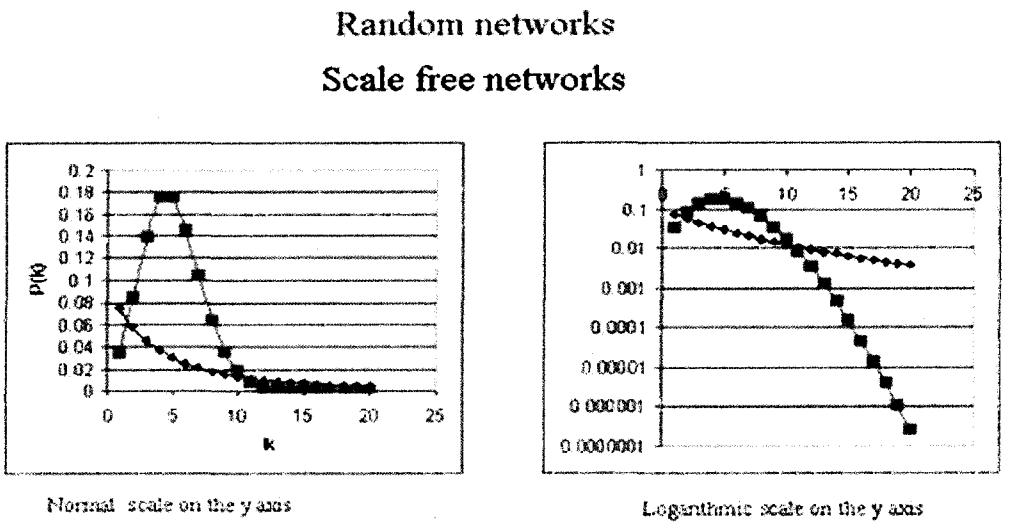

Figure 1. The distribution of connections for random networks (pink) and for scale-free networks (blue).[26]

The graph on the left in Figure 1 shows the distribution of connections in a random network (pink) which follow a Poisson distribution where the average number of connections is five, and this average defines a certain scale.[26] The exponential tail in a Poisson distribution makes observations much larger than the mean extremely unlikely.[26] The distribution of connections in a scale-free network (blue) is extremely skewed with a long tail and is described by a power-law.[26] When these distributions are plotted on a graph with logarithmic axes, a power law takes the form of a straight line.[14,26] A normal distribution can be characterized by its mean while the mean in a power law distribution does not represent the typical features of the power law

distribution. Power laws frequently describe distributions in income, word frequencies and city sizes.[27] The absence of scale in a network that follows a power law distribution has led them to be called scale-free.[28]

In a scale-free network, the nodes with a large number of connections are known as "hubs".[28] In the World Wide Web, hubs might be websites such as Yahoo or Google; among Hollywood actors the hubs are actors that have worked with the most people; among scientific collaboration networks, the hubs are the scientists who have collaborated with the most people or co-authored papers with the most people; in cells the hubs are the most connected molecules such as water, ATP or ADP and in an infectious disease transmission network, hubs are the people who are in contact with a large number of susceptible people. For example, early on in the AIDS epidemic an index patient (now known as "patient 0") in an AIDS cluster identified by the Center for Disease Prevention and Control (CDC) was linked to 250 other sexual contacts living in New York, San Francisco and other parts of the United States . The average number of sexual contacts reported by individuals in this "AIDS cluster" was 227 per year ranging from 20 to 1560 contacts per year.[21]

The structures of random and scale free networks are shown in Figure 2. Although both of these networks contain 130 individuals and 430 connections, more than 60% of individuals (green) can be reached from the five most connected individuals (red) in the scale-free network compared with only 27% in the random network.[28]

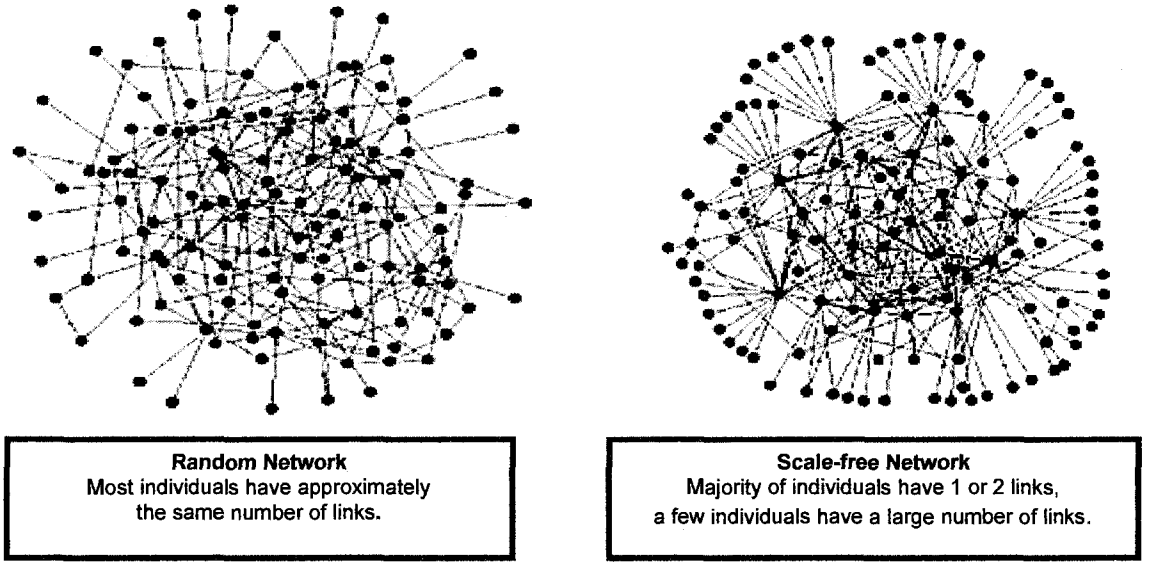

Figure 2. A random network compared to a scale-free network.[28]

Barabási [28-29] suggests there are two common mechanisms that underlie the development of scale-free networks in systems as diverse as the Internet (a physical network), the WWW (a virtual network) and Hollywood actor and scientific collaboration networks (social networks). These two mechanisms; growth and preferential attachment are absent from traditional random-graph models, but are present in many complex networks.[28]

Traditional graph-theory models assume that the number of nodes in a network is fixed meaning the network never changes over time.[29] In contrast, the WWW continually expands by the addition of new pages, the Internet by the installation of new routers and communication links; Hollywood actor, and scientific collaboration networks by new actors and scientists.[28] Random-graph models assume the connections between routers, web pages or individuals are distributed randomly, but in the real world many networks exhibit a phenomenon called "preferential attachment". In other words, the more popular nodes are the most attractive.[26, 28] For example, new web pages are far more likely to be linked to the most popular documents or search engines on the Web, rather than less popular ones, network engineers tend to connect their company or institution to the Internet through points that have a high bandwidth, new Hollywood actors try to perform in a movie with a Hollywood star and new scientists tend to collaborate with scientists well known in their field.[28]

Scale-free networks can be further identified by other characteristics. For example, Barabási and Albert [31] found that the clustering coefficient (the average of the clustering coefficients for each cluster of nodes in a network) [32-33] of a scale-free network is about five times higher than that of a random graph. Completely random networks have very small clustering coefficients compared to most real networks.[34, 35] In addition, the average path length (the mean distance between two nodes averaged over all pairs of nodes) by which any given node is linked to another in a scale-free network is smaller compared to the average path length of a random graph of the same size.[34]

Network structure has been shown to have an effect on the spread of disease. Recent results indicate that the spread of disease in a scale-free network deviates significantly from that of random or regular networks.[36] Infection in a random network spreads to the whole network only if the spreading rate exceeds a critical value or threshold.[36]

It has been suggested that in a scale-free network there is no critical threshold.[36-37] This absence of critical threshold could radically alter many of the standard

assumptions used in epidemic modeling.[37] In fact, Dezsö & Barabási [36] suggest that the loss of a critical threshold implies that even weakly infectious viruses can spread and prevail. They further suggest that this vanishing threshold is a consequence of the fact that a small number of individuals (nodes) have a large number of contacts (links), referred to as "hubs".[36] Once the hubs are infected, the virus is easily passed on to a significant fraction of individuals (nodes) in the whole network.[36] This concept is visually displayed by the drawing of the scale-free network in Figure 2.

The values for the critical threshold are determined by the exponent in the power law equation ($P(x) = Cx^{-\alpha}$).[27] The constant α, in the power law equation is the exponent of the power law and the constant C is determined by the requirement that the distribution $P(x)$ sum to 1, once α is fixed.[27] Values for the exponent have been generated primarily by two methods 1) ordinary least squares (OLS) where α = slope of the line and 2) maximum likelihood estimation (MLE).[27] In MLE, confidence intervals for the exponent can be generated using bootstrapping methods.[27] Usually, an exponent < 3 indicates a scale-free network however, exponent values less than 2 are rarely seen in real world networks.[37-38]

Newman [38] investigated the effect of network topology on the rate and pattern of disease spread in a sexual contact network. He identified three values for the exponent, which, when altered, can change the spread of disease in a sexual contact network.[38] For $\alpha < 3$, there is always epidemic behaviour even if the transmissibility of the virus is low, for $\alpha > 3.48$, no epidemic will ever occur even if the disease is highly transmissible and when α is between 3.0 to 3.48, the epidemic transition region, epidemics may, or may not occur.[38-39] Newman suggests that if a network is in the epidemic transition stage it is possible to prevent an epidemic by reducing the probability of transmission.[34] This could be done by shortening the duration of infectiousness, (by screening and treating for disease); lowering the transmission probability (through the use of condoms); lowering the number of people with whom the infected person has contact (decreasing the number of sex partners) and/or reducing the number of sexual contacts that the most sexually active individuals (hubs) have, resulting in an increase in the epidemic threshold and a decrease in the transmission of disease.

Many public health interventions aimed at preventing or reducing the spread of infection attempt to reduce the epidemic threshold.[40] However, Dezsö and Barabási [36] have shown that interventions directed to random individuals in a scale-free network are ineffective as they are unable to alter the basic properties of the threshold-free diffusion

process. They go on to suggest that interventions targeting the hubs within a scale-free network could restore the epidemic threshold.[36] In other words, targeting preventive efforts to individuals with the most contacts may be a better way of preventing or limiting the spread of disease rather than targeting everyone.[38]

Review of recent empirical data

Three recent studies have suggested that networks of sexual contacts may have a scale-free structure which has implications for the transmission of disease through networks. Liljeros and colleagues[19] analyzed data from a 1996 Swedish survey of sexual behaviour (N = 2810). They examined both the number of sexual partners over a one-year period and the total number of sexual partners over the respondent's lifetime. The cumulative distributions for both these variables were plotted on a graph with both *x* and *y* logarithmic axes and the data were found to follow a straight line.[19] This is consistent with power law dependence, indicating that the network of sexual contacts may be scale-free. The presence of individuals with sexual contacts much greater than the mean is another indication of power law behaviour in these data.[19] The average number of lifetime sexual contacts for women was seven, but one woman had 100. For men, the average lifetime number of sexual contacts was 15 but one man had 800.[19]

Values for the exponents were generated using OLS. For women, exponents were 2.54 (number of sexual partners over 1 year) and 2.1 (total number of lifetime sexual partners).[19] For men, exponents were 2.31 (number of sexual partners over 1 year) and 1.6 (total number of lifetime sexual partners).[19] These exponent values suggest that the network of sexual contacts may indeed be scale-free.

In 2004, Schneeberger and colleagues [18] analyzed four large datasets including the British National Survey of Sexual Attitudes and Lifestyles (NATSAL) the London Gay Men's Sexual Health Survey (LGMHS) and a study of sexual behaviours in rural Zimbabwe. They examined both the number of sexual partners over a one-year period and the total number of sexual partners over the respondent's lifetime. The cumulative distributions for both these variables from all datasets were found to follow a straight line when plotted on a graph with double logarithmic axes.[18] Again this is consistent with a power law dependence indicating that the networks may be scale-free.

For heterosexuals in both the NATSAL and Zimbabwean datasets the power-law model provided the best fit to the tail end of the distributions.[18] All values for the

exponents were generated using MLE. The value of the exponents ranged from 2.46 to 3.07 for men and from 2.51 to 3.68 for women.[18] Although a few of the upper 95% CI's of these exponents would place some of these networks in the region where there may be no epidemics, empirical evidence suggests that this is not the case in the real world where HIV and HCV among some groups of men and women is clearly an epidemic.

For gay men in both the NATSAL and LGMHS datasets, the power law model provided the best fit and the value for the exponents ranged from 1.57 to 1.75.[18] In NATSAL, the sample size for lesbians was extremely small and the researchers were not able to conclusively identify power law behaviour.[18] The value of the exponents ranged from 2.27 to 3.29 and the confidence intervals were very wide.[18]

In 2006, Latora and colleagues [17] analyzed data from a survey designed to cover a broad array of issues including sexual attitudes from a sample of 1000 women and men living in the capital city of Burkina Faso. They examined the number of sexual partners of 488 individuals in the last 12 months. The cumulative distributions for both men and women were plotted on a log-log scale.[17] The distribution of the number of sexual contacts in the last year for both women and men were fitted by a power law.[17] The exponent for men = 2.93 and for women = 3.9.[17] These results suggest that the network of sexual contacts among men may in fact be scale-free.

These separate analyses by Latora [17], Schneeberger [18] and Liljeros [19] and their colleagues of some of the largest empirical datasets of sexual contacts strongly suggests that the structure of sexual contact networks may be scale-free in a wide range of populations.

Review of current methods

Research relating to whether sexual networks are in fact scale-free remains controversial. This debate predominantly focuses on the methods used to estimate the value of the exponent (α) in the equation for the power law curve.[24]

The value of the exponent assists in determining whether a network is scale-free. or in other words if there is a critical threshold that allows for an infection to spread or persist.[18] Primarily two methods have been used to estimate the exponent of a power law distribution; maximum likelihood estimation (MLE) and ordinary least squares (OLS). MLE has been suggested as the preferable estimation method by some researchers as OLS has been known to produce biased and inaccurate results.[27, 41]

Goldstein et al.,[41] used a random deviate generator to produce a dataset of 10,000 samples from a known distribution with an exponent equal to 2.5. MLE and three types of linear fits commonly used by researchers for fitting to a power law distribution (full linear fit, linear fit of first 5 data points and linear fit on logarithmic bins to the log-log plot) were performed using least squares to estimate the exponent.[41] Two out of the four methods were found to have a severe bias; a 36% error (exponent = 1.590) using full linear fit and a 29% bias error (exponent = 1.777) using linear fit on logarithmic bins.[41] No bias was found using the linear fit of the first 5 points (exponent = 2.500) or with MLE (exponent = 2.500).[41]

However, the variance of the estimate using the linear fit of the first 5 points was much higher than the variance of the estimate using MLE, showing the stability of MLE in generating a true value for the exponent.[41] In addition, fitting the first 5 points of a dataset is not a reliable method for analyzing empirical data.[41] In real world data, power laws generally are not found over the entire range of data but rather over a limited part of the data and usually in the tail-end of the distribution.[27]

In a series of working papers starting in 2002, Handcock and Jones[42-44] suggested that the approach taken by Liljeros et al.,[19] when estimating the exponent for the distribution of number of partners obtained from a Swedish survey of sexual behaviours was statistically inappropriate.

They argued that using a linear fit of the distribution's extreme upper tail to estimate the exponent is a questionable practice as the statistical variation in values is not constant, excludes "0" frequencies introducing bias into the estimate of the exponent, and that high degree frequencies are sensitive to misreporting and population heterogeneity.[43] In addition they argue that estimates for the exponent based on number of lifetime partners may be biased due to temporal confounding and censoring.[43] Handcock and Jones [43-44] reanalyzed the sexual contact distributions from Sweden (Liljeros et al's data[19]) along with two other datasets (from Uganda and the USA) using the Yule model (another process that can generate power law distributions) and MLE which resulted in exponents > 3, above the infinite variance range, indicating that sexual contact networks are not scale-free.

They suggest that although sexual contact distributions are highly right skewed they are characterized by a finite variance supporting the existence of thresholds among sexual contact networks and therefore current interventions have the potential to reduce

the transmission of sexually transmitted infections in a sexual contact network.[43] They conclude that a unilateral behavioural process such as preferential attachment is unlikely to underlie empirical network degree distributions.[44]

In 2003, a response by Liljeros et al.,[45-46] suggests that restricting analysis to the number of partners reported in one year would limit our understanding of the structure of sexual contact networks as many contacts may be missed and diminish the effects of pathogens with long infectious periods such as HIV and other STIs left untreated such as syphilis or chlamydia. Liljeros et al.,[46] reanalyzed their datasets using OLS, MLE (power law fit) and MLE (Yule model). Interestingly there is little difference between the three methods when estimating the exponents for the number of lifetime partners as can be seen below in Table 1.

	No. of distinct partners during previous year			**No. of distinct partners in lifetime**		
	OLS Power law (kmen>5; kwomen>4)	MLE Power law (k>0)	MLE Yule (k>0)	OLS Power law (20<kmen<400) (kwomen>20)	MLE Power law (k>20)	MLE Yule (k>20)
P men	3.31 (3.11-3.51)	2.73 (2.65-2.84)	4.13 (4.0-4.7)	2.16 (1.86-2.46)	2.37 (2.26-2.50)	2.40 (2.28-2.53)
P women	3.54 (3.34-3.74)	3.26 (3.10-3.41)	6.23 (5.54 -6.98)	3.1 (2.8-3.4)	3.125 (2.77-3.62)	3.21 (2.85-3.68)

Table 1. Estimates of the tail exponent α and confidence intervals for the distribution of distinct sexual partnerships for Swedish men and women. [46] (Note: MLE = Maximum Likelihood Estimation, OLS = Ordinary Least Squares)

In addition, Liljeros et al., [46] agree that the variance of these distributions are finite but suggest that it is premature to argue that thresholds exist for all sexual contact networks as research has demonstrated that the transmission of disease, signals or other information is exceedingly different between networks with a power law decaying distribution and those with a Gaussian, Poisson or lognormal distribution. In addition the effect of variances so much larger than the mean for the distribution of the number of sexual contacts has not been fully incorporated into current statistical methods.[46-47]

More recently Handcock and Jones [44] compared different models to establish the best fit for three datasets (USA, Uganda, Sweden) using the reported number of heterosexual partners in the last years as the estimate for individual network degree. For all six networks examined, only one network was described by a power law model (Yule model) and the value of the exponent was > 3 suggesting that all networks examined

have an epidemic threshold (have a finite variance) and are not scale-free.[44] They conclude that there is not enough empirical evidence to support preferential attachment as a general behavioural model for the formation of sexual contacts.[44]

However, the assumptions in the derivation of the Yule model have been shown to result in distributions that have power-law behaviour but are not scale-free.[46, 48] The essential component of a model which produces scale-free behaviour is the phenomenon of preferential attachment - one which the Yule model does not have.[48] As described earlier, preferential attachment in a sexual contact network is one in which an individual with a large number of contacts is more likely to acquire another contact than an individual who previously has one or no contacts.[48] Preferential attachment in a sexual contact network could also be described as an individual who has already infected many others in a network is more likely to infect a new individual compared to an individual who has previously infected few or no other individuals.[48] In the case of the Yule model, this model assumes that all individuals are equally likely to spread the disease at all times and results in a geometric degree distribution (not scale-free).[48]

Recently Reed [48] compared two stochastic network models (Yule-tree and Reed-Hughes tree). It was shown that the growth of the epidemic is similar for both models.[48] However, the models differ in the resulting degree distributions.[48] The Reed-Hughes model results in scale-free distributions with exponents < 3, consistent with the numerical estimates obtained by Liljeros et al in 2001.[48] The Reed-Hughes tree model assumes that individuals who have already infected many others will have a higher probability of infecting more individuals.[48] The Reed-Hughes model seems more appropriate for the transmission of STIs as it recognizes heterogeneity in the number of contacts while the Yule model may be appropriate to describe the transmission of influenza or SARS.[48-49]

In a 2004 editorial, Pourbohloul and Brunham[39] credit Schneeberger et al., for increasing our understanding of the mechanisms relating to the spread of disease through sexual contact networks. Schneeberger et al's analysis of the formation and structure of sexual contact networks in three different populations clearly illustrated that the interventions required to reduce the spread of disease may vary greatly depending on how the sexual contacts in a network are formed and distributed.[39] However, Pourbohloul and Brunham also suggest that Schneeberger et al's results should be interpreted with caution as real sexual behaviour data are "cut-off" at some point.[39] In other words there is a maximum number of sexual partners that one individual can have.

Even though the distribution of sexual contacts in Schneeberger et al's analysis follows a power law the maximum cut-off implies that the variance in the number of partners is finite and therefore a critical threshold may exist in all the networks analyzed.[39]

Although empirical data is finite, the assumptions underlying the various models used to analyze current disease transmission and to predict future epidemics may produce substantially different results. For example, using the Yule model to predict the spread of disease assumes that all individuals are equally likely to spread the disease at all times; which intuitively does not capture the complexity of human social or sexual contact. In addition, misinterpreting the tail of a distribution during analysis could have severe consequences in preventing the transmission of disease.[50] The recent empirical data relating to the distribution of contacts in various sexual networks have shown that they contain a few individuals with a large number of contacts resulting in distributions with a very large variance. The recent mathematical evidence by Reed [48] seems to provide support for the results obtained by Liljeros[19], Schneeberger[18], Latora[17] and their colleagues suggesting that the networks of sexual contacts may indeed be scale-free.

In addition, while an epidemic threshold may exist because there is a limit to the number sexual partners one individual can have, and because sexual contact networks are finite in size, it would be a great deal lower then that seen in a randomly mixed network.[51-53]

It appears that much of the debate regarding the existence of scale-free networks revolves around the precise definition of a scale-free network; the statistical methods and mathematical models used to identify power law behaviour that result in a scale-free network and the methods used to estimate the parameter values for the exponent. For epidemiology, identifying the structure of a network and establishing whether a critical threshold exists for the spread of disease would have major implications in preventing or reducing the transmission of many STIs and blood-borne pathogens. As the structure of a network has an impact on the spread of disease, there is a need to try all available methods with empirical data and continue investigating which statistical methods are best so that we can determine whether a network of contacts in which disease is transmitted, such as sexual partners or injection drug users may be scale-free. [24] This relatively new area of research should be applied to the analysis of STIs and other blood-borne pathogens which are stable or increasing despite enhanced detection and therapy.

Future applications

The human immunodeficiency virus (HIIV) and hepatitis C virus (HCV) continues to spread among individuals who inject drugs (IDUs) and rates of injection equipment sharing have remained relatively unchanged since the mid-1990s suggesting that our interventions have been only partially effective.[54-70] The primary mode of HIV and HCV transmission among IDUs is the sharing of needles and other drug injection equipment. As the probability of transmission of HIIV and HCV is greater when sharing needles and other injection equipment compared to sexual contact, the application of the techniques described in this paper to networks formed by individuals who share drug injection equipment may reveal a previously unidentified risk factor that may help to explain the sustained transmission of HIV and HCV among IDUs. Identifying the structure of the network formed by individuals who inject drugs in relation to the spread of disease may help to develop additional interventions that target the network structure and therefore help to reduce the transmission of HIV and HCV among IDUs.

In addition, testing different generative mechanisms that generate power laws such as the Barabási and Albert (BA), Yule, Reed-Hughes or Copy model against empirical data would be an essential step to validate the existence of scale-free networks among disease transmission networks.

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3. Chapter Two

Changing perspectives: an alternative approach to help reduce the spread of disease among networks of individuals who inject drugs.

This chapter consists of the second of three manuscripts relating to this research that investigates whether the structure of the network of individuals who inject drugs and share injection equipment in Winnipeg, Canada may be scale-free. This second paper explores whether the methods used to identify the scale-free structure of sexual contact networks may be applied to networks of individuals who inject drugs. Two methods, ordinary least squares (OLS) and maximum likelihood estimation (MLE) reviewed in the previous manuscript were used to identify the structure of injection drug using networks through which disease may be transmitted and the results were compared.

Additional details relating to some of the methods and results in this paper are presented in the appendices listed below:

Changing perspectives: an alternative approach to help reduce the spread of disease among networks of individuals who inject drugs.

L. Pelude[1], Liljeros F [2], J. Wylie [3,4], G. Wells[1], L. Leonard[1] and A. Jolly, PhD[1,5]

[1] University of Ottawa, Ottawa, Canada,

[2] Stockholm University, Stockholm, Sweden

[3] Cadham Provincial Laboratory, Manitoba Health, Winnipeg, Canada

[4] University of Manitoba, Winnipeg, Canada

[5] Division of Modeling and Projections, Centre for Infectious Disease Prevention and Control, Public Health Agency of Canada, Ottawa, Canada

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Abstract

This paper explores whether the methods used to identify the scale-free structure of sexual contact networks may be applied to networks of individuals who inject drugs and share injection equipment. Two methods ordinary least squares (OLS) and maximum likelihood estimation (MLE) were used to identify the structure of injection drug using networks through which disease may be transmitted. Results indicate that the network of injection drugs users in Winnipeg, Canada may indeed be scale-free. In addition it was found that individuals who are in the tail end of the distribution (inject very frequently, ≥ 2,640 injections in one year) were significantly more likely to be aboriginal; to have an income > $40,000; have been paid (money or drugs) by someone to help them inject drugs; have injected at a hotel in the past 12 months; and have at least one member in their network who injected daily. Based on these findings, additional interventions are suggested that may help to reduce the transmission of HIV and HCV among injection drug users in Winnipeg, Canada.

Background

Among injection drug users (IDUs), the spread of the human immunodeficiency virus (HIV) and the hepatitis C virus (HCV) continues.[1-5] The practice of sharing needles, syringes and other drug injection equipment is generally acknowledged as carrying the

highest risk for the transmission of HIV and HCV among IDUs.[6-21] Sharing equipment is defined as knowingly or unknowingly using a needle or syringe, filter, water or cooker which has been previously used by someone else.

Currently, most research studies that examine injection practices among IDUs, have found that at least 20% and up to 75% of IDUs report using previously used injection equipment in the six months prior to interview.[7,13,21,22] Epidemiological research has been primarily devoted to identifying factors associated with individual injection risk practices and in particular those factors associated with sharing drug injection equipment. As a result, intervention programs have been designed and implemented to modify the factors associated with individual injection risk practices.

Social network analysis (SNA) has been used to investigate the spread of HIV and HCV among IDUs. SNA is a research method that goes beyond the level of the individual by examining the relationships between people.[23-25] A network is the structure of relations formed between individuals, objects or groups (e.g., family members, organizations, countries, cells or computers). Network analysis provides the method to describe the way in which individuals are connected through relationships.[26]

Social network analyses of IDUs' injection practices have found that various network variables have a significant effect on the injection risk practices of individual IDUs. For example, Latkin [27] found that the number of people in an IDU's network was positively associated with needle sharing, while Neaigus [28] documented that IDUs with a greater proportion of friendships with non-IDUs were less likely to engage in injection-related risk practices. Overall, SNA indicates that IDUs' social networks affect individual IDUs' injection related risk practices and, thereby, the transmission of HIV and other blood-borne pathogens.

Clearly, both standard epidemiological research and SNA have facilitated our understanding of the transmission of disease and, in this context, the transmission of HIV and HCV among IDUs. However, HIV and HCV continues to spread among IDUs and rates of injection equipment sharing have remained relatively unchanged since the mid-1990s, which suggests our interventions have been only partially effective, and that processes beyond individual and social network factors play a role in the sustained spread of HIV and HCV among IDUs. Recently the distribution of sexual contacts has been examined in order to identify the structure of sexual contact networks.

Most infectious diseases are spread by some type of contact between an infected individual and a susceptible individual. Therefore, how all the individuals are

connected within a network is a crucial factor in the transmission of disease.[29-34] Traditionally, epidemiologic models assume that the population of susceptible individuals are randomly mixed, one where all individuals are equally likely to be infected by contact with an infected individual.[30,35]

The distribution of the frequency of contacts in a network has been shown to follow distinct patterns; there are 1) random networks; where links between individuals are created randomly but on average each individual has the same number of contacts; 2) regular networks, where links created between individuals follow precise rules, (i.e., each individual has exactly the same number of contacts) and; 3) small-world networks, where links are created through a combination of randomness and rules.[36] Recently, some small world networks have been found to be scale-free.[37] Individuals in a scale-free network do not have a typical or average number of contacts. Rather, the majority of individuals have a small number of contacts while a small number of individuals have a large number of contacts.[29-30,32,36,38] The degree of distribution in a scale-free network (the frequency with which individuals with a certain number of contacts occur in a network) is described by a power law $y = Cx^{-\alpha}$.[32,38-39]

Network structure has been shown to have an effect on the initial spread and long-term behaviour of any infectious disease.[40] The spread of disease in a scale-free network significantly deviates from that of a random network, where infection spreads to the whole network only if the spreading rate exceeds a critical value or threshold.[41] The constant α, in the power law equation ($y = Cx^{-\alpha}$) is called the exponent of the power law. An exponent < 3 indicates a scale-free network in which there is no critical value or threshold.[42-44] However, exponent values less than 2 are rarely seen in real world networks.[43-44]

Newman [43] investigated the effect of network structure on the rate and pattern of disease spread in a sexual contact network. He identified three values for the exponent which, when altered, change the spread of disease in a sexual contact network. If $\alpha < 3$, there is always epidemic behaviour even if the transmissibility of the pathogen is low; if $\alpha > 3.48$, it is very difficult to determine whether the network is scale free and whether an epidemic will occur, and when α is between 3.0 to 3.48, the epidemic transition region, epidemics may or may not occur.[33,43] Newman [43] suggests that if a network is in the epidemic transition stage it is possible to reduce the probability of transmission by traditional prevention strategies such as shortening the duration of infectiousness, by

screening and treating for disease or lowering the transmission probability through the use of condoms.

As network structure has been shown to affect the transmission of disease in sexual contact networks then by analogy, identifying the structure of contacts formed by individuals who inject drugs may also help to define transmission dynamics which can be used to develop more effective HCV and HIV interventions.

In this paper we explore whether the methods currently used to identify the scale-free structure of sexual contact networks may be applied to networks of individuals who inject drugs.

Methods

A cross-sectional pilot study was conducted in 2000 among 156 individuals who inject drugs and live in Winnipeg, Canada. Participants were recruited anonymously through posters placed in community clinics, drop-in venues, locations frequented by IDUs, and by word of mouth. People who had injected within the past 6 months, aged 15 or more, and were positive for Hepatitis C were invited to participate. The study design was approved by the Health Research Ethics Board of the University of Manitoba and the Winnipeg Regional Health Authority Research Review Committee. The analysis specific to this paper was also approved by the Ottawa Hospital Research Ethics Board.

A questionnaire containing information on the participant's demography and drug use behaviours, and, by proxy, those of their drug, sex, and social support networks was administered by the study nurse. The frequency of individuals' sharing injection equipment was not available. However, since frequency of injection has been associated with sharing of drug injection equipment among IDUs and an increased risk of HIV & HCV infection.[45-49], we examined the distribution of the frequency of injection over one year in order to determine if the drug injection equipment sharing networks may be scale-free. Complete data for the frequency of injection was available for 142 participants.

Scale-free networks are characterized by power law behaviour in the tail of the cumulative distribution, $P(x) = Cx^{-\alpha}$; the probability $P(x)$ that x has a value greater or equal to x and a value for the exponent (α) of less than 3.[32,34,39] However, exponent values less than 2 are rarely seen in real world networks. We plotted the cumulative distribution of the frequency of injection over a 1- year period on a graph with logarithmic axes by sorting the frequency of injection in ascending order and then ranking by

cumulative percent. For example, 100% of respondents injected at least once during the past year; 90% at least 18 times, 76% at least 80 times, 50% at least 500 times, 14% at least 2,640 times and so on. These ranks are then plotted as a function of their frequency. Generally, a power law cannot hold strictly over the entire range of data, particularly in real-world distributions, but only over a limited part of the data, usually in the tail end of the distribution.[39] A curve was fitted to the entire distribution and then to the tail-end of the distribution using ordinary least squares (OLS) and maximum likelihood estimation (MLE) methods.

Both OLS and MLE have been used to identify the structure of sexual contact networks. OLS uses the cumulative distribution (1 data point could represent 5 individuals with the same number of reported injections) while MLE uses the frequency distribution (plots each individual data point). The relationship between these distributions is that the slope for the frequency distribution minus one equals the slope for the cumulative distribution.

However, studies in various disciplines have shown that both methods generate similar exponents regardless whether they used OLS or MLE.[50-51] Therefore, both methods were used to see how they perform in terms of generating a value for the exponent and the results are compared

Determining the start of the tail is subjective, and requires judgment about the value above which the distribution follows a power law.[39] The distribution must deviate from the power law form below some minimum value because for any positive value of the exponent α, the function $P(x) = Cx^{-\alpha}$ diverges as x gets closer to 0.[39] The approximate point where the tail region of the distribution begins can be observed on a cumulative degree plot.[32]

Our choice of a starting point for the tail begins at 2,640 injections over a one year period. In the log-log plot of the cumulative distribution of the frequency of injection (Figure 2) we can observe that the distribution appears to go straight at around 2,500 injections.

We deleted one record of a participant who reported 24,000 injections per year over 240 days. This frequency would be equal to 100 injections per day if awake 20 hours a day and it was considered by one of us to be physically impossible (LP). Graphs were plotted using both Curve Expert Version 1.38 [52] and Mathcad 12 [53] with similar results. The exponent was determined using both OLS: $y = Cx^{-\alpha}$ and MLE as described by Newman (Figure1).[39]

$$\alpha := 1 + n \cdot \left(\sum \ln\left(\frac{data}{xmin} \right) \right)^{-1}$$

Figure 1: MLE method [39] Note: MLE uses the frequency distribution to estimate the exponent (slope) (α) = exponent; n = 20; ln = log; data = frequency of injection data; xmin = start of the tail end of the distribution (2,640 injections)

Best fit was determined using the correlation coefficient and the standard error of the estimate for the OLS method. Bootstrapping methods [54] were used to estimate 95% confidence intervals for the exponent using MLE. Differences in people who injected more frequently than 2,640 times in the previous year compared with people who injected less frequently were calculated used χ^2 tests.

Results

Descriptives

Sociodemographic results and drug injection related practices are presented in Table 1. Overall, half of the participants were men and the average age was 34 years, more than two-thirds were aboriginal and most reported their annual income as $20,000 or less. The drug most frequently injected by participants was cocaine (62%) followed by Talwin and Ritalin, morphine, other drugs, and heroin. Over two-thirds reported injecting in their own house or apartment, almost half reported injecting at a Hotel (48.1%) and more than half reported injecting in both private (home or apartment) or public places (shelters, street, hotels) in the past year.

Just over 70% of participants reported ever having used a needle previously used by someone else and 43% of those reported doing so in the past year. Sixty-five percent of participants reported ever using water, filters or cookers previously used by someone else. The average annual number of injections reported was 1,377 (range 1-15,000). Eighty-six percent (n = 122) of IDUs reported injecting 2,640 times a year or less while 14% (n=20) reported injecting greater or equal to 2,640 times in a year and 7% (n = 10) reported injecting 4,320 times a year or more.

On average, almost 60% of each participant's social network were also IDUs and almost 50% of participants reported having at least one network member who injected daily. The average network density was 0.76 which describes the ratio of the actual number of connections present to the maximum possible, ranging from 0 (if there are no connections present) to 1 if all possible connections are present.

Variable	N = 156 n (%)
Gender	
Male	76 (48.7)
Female	74 (47.4)
Transgender (male to female)	6 (3.8)
Age	
Mean (SD)	33.5 (8.82)
Median	34
Mode	37
Min – Max	16 – 54
Ethnicity (N =156)	
Aboriginal	104 (66.7)
Caucasian	49 (31.4)
Other	2 (1.3)
Not identified	1 (0.6)
Average annual income[1]	
< $5,000	13 (11.5)
$5,000 – 20,000	63 (55.8)
$20,000 – 40,000	21 (18.6)
>$40,000	16 (14.2)
Drug most frequently injected [1]	
Cocaine	96 (62.3)
Talwin & Ritalin	26 (16.9)
Morphine	13 (8.4)
Other	10 (6.5)
Heroin	9 (5.8)
Has injected in own house/apt in past 12 months (N = 156)	
No	49 (31.4)
Yes	107 (68.6)
Has injected in a hotel in past 12 months (N = 156)	
No	81 (51.9)
Yes	75 (48.1)
Injects in both private & public places (N = 156)	
No	69 (44.2)
Yes	87 (55.8)
Has ever used a needle previously used by someone else (N = 156)	
No	44 (28.2)
Yes	112 (71.8)
If ever used a needle previously used by someone, did so in the past year [1]	
No	53 (57.0)
Yes	40 (43.0)
Has ever used other injection equipment (water, filters, cookers) previously used by someone else [1]	
No	51 (34.9)
Yes	95 (65.1)
Number of times injected over the past year [1]	
Mean (SD)	1377 (2502.992)
Median	480
Mode	360
Variance	6264971
Min – Max	1 – 15,000
Injected greater or equal to 2,640 times in a year [1]	
No	122 (85.9)
Yes	20 (14.1)

[1] Does not add up to 156 due to missing values

Table 1. Sociodemographic and drug injection practices in 156 IDUs, Winnipeg, Canada, 2001.

There was a large variation in the frequency of injection reported. The frequency of injection was non normal, with by far the majority of people reporting a small number of injections and very few reporting a large number of injections (Figure 2)

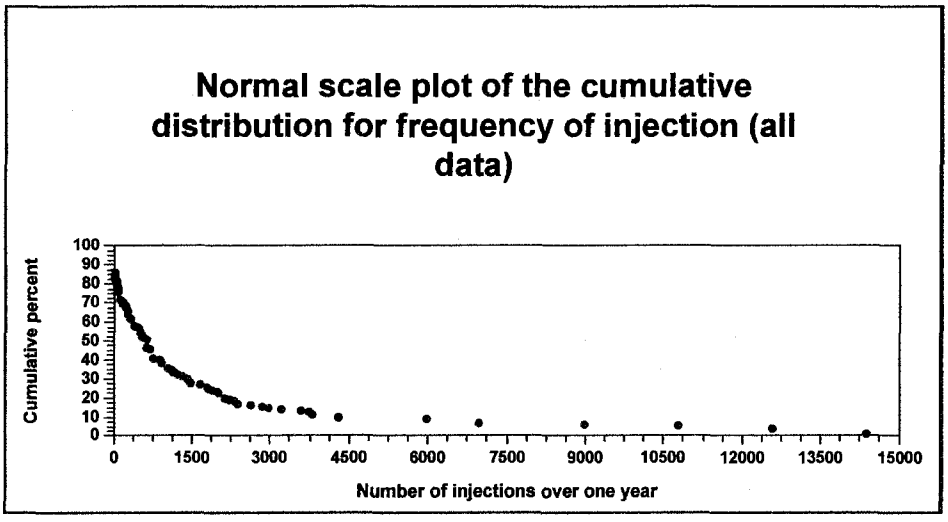

Figure 2. Normal scale plot of the distribution of the frequency of injection over one year in 142 IDUs, Winnipeg, Canada, 2001.
Mean 1,377 injections; median 480; 25% quartile 79, 75% quartile 1440; IQR = 1361; min 1; max 15,000)

On a normal scale (Figure 2), the distribution of the frequency of injection is extremely positively skewed with a long tail, suggesting it may be described by a power law.

The graph below (Figure 3) shows that a log-log plot of the entire data set using OLS, is best fit with the Hoerl Model, y=abx xc, which is one of the various forms of power models (c = slope of the line or the exponent and a = y intercept).

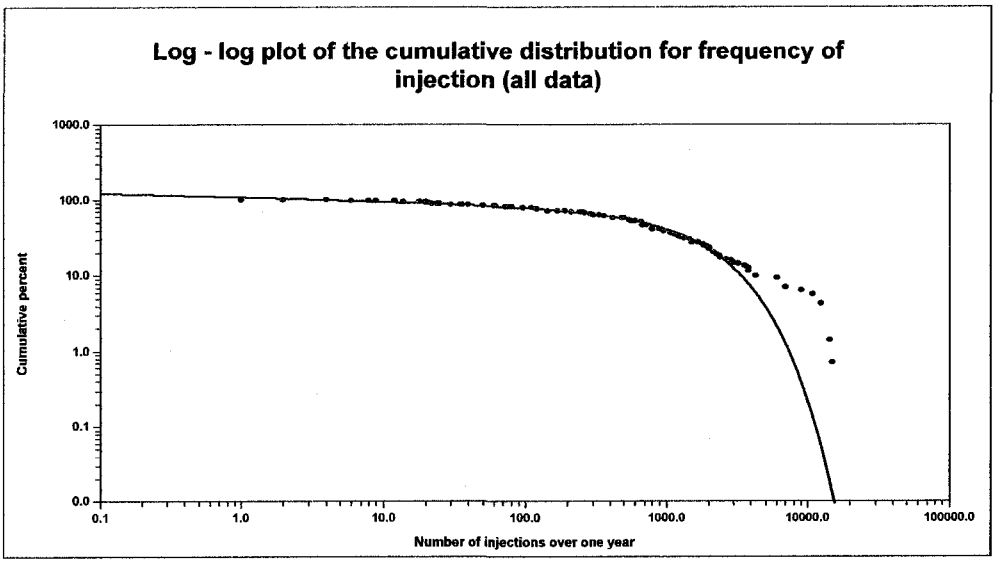

Figure 3. Log-log plot (OLS method) of the cumulative distribution for the frequency of injection over one year in 142 IDUs, Winnipeg, Canada, 2001. — Fitted line ····· Empirical data
Hoerl Model: $y=ab^x x^c$
Coefficients, C =108.2166 b = 0.99942967 c = -0.060672548
Standard Error: 2.5767712 Correlation Coefficient: 0.9966093

We then plotted the data using OLS from the tail-end of the distribution (≥ 2,640 injections) in a log-log plot which follow a straight line consistent with a power law (Figure 4). Also, the model that best fits the data is the power law model.

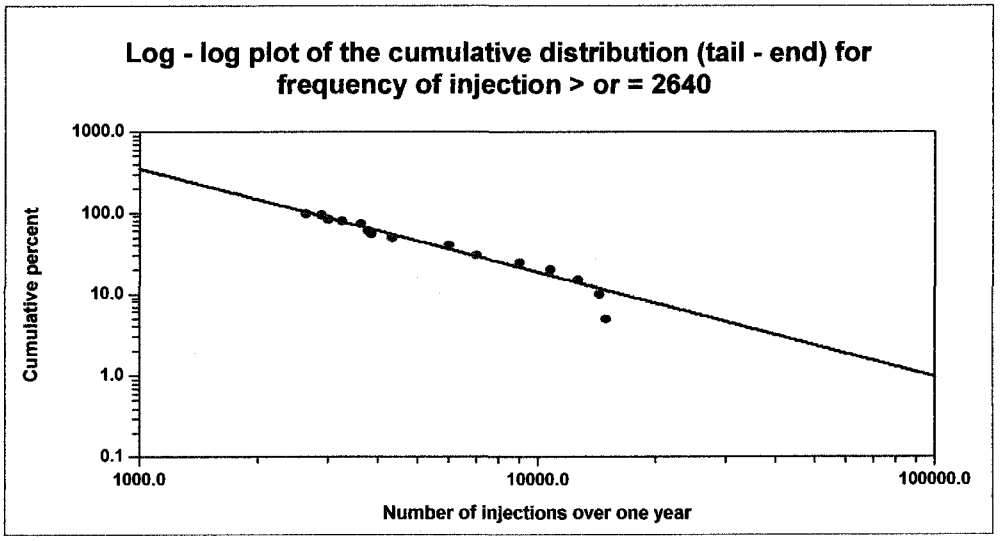

Figure 4. Log-log plot (OLS method) of the cumulative distribution (tail-end) for the frequency of injection over one year in 20 IDUs, Winnipeg, Canada, 2001. — Fitted line ····· Empirical data
Power Fit: $y = Cx^{-\alpha}$ Coefficient Data: C = 2338451.6 α = -1.2750789
Standard Error: 4.4008054 Correlation Coefficient: 0.9911411

Using the MLE method described in Figure 1 [39] and bootstrapping methods, [54] the model generated an exponent of 2.4 with 95% CI 2.09, 3.29 (Figure 5).

minx = 2640, maxx = 15,000, Estimates = Bootstrap (data, minx, maxx, 0.05)

$$\text{Estimates} = \begin{pmatrix} 2.492 \\ 2.083 \\ 3.289 \end{pmatrix}$$

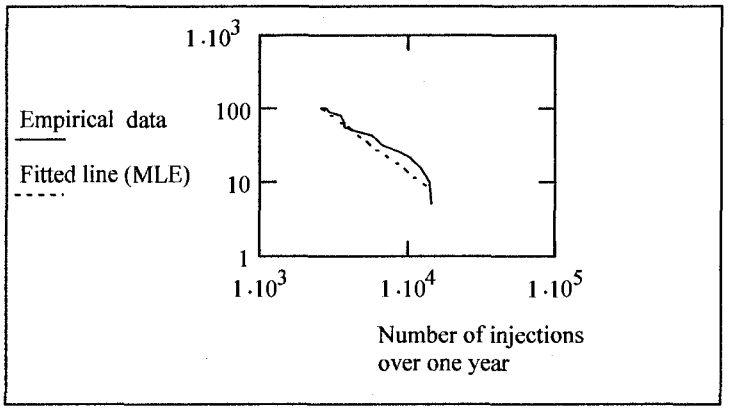

Figure 5. Log-log plot (MLE method) of the frequency distribution (tail-end) for the frequency of injection over one year in 20 IDUs, Winnipeg, Canada, 2001. — Fitted line — Empirical data
Minx = the start of the tail-end of the distribution; Maxx = the maximum value of the tail end of the distribution; 0.05 = 95% confidence limits. Estimates are the result of the MLE equation which generates a vector with three values. The first one is the estimate of the exponent; the second and the third values are the upper and lower limits of the 95% confidence interval.

Therefore the exponent (α) derived using OLS was 1.28; while MLE yielded α= 2.4.

Further investigation into the 20 individuals who inject very frequently (≥ 2,640 injections in one year) and are located in the tail end of the distribution revealed that they were significantly more likely to be aboriginal (p = 0.011); to have an income > $40,000 ($p$ = 0.007); have been paid (money or drugs) by someone to help them inject drugs (p = 0.035); have injected at an hotel in the past 12 months (p = 0.039); and have at least one member in their network who injected daily (p = 0.014) (Table 2).

Variable	Injects ≥ 2640 times in 1 year N = 20 n (%)	Injects < 2640 times in 1 year N = 122 n (%)	X^2 (df = 1)	p
Ethnicity†				
Aboriginal	17 (94.4%)	78 (64.5%)	6.510	0.011
Caucasian	1 (5.6%)	43 (35.5%)		
Income †				
≤ $40,000	9 (60.0%)	76 (90.5%)		0007*
> $40,000	6 (40.0%)	8 (9.5%)		
Has ever been paid (money or drugs) by someone to help them inject drugs †				
No	5 (25.0%)	60 (50.4%)	4.444	0.035
Yes	15 (75.0%)	59 (49.6%)		
Has injected in a hotel in the past 6 months				
No	6 (30.0%)	67 (54.9%)	4.271	0.039
Yes	14 (70.0%)	55 (45.1%)		
Has at least 1 member in their network who injects daily†				
No	5 (26.3%)	69 (56.6%)	6.029	0.014
Yes	14 (73.7%)	53 (43.4%)		

* Fisher's Exact Test (2-sided); † Does not add up to 142 due to missing data.

Table 2. Univariate results: Sociodemographic and drug injection related practices among 142 IDUs in Winnipeg, Canada 2001.

Discussion

The generated values for the exponent of < 3 using both OLS and MLE provides a strong indication that the IDU network through which infection is transmitted may also be scale-free

The exponent is the slope of the distribution and is directly related to the mean degree (number of injections) of the distribution and its variance which determine whether there is a critical or threshold spreading rate for an infection to persist.[32] The upper 95% CI falls into the epidemic transition region where an epidemic may or may not occur.[43] However, epidemic threshold values generated for a sexual contact network such as Newman's may not be the same for a network of IDUs who share drug injection equipment which carries a much higher probability of disease transmission. In reality, the prevalence of HIV infection among Winnipeg IDUs, based on two cross-sectional surveys, increased from 2.3% in 1986-90 to 12.6% in 1998, consistent with our analysis that the epidemic is still spreading.[55]

The over representation of aboriginals in the tail end of the distribution is troubling, but not surprising given the recent increases of HIV/AIDS reported among Aboriginal peoples in Canada. Before 1993, 1.2% of reported AIDS cases were among Aboriginal peoples and 10.9% were attributed to injecting drug use.[56] In 2003 13.4% of reported AIDS cases were among Aboriginal peoples and 58.3% were attributed to

injecting drug use.[56] In 1998, 18.8% of positive HIV test reports were among Aboriginal peoples and in 2003 this increased to 25.3%.[56] Injection drug use was the most common exposure reported among Aboriginal peoples between 1998 and December 31, 2003.[56] In addition, recent results from Vancouver reported that more Aboriginal people frequently injected cocaine and speedballs and went on binges of injecting drugs compared to Non-Aboriginals.[47] Also, frequent cocaine and speedball injection were independent predictors of HIV infection among Aboriginal men and women, while Aboriginal women were twice as likely to be infected with HIV if they reported going on binges of injection drug use.[47]

The significant association between high income and high frequency injectors could indicate involvement in the drug trade. Selling drugs is financially lucrative and ensures a steady drug supply to support personal drug habits. A report characterizing Edmonton's drug scene found that IDUs who reported dealing drugs could collect as much as $7,500 in one month.[57]

There is some controversy in the literature over what is the best method to determine the exponent.[58] If a model is linear, the MLE and OLS estimators are the same. However, if a model is not linear (such as our data), the variance of the ML estimator is less than the variance of other estimators (i.e. OLS) and therefore is preferable.[39, 59-60]

The MLE method used in this study has limitations in its use for finite distributions such as this one.[39] However, it is obvious that the variance in the frequency of injection is very high, just like that of a scale-free network. Therefore, while an epidemic threshold may exist because there is a limit to the number of times an individual can inject in a day or year, and because injection drug using populations are finite in size, it would be a great deal lower then that seen in a randomly mixed network.[30, 60-61]

Using frequency of injection as a proxy for frequency of sharing injection equipment may at first appear to be a serious limitation to generating an accurate estimate of the exponent which assists in determining whether the network may be scale-free. However, in reality, frequency of injection may in fact more accurately reflect the nature of contact patterns among IDUs. Individuals who inject drugs may be more likely to truthfully describe the frequency with which they inject compared to describing how often they share needles or other drug injection equipment.

Frequency of injection is more likely to capture the potentially multiple routes of disease transmission beyond just the sharing of needles such as the sharing of spoons,

cookers, filters, water or using equipment picked up off of coffee tables, the street or out of biohazard containers without knowing if it had previously been used by someone else. For example, high frequency injectors may in fact not share needles but share cookers, filters, water or may just pick up a cooker without knowing if it has been used by someone else.

Furthermore, high frequency injectors are more likely to be placed in a position where they need to share or use injection equipment previously used by someone else. Frequent injection patterns decrease the chance that an individual will have sterile or unused equipment for every injection episode.[62-63]

Despite these limitations, this initial examination of the distribution of the frequency of injection among IDUs has illustrated the exciting potential this new approach has for identifying another process through which HIV and HCV may be spread among IDUs.[31]

This analysis suggests that the transmission of HIV and HCV among IDUs is not just a result of risky individual injection practices and the relationships between individuals, but may, partly be a result of the network structure created by IDUs themselves, which helps to explain the ongoing transmission of HIV and HCV despite interventions.

Randomly targeted interventions have little impact on the spread of disease in a scale-free network. Therefore, interventions that change the scale-free network structure are required to reduce the transmission of disease. For example, a post-hoc analysis of the contact pattern between farms and markets in the 2001 foot-and-mouth (FMD) disease epidemic in the United Kingdom revealed a scale-free network.[30] with the majority of farms or markets having only one neighbouring farm or market while a few (hubs) had a large number of neighbouring farms or markets through which FMD was rapidly spread.[30] Culling the livestock in farms or markets with a large number of contacts (hubs) would have significantly reduced or stopped the epidemic from spreading.[30]

In 1996, Latkin [64] successfully implemented a network level intervention aimed at reducing drug injection equipment sharing among networks of IDUs. Participants were individual injection drug users who brought in members of their injection drug using network. Participants and their contacts were then randomly assigned to two groups; those who received the intervention and those who did not.[60] The intervention utilized self-help, network-centered and psycho educational approaches to changing network

member's behaviours related to risky injection practices.[60] Results of this network level intervention revealed that participants in the non-intervention group were 2.8 times more likely to report needle sharing and 2.7 times more likely to report sharing cookers.[60] These studies in applied prevention emphasize the need to understand the contact patterns of susceptible at risk populations.

Results from this pilot study among Winnipeg IDUs indicate that identifying the network structure is possible by examining the distribution of the frequency of injection (therefore, the frequency of contacts) and has yielded potential new interventions that could be implemented to help reduce the transmission of HIV and HCV. Specifically, implementing needle exchange programs, peer outreach, or safer injection facilities in or near the hotels frequented by those in the tail-end of the distribution (very high frequency injectors) may help to interrupt the disease transmission network and significantly reduce the spread of HIV and HCV among this network of IDUs.

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4. Chapter Three

Scale free networks among injection drug users in Winnipeg, Canada.

This chapter consists of the third and final manuscript relating to this research which investigates whether the structure of the network of individuals who inject drugs and share injection equipment in Winnipeg, Canada may be scale free. In this paper, the emphasis is on corroborating the two methods, ordinary least squares (OLS) and maximum likelihood estimation (MLE) which were used to identify network structure in the previous paper. In addition, factors associated with the structure of drug injecting networks are presented and interventions that may assist to reduce the transmission of HIV and HCV among injection drug users are recommended based on the results presented in this paper. This analysis focuses on a specific group of interest, individuals who have gone on binges of injection drug use.

Additional details relating to some of the methods and results in this paper are presented in the appendices listed below:

Scale free networks among injection drug users in Winnipeg, Canada.

L. Pelude[1], Liljeros F [2], J. Wylie [3,4], G. Wells[1], L. Leonard[1] and A. Jolly, PhD[1,5]

[1] University of Ottawa, Ottawa, Canada

[2] Stockholm University, Stockholm, Sweden

[3] Cadham Provincial Laboratory, Manitoba Health, Winnipeg, Canada

[4] University of Manitoba, Winnipeg, Canada

[5] Division of Modeling and Projections, Centre for Infectious Disease Prevention and Control, Public Health Agency of Canada, Ottawa, Canada

Keywords: Injection drug use, network analysis, scale-free networks

Abstract

This paper explores whether frequency of injection patterns among individuals who inject drugs may be used to identify the structure of their injection equipment sharing networks. Identifying the structure of any infectious disease network has important implications in relation to the spread of disease. In a scale-free network, epidemic thresholds are non-existent or if present are much lower than that seen in a randomly mixed network. As a result, even pathogens with low transmissibility may spread easily through this type of network.

Results indicate that the network of injection drugs users in Winnipeg, Canada may indeed be scale-free. An exponent of < 3 was generated using MLE with 95% CIs that were also < 3 indicating that the frequency of injection during binge drug use and consequently the injection sharing networks among IDUs may be scale-free. Results from the multivariate analysis revealed that high frequency injectors or those located in the tail end of the power law distribution were significantly more likely to have injected cocaine or Talwin & Ritalin and obtained their needles from a dealer. These results suggest new interventions that could be implemented by the current needle exchange program to help reduce the transmission of human immunodeficiency virus and hepatitis C among this network of individuals who inject drugs in Winnipeg, Canada.

Background

In the last two decades the human immunodeficiency virus (HIV) and the hepatitis C virus (HCV) have emerged as epidemics among many groups of injection drug users (IDUs). HIV/AIDS epidemics among IDUs have been documented in 114 countries and on every continent.[1] Explosive epidemics have occurred in cities across the world such as New York, Vancouver, Bangkok, Manipur and Odessa. In some IDU populations, HIV prevalence has been documented at 30% and up to 80% in a short period of time.[2-5] Injection drug use accounts for approximately 63% of new HCV infections in Canada and the US. [6-7]

Consequently, understanding the dynamics of disease transmission through a population requires a versatile approach. The transmissibility of the pathogen, duration of infection and the introduction of an infectious individual into a susceptible population contribute to the complexities of disease transmission.

However, the ability of a pathogen to spread depends also on a number of factors that may or may not be modifiable. In terms of the spread of HIV and HCV among IDUs; individual practices (not using previously used injection equipment), social networks (effect of social relationships on individual injection practices) and network structure (frequency of contacts and how they are distributed between members of an injection drug using network) are some of the factors that may influence the spread of disease.

The practice of sharing or using previously used needles, syringes and other drug injection equipment (filters, water or cookers) plays a significant role in the transmission of HIV and HCV among IDUs. [8-22] This practice usually requires contact with another individual who injects drugs. Therefore, when attempting to determine or predict the spread of HIV and HCV among IDUs, a crucial factor is the identification of the contact patterns in the network of IDUs.

Most epidemiological models used to predict the spread of disease assume a completely homogenous population, one where all individuals are equally likely to be infected by contact with an infected individual.[23-26] In relation to the transmission of HIV and HCV among IDUs it is not reasonable to assume that contacts are random and that there is homogeneity in the distribution of contacts. [24,27] Heterogeneity in the number of contacts has been incorporated into the standard model however, it continues to assume random mixing with respect to how contacts are formed and that the number of contacts

per individual follows a normal distribution.[24, 27-28] As is the case with most social interactions, contacts among IDUs, for the most part, are not a random act. Factors such as how contacts are formed; the duration of contacts, and simultaneous contacts are not addressed by this standard model.

A more recent approach to determining the spread of disease has been to identify the structure of a network by examining the frequency and distribution of contacts. Three recent studies have suggested that networks of sexual contacts may have a scale-free structure which has implications for the transmission of disease through networks. The distribution of the frequency of contacts in a network has been shown to follow distinct patterns; there are 1) random networks; where links between individuals are created randomly but on average each individual has the same number of contacts; 2) regular networks, where links created between individuals follow precise rules, (i.e., each individual has exactly the same number of contacts) and; 3) small-world networks, where links are created through a combination of randomness and rules.[29]

Recently, some small world networks have been found to be scale-free.[30] Individuals in a scale-free network do not have a typical or average number of contacts. Rather, the majority of individuals have a small number of contacts while a small number of individuals have a large number of contacts.[23, 27, 29, 31-32]

Network structure has been shown to have an effect on the initial spread and long-term behaviour of any infectious disease.[33] The spread of disease in a scale-free network significantly deviates from that of a random network, where infection spreads to the whole network only if the spreading rate exceeds a critical value or threshold.[34] In a scale-free network there is no critical value or threshold.[35-37]

The concept that network structure affects the transmission of disease can also be applied to networks of individuals who inject drugs. In a previous paper we explored whether the methods currently used to identify the scale-free structure of sexual contact networks may be applied to networks of individuals who inject drugs. In a previous pilot study conducted among a group of IDUs living in Winnipeg, Canada it was found that the distribution of the frequency of injection among IDUs was highly right skewed with by far the majority of people reporting a small number of injections and very few reporting a large number of injections.[38] Results indicated that it was possible to identify the network structure by examining the distribution of the frequency of injection and therefore, the frequency of contacts and that the networks of IDUs through which infection is transmitted may be scale-free. In addition, defining transmission dynamics based on

network structure may suggest additional interventions that may help to significantly reduce the spread of HIV and HCV among this network of IDUs.

In this paper, the emphasis is on corroborating the methods used to identify network structure on a larger sample and identifying the factors associated with drug injecting networks. The analysis will focus on a specific group of interest, individuals who have gone on binges of injection drug use. Binges are episodes of injection drug use in which individuals inject repeatedly in a relatively short time and then go back to their usual use or stop injecting for a period of time. During binges of drug use, individuals are at greater risk of sharing injection drug equipment and consequently the risk of transmitting disease is increased.[39-42]

Methods

Data

A cross-sectional study was conducted from December, 2003 to September 2004 of 435 individuals who inject drugs and live in Winnipeg, Canada. Participants were invited to participate through posters placed in community clinics, drop-in venues, locations frequented by IDUs, and by word of mouth. Participants had to be aged 15 or more and have injected drugs in the 6 months prior to being interviewed. A study nurse administered all the questionnaires and collected a blood specimen for HCV, HBV and HIV serological testing. Participants provided written or oral consent and they received $40 Cdn for their participation. The study design was approved by the Health Research Ethics Board of the University of Manitoba and the Winnipeg Regional Health Authority Research Review Committee. The analysis specific to this paper was also approved by the Ottawa Hospital Research Ethics Board.

Questionnaire

The questionnaire was divided into three parts. The first section obtained information on the participant's socio-demographics, drug use, drug injection practices, needle exchange program (NEP) use, sexual behaviours, self-perceived drug dependency, social support and depression. Section 2 gathered information from the participant on their drug, sex and social support networks. Participants were asked to list people (maximum of 20) they had more than casual contact with in the past 30 days and related contact information. The final section obtained detailed information relating specifically to their injection drug using network (maximum of 5 IDUs).

Analysis

Network Structure

The focus is on describing the frequency distribution (degree distribution) of the participant's sharing injection equipment contacts. Individual numbers for the frequency with which participant's shared injection equipment was not available. However, since frequency of injection during binge drug use has been strongly associated with sharing of drug injection equipment among IDUs and an increased risk of HIV and HCV infection in previous studies, [10, 39-44] we examined the distribution of the frequency of injection during binge drug use over a 6 month period in order to determine if the drug injection equipment sharing networks may be scale-free. In this data set, there was a positive relationship between the frequency of injecting while bingeing with sharing needles, r = .15, p (one-tailed) = < .05. Although frequency of injection accounts for a very small percentage of the variation in needle sharing, a scatter plot of the two variables illustrates that as frequency of injection increases so does the frequency of sharing needles (Figure 1)

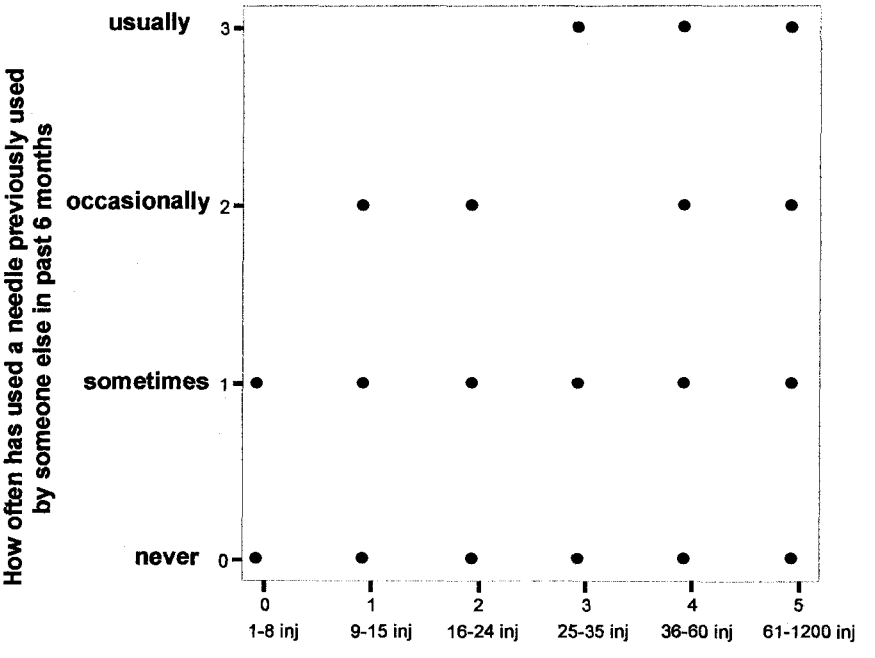

Figure1. Correlation between frequency of injection during binge drug use and frequency of sharing needles *among 242 IDUs in Winnipeg, Canada 2004.*

Of the 435 participants enrolled in this study, 248 reported binges of drug use in the six months prior to interview. As the number of days of binge drug use varied for each participant the frequency of injection during binge drug use was calculated by multiplying the total number of days of binge drug use by the number of injections per day for a total of 242 participants with complete data.

Scale-free networks are characterized by power law behaviour in the tail of the cumulative distribution, $P(x) = Cx^{-\alpha}$; the probability $P(x)$ that x has a value greater or equal to x and a value for the exponent α of less than 3.[32, 45-46] However, exponent values less than 2 are rarely seen in real world networks. [36-37]

The cumulative distribution of the frequency of injection during binge drug use in the past 6 months was plotted on a graph with logarithmic axes (method described in Chapter two).[38] A curve was fitted to the entire distribution and then to the tail-end of the distribution using ordinary least squares (OLS) and maximum likelihood estimation (MLE) methods.

Both OLS and MLE have been used to identify the structure of sexual contact networks. OLS uses the cumulative distribution (1 data point could represent 5 individuals with the same number of reported injections) while MLE uses the frequency distribution (plots each individual data point). The relationship between these distributions is that the slope for the frequency distribution minus one equals the slope for the cumulative distribution.

However, studies in various disciplines have shown that both methods generate similar exponents regardless whether they used OLS or MLE. [47-48] Therefore, both methods were used to see how they perform in terms of generating a value for the exponent and the results are compared

Determining the start of the tail is subjective, and requires judgment about the value above which the distribution follows a power law.[46] The approximate point where the tail region of the distribution begins can be observed on a cumulative degree plot.[32] Our choice of a starting point for the tail begins at ≥ 63 injections during binge drug use (n = 71).

Graphs were plotted using both Curve Expert Version 1.38 and Mathcad 12.[49-50] The exponent was determined using OLS: $y = Cx^{-\alpha}$ and MLE described by Newman (Figure 2).[46]

$$\alpha := 1 + n \cdot \left(\sum \ln\left(\frac{\text{data}}{\text{xmin}} \right) \right)^{-1}$$

Figure 2: MLE method [46] Note: MLE uses the frequency distribution to estimate the exponent (slope) (α) = exponent; n = 71; ln = log; data = frequency of injection data; xmin = start of the tail end of the distribution (63 injections)

Best fit was determined using the correlation coefficient and the standard error of the estimate for OLS. Bootstrapping methods were used to estimate 95% confidence intervals for the exponent using MLE.[51]

Statistical analysis

Descriptives for those individuals who reported binges of injection drug use were obtained for socio-demographics, drug use, drug injection practices, NEP use, self-perceived drug dependency, social support and depression. Spearman's Rho was used to assess the relationship between frequency of injection during binge drug use and sharing needles. Univariate analysis to describe the differences in people who injected greater or equal to 63 injections during binge drug use compared with people who injected less frequently were conducted using X^2 or Fisher's exact when appropriate. Logistic regression was used to analyze the binary dependent variable frequency of injection during binge drug use. Variables with p values of 0.05 or less that were considered to be potentially useful by current NEP staff in order to identify high frequency injectors were considered for inclusion in multivariate analysis. Logistic regression model building procedures followed those described by Field 2005.[52] Multivariate analysis was conducted using the stepwise backward method. Removal criterion for the variables entered was assessed using the likelihood ratio test. All statistical analysis was done using SPSS version 12.[53] Residuals were examined to assess the final fit of the logistic regression model. Variables that were entered into the multivariate analysis were also checked for multicollinearity. The tolerance values and variance inflation factors were within acceptable limits.

Network Visualization

Two components of the larger network are used to visually illustrate the variation in the transmission of disease in relation to a participant's place in this social network of IDUs. Networks were constructed by Wylie et al., 2006 [54] using Pajek [55], a social network analysis program where the relationships between individual IDUs and their contacts (egocentric networks) were plotted to delineate the various networks for each participant

and then linked to form the larger (sociometric) network. The methods to construct this network have been described previously.[52] Individual network components were extracted for this analysis using Pajek.[55]

Results

Descriptives

A summary of statistics relevant to this analysis for the 242 participants who reported binges of drug use are presented in Table 1. Overall, almost half of the participants identified as aboriginal, average age was 35, just over half of the participants were men and the main source of income reported was government support or money from family and friends. The majority had less then a grade 12 education and reported having stable housing. More than half were HCV positive (54%), one third were HBV positive (31%) and 7% were HIV positive.

Greater than two thirds had injected cocaine, 41% had injected morphine, 34% Talwin & Ritalin (T&Rs) and 30% crack in the past 6 months. Just over 60% reported ever having used a needle previously used by some one else and 23% had done so in the past 6 months Forty percent had used water, filters or cookers previously used by someone else. Almost three-quarters of participants had obtained their needles from friends, family members or their partners, 67% from a pharmacy or a NEP and 21% from a dealer.

Typically, runs of binge drug use lasted 6 days and participants injected on average 17 times per day. The average number of injections during binge drug use in the past 6 months was 76 (range 2-1,200). Seventy-one percent (n = 171) reported injecting less than 63 times in the past 6 months during binge drug use while 29% (n = 71) injected greater or equal to 63 times.

Variable	N = 242 n (%)
Gender	
Male	137 (56.6)
Female	102 (42.1)
Transgender (male to female)	3 (1.2)
Age	
Mean (SD)	35 (9.501)
Median	36
Mode	31
Min – Max	16-60

Ethnicity	
Aboriginal	110 (45.5)
Caucasian	90 (37.2)
Metis	36 (14.9)
Other	6 (2.5)
Main source of income	
Regular employment	60 (24.8)
Gov't support (welfare, EI, pension) or $ family & friends	146 (60.3)
Illegal activities (sex trade, dealing, panhandling, stealing)	36 (14.9)
Education	
< than grade 12	171 (70.7)
Completed grade 12	71 (29.3)
Current housing [†]	
Stable (own, family or friend's home, treatment centre, rooming house)	194 (81.5)
Unstable (shelter, hotel, on the street, vehicle)	44 (18.5)
Drugs injected in past 6 months [$]	
Cocaine	168 (69.4)
Morphine	101 (41.7)
Talwin & Ritalin (T&Rs)	83 (34.3)
Crack	74 (30.6)
Drug most frequently injected in past 6 months [†]	
Cocaine	87 (36.3)
Talwin & Ritalin (T&Rs)	56 (23.3)
Morphine	38 (15.8)
Has injected in own house/apt in past 6 months	
No	96 (39.7)
Yes	146 (60.3)
Has injected at friend's house/apt in past 6 months	
No	58 (24.0)
Yes	184 (76.0)
Has injected in a hotel in past 6 months	
No	130 (53.7)
Yes	112 (46.3)
Has injected in a public place in past 6 months	
No	156 (64.5)
Yes	86 (35.5)
Has ever used a needle previously used by someone else [†]	
No	80 (36.9)
Yes	137 (63.1)
Has used a needle previously used by someone else in the past 6 months [†]	
No	93 (38.4)
Yes	57 (23.6)
Has used other injection equipment (water, filters, cookers) previously used by someone else in the past 6 months [†]	
No	132 (56.9)
Yes	100 (43.1)
Number of days binges lasted in past 6 months	
Mean (SD)	5.5 (13.091)
Median	3
Mode	2
Variance	171.379
Min – Max	1-183
Number of injections per day of binge	
Mean (SD)	17 (24.676)
Median	10
Mode	10
Variance	608.902
Min – Max	1-300

Frequency of injection during binge drug use in the past 6 months (Total number of days binged x number of injections per day)	
Mean (SD)	76
Median	35
Mode	60
Variance	24084.23
Min – Max	2-1200
Injected greater or equal to 63 times during binge drug use in the past 6 months	
No	171 (70.7)
Yes	71 (29.3)
Drugs most frequently injected during binge drug use in past 6 months [†]	
Cocaine	92 (38.2)
T&Rs	54 (22.4)
Morphine	34 (14.1)
Where obtained needles from in past 6 months [§§]	
Friends/family/partner	173 (71.5)
Pharmacy	163 (67.4)
NEP	162 (66.9)
Dealer	50 (20.7)
Someone on the street	44 (18.2)
Shooting gallery owner	18 (7.4)
Network component size (# of contacts in component)	
Mean (SD)	39
Median	26
Mode	7
Min – Max	2-138
Network component size ≥ 85 (# of contacts in component)	
No	210 (86.8)
Yes	32 (13.2)
HCV [†]	
Negative	99 (45.6)
Positive	118 (54.4)
HIV [†]	
Negative	200 (93.5)
Positive	14 (6.5)
HBV [†]	
Negative	149 (68.7)
Positive	68 (31.3)

[†] Does not add up to 242 due to missing values [§] For each drug N = 242 [§§] For each location N = 242

Table 1. Sociodemographic and drug injection practices in 242 IDUs, Winnipeg, Canada, 2004.

Network Structure

There was a large variation in the frequency of injection reported during binge drug use. The frequency of injection was non normal, with by far the majority of people reporting a small number of injections and very few reporting a very large numbers of injections. The distribution is extremely positively skewed with a long tail suggesting it may be described by a power law (Figure 3).

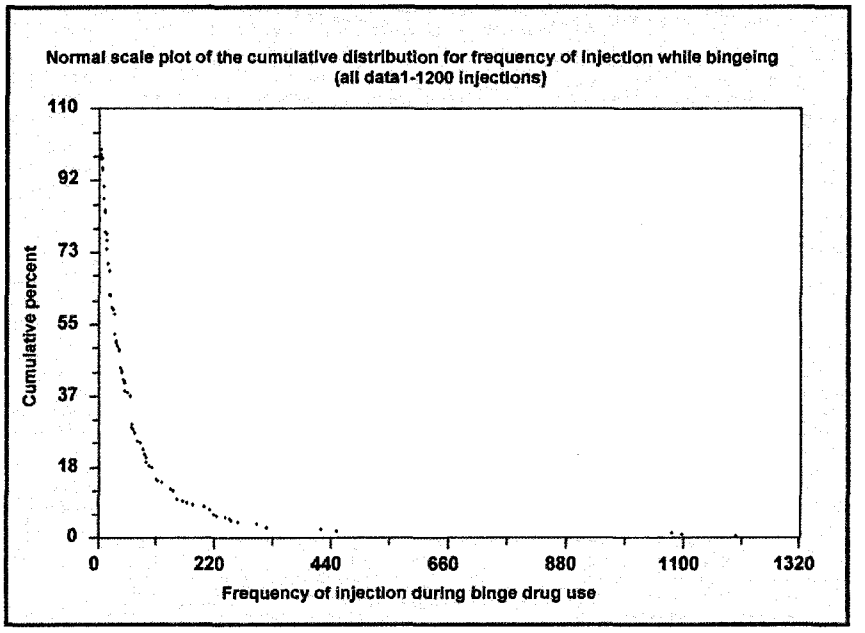

Figure 3. Normal scale plot of the cumulative distribution for frequency of injection during binge drug use over a 6 month period in 242 IDU, Winnipeg, Canada, 2004.
(Mean 76 injections; median 35; mode 60; std. dev 155.191; variance 24084.23; min 1; max 15,000)

The next graph (Figure 4) shows that a log-log plot of the entire data set, using OLS, is best fit with a shifted power model (y=a*(x-b)^c), one of the various forms of power models (c = slope of the line or the exponent and a = y intercept). On this plot we can observe that the distribution appears to go straight at around 60 injections.

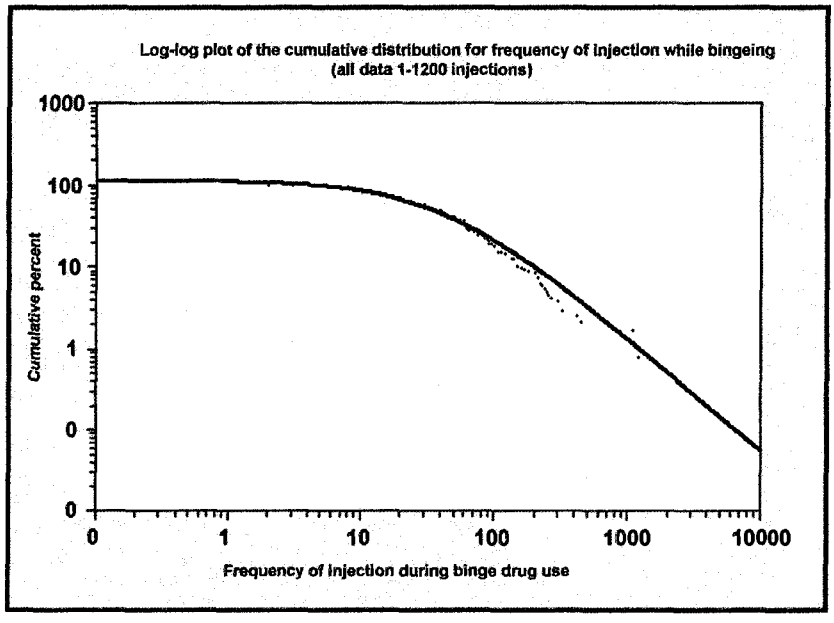

Figure 4. Log-log plot (OLS method) of the cumulative distribution for frequency of injection during binge drug use over a 6 month period in 242 IDUs, Winnipeg, Canada, 2004. — Fitted line ····· Empirical data
Shifted Power Fit: y= a*(x-b)^c
Coefficient Data: a = 19935.651 b = -40.654318 c = -1.3896347
Standard Error: 2.5661998 Correlation Coefficient: 0.9967647

Data from the tail-end of the distribution (≥ 63 injections) were plotted on a log-log plot (Figure 5) using OLS. The vapour pressure model (exponential family) fit the data best.

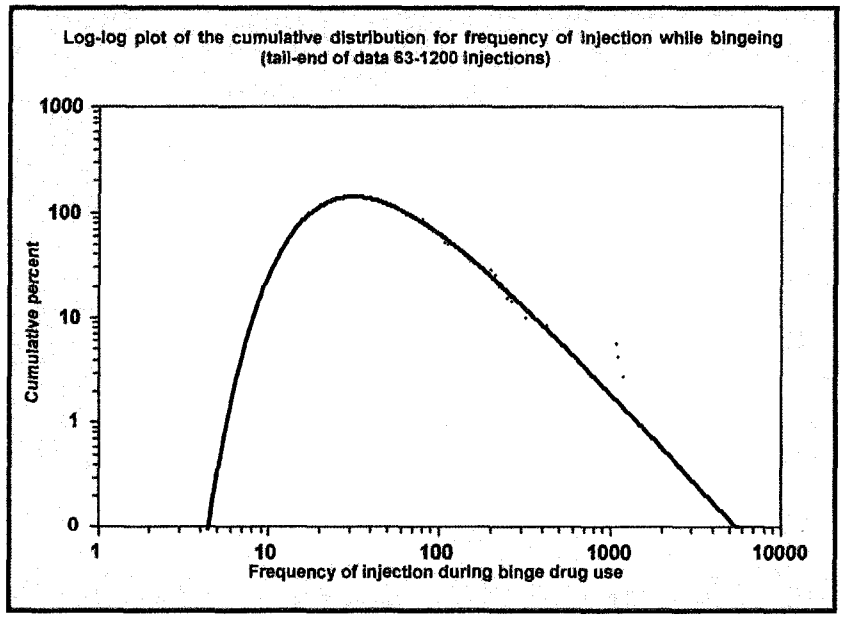

Figure 5. Log-log plot (OLS method) of the cumulative distribution (tail-end) for frequency of injection during binge drug use over a 6 month period in 71 IDUs, Winnipeg, Canada, 2004. — Fitted line ····· Empirical data
Vapor Pressure Model: y= exp (a+b/x+cln(x))
Coefficient Data: a = 12.665791 b = -54.198201 c = -1.7370512
Standard Error: 2.1363721 Correlation Coefficient: 0.9977386

These results using OLS are not surprising given that our data is not normally distributed. The value of the exponent in the model is the slope of the distribution (the straight line) and is directly related to the mean degree (number of injections) of the distribution and its variance.[32] If a model is linear, using OLS or MLE would likely generate similar results. However, if a model is not linear (such as our data), the variance of the ML estimator is less than the variance of other estimators (i.e. OLS) and therefore is the preferable estimation method.[24, 46, 56]

Using the MLE method described in Figure 2 and bootstrapping methods,[51] the model generated an exponent of 2.26 with 95% CI 2.04, 2.57 (Figure 6).

minx = 63, maxx = 1,200, Estimates = Bootstrap (data, minx, maxx, 0.05)

$$\text{Estimates} = \begin{pmatrix} 2.261 \\ 2.042 \\ 2.566 \end{pmatrix}$$

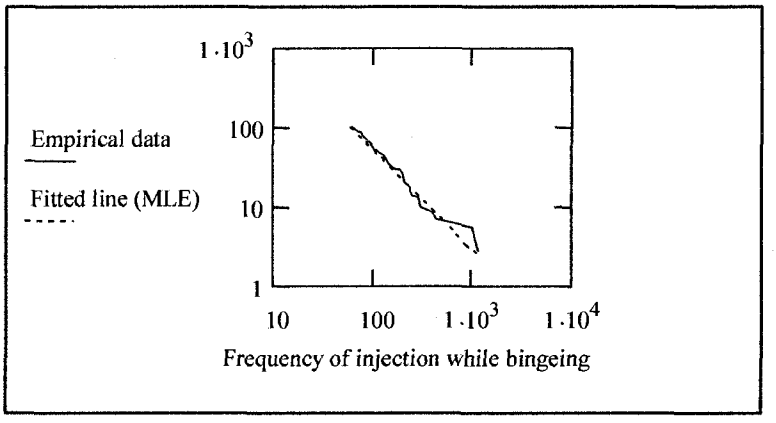

Figure 6. Log-log plot (MLE method) of the frequency distribution (tail-end) for the frequency of injection during binge drug use over a 6 month period among 71 IDUs, Winnipeg, Canada, 2004. — Fitted line — Empirical data Minx = the start of the tail-end of the distribution; Maxx = the maximum value of the tail end of the distribution; 0.05 = 95% confidence limits. Estimates are the result of the MLE equation which generates a vector with three values. The first one is the estimate of the exponent; the second and the third values are the upper and lower limits of the 95% confidence interval.

Univariate analysis

Results using the MLE method suggest that the network of IDUs who share needles or syringes may be scale-free. Significant differences in injection practices, drug use, location of injection, where participants obtained needles and self-perceived drug dependency were observed between those individuals who inject very frequently during binge drug use (are in the tail end of the distribution n= 71) compared to those who do

not inject very frequently (n = 171). These results are presented in Table 2. Of particular interest is that participants in the tail end were significantly more likely to be HCV positive, have injected cocaine, crack, Talwin and Ritalin (T&Rs), injected at a hotel or in a public place (street, empty house, shooting gallery, car, public washroom), have obtained needles from local NEPs, pharmacies and also from dealers and shooting gallery owners.

Variable	Injects ≥ 63 times while bingeing N = 71 n (%)	Injects < 63 times while bingeing N = 171 n (%)	X^2 (df = 1)	*p*
Injected cocaine in the past 6 months				
No	11 (15.5)	63 (36.8)	10.772	0.001
Yes	60 (84.5)	108 (63.2)		
Injected T&Rs in the past 6 months				
No	40 (56.3)	119 (69.6)	3.910	0.048
Yes	31 (43.7)	52 (30.4)		
Injected crack in the past 6 months				
No	39 (54.9)	129 (75.4)	9.941	0.002
Yes	32 (45.1)	42 (24.6)		
Injected at a hotel in the past 6 months				
No	28 (39.4)	102 (59.6)	8.244	0.004
Yes	43 (60.6)	69 (40.4)		
Injected in a public place in the past 6 months				
No	31 (43.7)	125 (73.1)	18.978	<0.001
Yes	40 (56.3)	46 (26.9)		
Obtained needles from a NEP in the past 6 months				
No	16 (22.5)	64 (37.4)	5.028	0.025
Yes	55 (77.5)	107 (62.6)		
Obtained needles from a pharmacy in the past 6 months				
No	9 (12.7)	70 (40.9)	18.222	<0.001
Yes	62 (87.3)	101 (59.1)		
Obtained needles from a dealer in the past 6 months				
No	44 (62.0)	118 (86.5)	18.488	<0.001
Yes	27 (38.0)	23 (13.5)		
Obtained needles from a shooting gallery owner in the past 6 months				
No	60 (84.50	164 (95.9)	9.469	0.002
Yes	11 (15.5)	7 (4.1)		
Self-perceived drug dependency				
Minimal	22 (31.0)	80 (46.8)	5.135	0.023
Moderate-extreme	49 (69.0)	91 (53.2)		
HCV [†]				
Negative	22 (34.4)	77 (50.3)	4.628	0.031
Positive	42 (65.6)	76 (49.7)		

[†] Does not add up to 242 due to missing values

Table 2. Univariate results: Drug injection related practices among 242 IDUs in Winnipeg, Canada, 2004.

Multivariate analysis

Since there were a number of variables significantly associated with high frequency injectors during binge drug use, variables that were considered to be potentially useful to identify high frequency injectors by current NEP staff were considered for inclusion in multivariate analysis. Most NEPs collect statistics on their contacts with individual clients. Information given by clients to NEP staff is considered anonymous, As such; information such as name, address or other identifying client information is not collected. In Winnipeg statistics collected include gender, type of contact (person, telephone, home visit), supplies given (needles, sterile water, glass stems, screens) and any medical intervention (testing, vaccination). Since many contacts with NEP clients are brief and establishing trusting relationships with NEP clients requires time, variables that were considered to be non-invasive and easy to ask were selected for inclusion into the logistic regression model. These variables included type of drug injected (cocaine and T&Rs), injected at a hotel, and if needles were obtained from a dealer.

Multivariate logistic regression revealed that three variables, injecting cocaine or T&Rs and obtaining needles from a dealer, remained positively associated with individuals who are high frequency injectors (injecting ≥ 63 times during binge drug use) and are located in the tail end of the distribution. High frequency injectors were 4 times more likely to have injected cocaine, 2.5 times more likely to have injected T & Rs and 3.5 times more likely to have obtained needles from a dealer compared with those who injected less frequently (Table 3).

Variable	OR (95% CI)	*p* value
Injected cocaine in the past 6 months		
No	Ref	
Yes	4.17 (1.89, 9.16)	< 0.001
Injected T & Rs in the past 6 months		
No	Ref	
Yes	2.58 (1.33, 5.0)	0.005
Obtained needles from a dealer in the past 6 months		
No	Ref	
Yes	3.55 (1.79, 7.03)	< 0.001

Table 3. Multivariate final model for frequency of injection during binge drug use in a 6 month period among 242 IDUs in Winnipeg, Canada, 2004.

Network visualization

The network generated by this study consists of the 435 participants and their contacts for a total of 4,166 individuals. From this network 227 individual components

were found ranging in size from 2 to 138 members. Numbers from 1-435 represent the study participants while numbers from 1001 – 435005 represent their contacts.

Two components of the larger network are presented below to visually illustrate the variation in the risk of disease transmission in relation to a participant's place in this social network of IDUs. These two components illustrate the varied potential for the transmission of HIV or HCV among members of a network. The boxes denote men while the circles represent women. For the study participants (1-435), red indicates an individual who is HCV positive while blue indicates HCV negative. HIV and HCV status is unknown for the contacts (black).

Component 5 (Figure 7) consists of 10 study participants and their 75 contacts representing a larger component of the network. All of the study participants in component 5 are HCV positive except for one individual (97) and have a greater proportion of IDU contacts in their personal networks. Two study participants are in the tail end of the distribution (high frequency injectors during binge drug use) (10, 11), one participant reported binge drug use but is not in the tail end of the distribution (97), two participants have shared needles in the past 6 months (11, 53), all reported having injected T&Rs while only two had injected cocaine (11, 19) in the past 6 months. No study participant had obtained their needles from a dealer.

In comparison, Component 41 (Figure 8) represents a medium sized component consisting of 7 study participants and their 44 contacts. Only 3 out of the 7 study participants are HCV positive (100, 103, 117) and overall they have fewer IDUs as contacts in their personal networks. None of the study participants are in the tail end of the distribution (high frequency injectors during binge drug use) however 2 of the study participants reported binge drug use (103, 110). None reported sharing needles or obtaining their needles from a dealer. Four reported injecting cocaine (73, 103, 105, 110) and only 1 study participant (100) reported injecting T&Rs. However, 2 study participants (111, 117) did not inject cocaine or T&RS in the past six months. These two components illustrate the different risk potentials for the transmission of HIV or HCV among IDUs relative to where individual IDUs are situated in the larger network. Component 5 carries the higher risk of disease transmission compared to Component 41.

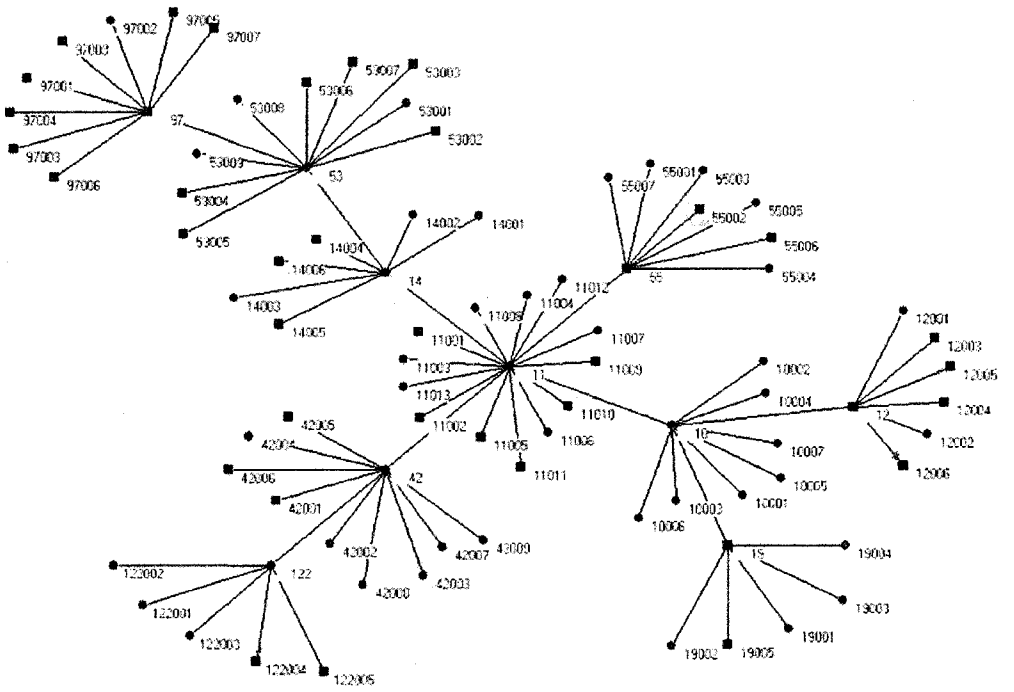

Figure 7: Component # 5, Size of network = 85 IDUs in Winnipeg, Canada, 2004.
Red: HCV positive, blue: HCV negative, circles: women, boxes: men

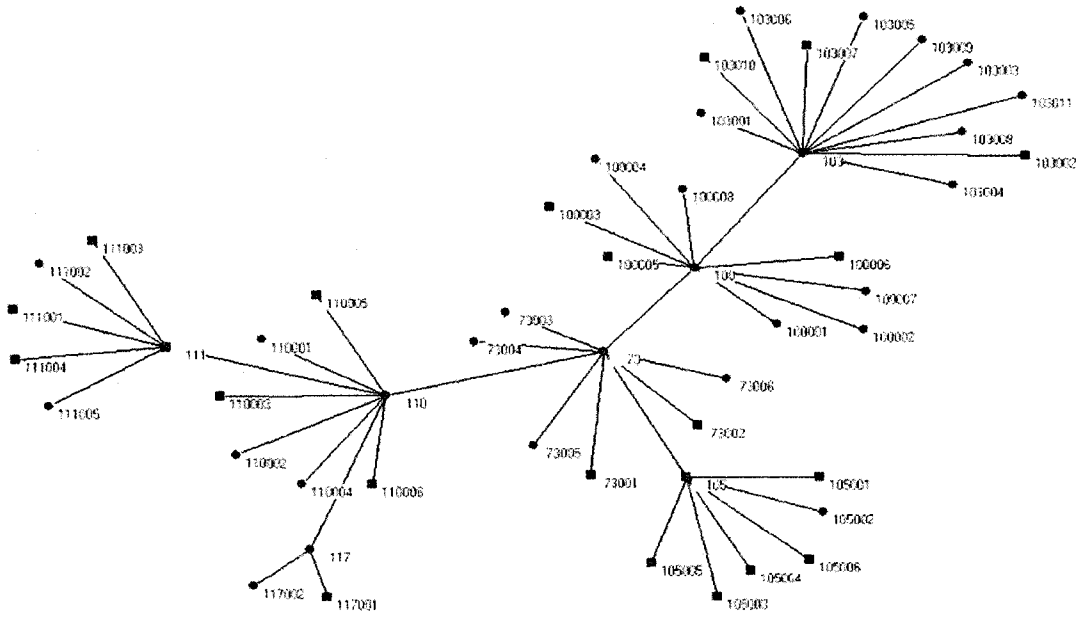

Figure 8: Component # 41: Size of network = 51 IDUs in Winnipeg, Canada, 2004.
Red: HCV positive, blue: HCV negative, circles: women, boxes: men

Discussion

The emphasis of this paper was on corroborating the techniques used in the pilot study (Chapter Two). The exponent of < 3 (including 95% CIs) derived using MLE indicates that the frequency of injection among individuals during binge drug use may be scale-free replicating results previously reported.[38] As frequency of injection and binge drug use are associated with sharing of drug injection equipment and an increased risk of HIV and HCV infection this finding provides a strong indication that networks of IDUs through which infection is transmitted may also be scale-free. Although frequency of injection during binge drug use is used as a proxy for sharing injection equipment, in reality, frequency of injection may in fact more accurately reflect the nature of contact patterns among IDUs. Individuals who inject drugs may be more likely to truthfully describe the frequency with which they inject compared to how often they share needles or other drug injection equipment. After 20 years of prevention messages in relation to the risks of disease transmission when sharing injection equipment, IDUs may be less comfortable admitting to sharing then to reporting the frequency with which they inject. More than 70% of participants in this study were aware of the risks of transmitting HIV and HCV when sharing drug injection equipment.

Furthermore, frequency of injection is more likely to capture the potentially multiple routes of disease transmission beyond just the sharing of needles such as the sharing of spoons, cookers, filters, water or using equipment picked up off of coffee tables, the street or out of biohazard containers without knowing if it had previously been used by someone else. For example, high frequency injectors may in fact not share needles but share cookers, filters, water or may just pick up a cooker without knowing if it has been used by someone else. In this study more people reported sharing other injection equipment (43%) than needles (22%) (p = <0.001). Sharing other injection equipment has been shown to be a significant factor in the transmission of HIV and HCV among people who inject drugs.

It is also important to be aware that NEPs currently distribute a small proportion of the sterile needles required. It has been projected that approximately 1,000 needles are required per IDU per year. In Ontario, it is estimated that 53 needles are distributed per injector per year. In Montreal and in Ottawa it is estimated that NEPs distribute approximately 5% of the needles required by IDUs.[57]

In Ontario, 100% coverage has yet to be achieved and a wide variation in distribution levels exists. For instance, in 2002 NEPs reported that they distributed

between 1 and 474 needles per IDU per year.[57] Insufficient needle distribution may also exist in Winnipeg as participants in the tail-end of the distribution (high frequency injectors) were significantly more likely to be certain they could not use a clean needle every time they injected (p = 0.013) and to have used a needle previously used by someone else in the past 6 months (p = 0.002) compared to those not in the tail–end of the distribution.

High frequency injectors are more likely to be placed in a position where they need to share or use injection equipment previously used by someone else. Frequent injection patterns decrease the chance that an individual will have sterile or unused equipment for every injection episode.[39, 42]

Given that 1) sharing needles does not capture the sharing of all drug injection equipment; 2) frequency of sharing may be underreported; 3) frequency of injection is accepted as related to frequency of sharing in the HIV and substance use field and 4) most NEPs do not distribute an adequate supply of needles it is quite probable that frequency of injection is in reality the variable which better reflects the actual structure or contact patterns of injection drug user's networks.

The MLE method used in this study has limitations in its use for finite distributions such as this one.[46] However, it is obvious that the variance in the frequency of injection is very high, just like that of a scale-free network. Therefore, while an epidemic threshold may exist because there is a limit to the number of times an individual can inject in a day or year, and because injection drug using populations are finite in size, it would be a great deal lower then that seen in a randomly mixed network.[23, 58]

The inability of the OLS method to fit a power model to our data is not surprising. Previous work in this area has established that linear fits commonly used by researchers for fitting to a power law distribution contain a severe bias.[46, 56] If a model is linear, the MLE & least squares estimators are the same. However, if a model is not linear (such as our data), the variance of the ML estimator is less than the variance of other estimators (i.e. least squares) and therefore is preferable.[24, 46, 56]

Multivariate analysis revealed the potential for existing NEP program staff to identify high frequency injectors or those located in the tail end of the distribution. High frequency injectors in Winnipeg, Canada were significantly more likely to have injected cocaine, to have injected T&Rs and to have obtained needles from a dealer. Since NEP programs currently collect statistics on contacts with clients, additional questions could be asked relating to where NEP clients have obtained their needles and if they inject

cocaine or T&Rs without breaking the anonymity of the NEP client . Consequently, high risk individuals in the tail end of the distribution could be identified and interventions such as ensuring an adequate supply of sterile needles, clean equipment and reinforcing the message of not sharing injection equipment could be implemented. Interventions which focus on changing the contact patterns of high frequency injectors in a network known to be scale-free may help to significantly reduce the spread of HIV and HCV among this network of IDUs. These results also provide evidence for implementing new NEP program initiatives such as supplying dealers with adequate supplies of sterile needles and clean injection equipment (such as water, cookers and filters).

Finally, visualizing the network components of individuals who inject drugs emphasizes the need to understand the frequency and distribution of the contact patterns among IDUs (network structure). It becomes obvious that the risk of disease transmission is related not only to individual practices (using previously used injection equipment) and the effect of social relationships on individual injection practices but is also influenced by the structure of the network and an individual's location within that network.

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5. Discussion: All three manuscripts

The primary goal of this research was to identify whether the network structure of individuals who inject drugs and share injection equipment in Winnipeg, Canada may be scale free by using techniques previously used to identify the structure of sexual contact networks in Sweden, Britain, Zimbabwe and Burkina Faso.

In a series of three papers the scientific literature relating to scale-free networks from a variety of disciplines including physics, epidemiology, mathematics, biology and computer science was reviewed and integrated; the methods used to identify scale-free networks were tested and compared using data from two network studies (a pilot study and a main study) and potential new interventions that could be implemented to help reduce the transmission of HIV and HCV among individuals who inject drugs by the existing needle exchange program were recommended based on the results.

In the first manuscript, the capacity of research that identifies only individual risk factors and the effects of social relationships to predict or determine the spread of disease was discussed. In addition, the literature relating to the ability of standard epidemiological models to fully capture the heterogeneity of contact patterns in relation to the transmission of disease was reviewed.

This review suggested that a more recent approach used to determine the spread of disease involved the identification of the structure of a network. This approach, which emerged from the disciplines of physics and graph theory examines the frequency and distribution of contacts among members of a network. Three types of networks have been identified; 1) random networks; where links between individuals are created randomly but usually each individual has the same number of contacts; 2) regular networks, where links created between individuals follow precise rules, (i.e., each individual has exactly the same number of contacts) and; 3) small-world networks, where links are created through a combination of randomness and rules.[1] More recently, some small world networks have been found to be scale-free.[2] Individuals in a scale-free network do not have a typical or average number of contacts. Rather, the majority of individuals have a small number of contacts while a small number of individuals have a large number of contacts.[1, 3-7]

Three studies examining the structure of sexual contact patterns revealed that the distribution of sexual contacts was scale-free in a wide range of populations.[3, 5, 7]

This finding has important epidemiological implications. It has been shown that spread of disease in a scale-free network significantly deviates from that of a random network, where infection spreads to the whole network only if the spreading rate exceeds a critical value or threshold.[8]. In a scale-free network there is no critical value or threshold.[9-11]

Scale-free networks are characterized by power law behaviour in the tail of the cumulative distribution, $P(x) = Cx^{-\alpha}$; the probability $P(x)$ that x has a value greater or equal to x and a value for the exponent of less than 3.[5, 7, 12] The value of the exponent assists in determining whether the network is scale-free. Two methods; ordinary least squares (OLS) and maximum likelihood estimation (MLE) have been used to generate the value for exponent. The method which produces the most accurate results has been debated in the literature. Previous work in this area reported that linear fits commonly used by researchers for fitting to a power law distribution contain a severe bias.[12-13] If a model is linear, the MLE & least squares estimators are the same. However, if a model is not linear, the variance of the ML estimator has the smallest variance compared to other estimators (i.e. least squares) and therefore is preferable.[12-13] However, studies in various disciplines have shown that both methods generate similar exponents regardless whether they used OLS or MLE.[14-15].

In addition, controversy remains regarding the ability of MLE to generate an accurate value for the exponent when the distributions being studied are finite. The absence of an epidemic threshold in a scale-free network is related to the infinite variance of the frequency of contacts in a scale-free network. However, the human population is finite and there is a limit to the number of sexual contacts an individual can have and a limit to the number of times an individual can share drug injecting equipment. It is has been shown that the variance in the frequency of sexual contacts is very high and through research presented in two of these papers, that the frequency of injection and therefore the frequency of sharing injection equipment among IDUs is very high, just like that of a scale-free network. Therefore, while an epidemic threshold may exist because there is a limit to the number of sexual contacts or number of times an individual can inject in a day or year, and because sexual contact and injection drug using populations are finite in size, it would be a great deal lower then that seen in a randomly mixed network.[4, 16]

The background paper (Chapter One) concluded that both standard epidemiological research and social network analysis have facilitated our understanding of the transmission of disease and the transmission of HIV and HCV among IDUs.

However, the impetus for this research was the continued spread of HIV and HCV among IDUs together with the fact that rates of injection equipment sharing have remained relatively unchanged since the mid-1990s which suggested that our interventions have been only partially effective. We hypothesized that perhaps processes beyond individual and social network factors such as the existence or non-existence of critical thresholds may play a role in the sustained spread of HIV and HCV among IDUs.

The second manuscript (Chapter Two) explored whether the methods used to identify the scale-free structure of sexual contact networks may be applied to networks of individuals who inject drugs. As controversy continued in the literature regarding which method generated the most accurate value for the exponent, both the OLS and MLE methods were used. Results from the pilot study using both methods indicated that the frequency of injection among a network of IDUs in Winnipeg, Canada may be scale-free. As frequency of injection is associated with sharing of drug injection equipment this finding provided a strong indication that networks of IDU through which infection is transmitted may also be scale-free. The upper 95% CI for the exponent generated by MLE falls into what has been called the epidemic transition region where an epidemic may or may not occur.[10] However, those epidemic threshold values were generated for a sexual contact network and may not be the same as for a network of IDUs who share drug injection equipment which carries a much higher probability of disease transmission. In reality, the prevalence of HIV infection among Winnipeg IDUs, based on two cross-sectional surveys, increased from 2.3% in 1986-90 to 12.6% in 1998, consistent with our analysis that the epidemic is continuing to spread.[17]

The sample size for the pilot study was inadequate for multivariate analysis however it was observed that individuals who inject very frequently (≥ 2,640 injections in one year) and are located in the tail end of the distribution were significantly more likely to be aboriginal; to have an income > $40,000; have been paid (money or drugs) by someone to help them inject drugs; have injected at an hotel in the past 12 months; and have at least one member in their network who injected daily. These results clearly indicated that identifying the network structure is possible by examining the distribution of the frequency of injection (therefore, the frequency of contacts). In addition, results indicated that interventions which focused on targeting the contact patterns of high frequency injectors could be implemented and may help to significantly reduce the spread of HIV and HCV among this network of IDUs.

In the final manuscript (Chapter Three), results from the pilot study were corroborated. An exponent of < 3 was generated using MLE with 95% CIs that were also < 3 indicating that the frequency of injection among individuals bingeing on injection drugs and consequently the injection sharing networks may be scale-free. Limitations to the methodology were discussed including the inability of the OLS method to fit a power model to the main study data and the limitations of MLE in its use for finite distributions such as this one.

The Winnipeg network studies were the best studies available at the time to analyze the structure of a network of individuals who inject drugs. Individual numbers for the frequency with which participant's shared injection equipment were not available for either study. Although identifying a variable that could potentially assess the network structure was challenging the outcome has resulted in the use of a variable that may in fact more completely capture the multiple methods of disease transmission among people who inject drugs and reduce the high cost and complex data collection associated with collecting network data.

Frequency of injection and frequency of injection during binge drug use has been associated with sharing of drug injection equipment among IDUs and an increased risk of HIV and HCV infection in previous studies.[18-25] Therefore, the distribution of the frequency of injection over 1 year (pilot study) and during binge drug use (main study) over a 6 month period was examined in order to determine if the drug injection equipment sharing networks may be scale-free.

There was a statistically weak correlation (0.15) between frequency of injection and sharing needles in the main study. This correlation suggests that using frequency of injection as a proxy for frequency of sharing injection equipment may at first appear to be a serious limitation to generating an accurate estimate of the exponent which assists in determining whether the network may be scale-free. However, in reality, frequency of injection may in fact more accurately reflect the nature of contact patterns among IDUs. Individuals who inject drugs may be more likely to truthfully describe the frequency with which they inject compared to describing how often they share needles or other drug injection equipment.

After receiving 20 years of prevention messages in relation to the risks of disease transmission when sharing injection equipment, IDUs may be less comfortable admitting to sharing then to reporting the frequency with which they inject. Results from the main

study found that more than 70% of participants were aware of the risks of transmitting HIV and HCV when sharing drug injection equipment.

In addition, the correlation coefficient is simply a number between 0 and 1 and does not lend itself to commonsense interpretation.[26] Increased frequency of injection is accepted in the field of HIV and substance use as related to increased sharing of drug injection equipment. Therefore this variable has content validity as it would be accepted by experts in the field as representative of the frequency of sharing drug injection equipment.

Furthermore, frequency of injection is more likely to capture the potentially multiple routes of disease transmission beyond just the sharing of needles such as the sharing of spoons, cookers, filters, water or using equipment picked up off of coffee tables, the street or out of biohazard containers without knowing if it had previously been used by someone else. For example, high frequency injectors may in fact not share needles but share cookers, filters, water or may just pick up a cooker without knowing if it has been used by someone else. In this study more people reported sharing other injection equipment (43%) than needles (22%) (p = <0.001). Sharing other injection equipment has been shown to be a significant factor in the transmission of HIV and HCV among people who inject drugs.

It is also important to be aware that NEPs currently distribute a small proportion of the sterile needles required. It has been projected that approximately 1,000 needles are required per IDU per year. In Ontario, it is estimated that 53 needles are distributed per injector per year. In Montreal and in Ottawa it is estimated that NEPs distribute approximately 5% of the needles required by IDUs.[27] In Ontario, 100% coverage has yet to be achieved and a wide variation in distribution levels exists. For instance, in 2002 NEPs reported that they distributed between 1 and 474 needles per IDU per year.[27] These estimates are supported by results from the main study where participants in the tail-end of the distribution (high frequency injectors) were significantly more likely to be certain they could not use a clean needle every time they injected (p = 0.013) and to have used a needle previously used by someone else in the past 6 months (p = 0.002) compared to those not in the tail–end of the distribution.

High frequency injectors are more likely to be placed in a position where they need to share or use injection equipment previously used by someone else. Frequent injection patterns decrease the chance that an individual will have sterile or unused equipment for every injection episode.[24-25] Given that 1) sharing needles does not

capture the sharing of all drug injection equipment; 2) frequency of sharing may be underreported; 3) frequency of injection is accepted as related to frequency of sharing in the HIV and substance use field and 4) most NEPs do not distribute an adequate supply of needles it is quite probable that frequency of injection is in reality the variable which better reflects the actual structure or contact patterns of injection drug user's networks.

The estimate of the exponent using frequency of injection is less than 3 in both studies indicating that the structure of the injection equipment sharing networks may be scale-free. In addition, both studies showed there was a large variation in the frequency of injection and a small proportion of people who are very high frequency injectors. High frequency injectors are more likely to share or use previously used injection equipment. 24-25 These results indicate that interventions that target high frequency injectors (people located in the tail-end of the distribution) may be more successful in reducing the transmission of HIV and HCV among people who inject drugs in Winnipeg, Canada compared to interventions that target all injection drug users equally.

Another limitation that could be put forward relates to the disease propagation model which is based on an undirected network. For example, sexual networks are undirected (doesn't matter who is infected, the disease can be transmitted). It could be argued that sharing injection equipment must be inherently directional (only the person who borrows the injection equipment can be infected). This argument may seem at first glance to make intuitive sense however; the true nature of sharing drug injection equipment is more complex. Many scenarios may in fact take place during drug injection episodes. Some people may share with multiple partners, some may share with only one partner and are not aware that the person they share with also shares with others, some people may inject in large groups where needles and other injection equipment are left on a table for all to use, some people may never share needles but always share cookers, spoons, water or filters, some people may use or buy other people's washes (filters or syringes that still contain small amounts of a drug) and some people may take previously used needles from an open biohazard container or pick up a needle, spoon, filter or water without knowing if it had been previously used by someone else. The large variation in how drug injection equipment may be "shared" suggests that it would be sensible to assume that drug injection equipment networks are non-directional in order to capture the large disparity in how injection equipment may be shared.

Despite these limitations, this exciting new approach has shown that identifying the network structure may be possible by examining the distribution of the frequency of

injection (therefore, probably, the frequency of contacts). These results are the first using interdisciplinary methods from epidemiology and statistical physics applied directly to a population in which HIV and HCV is spreading rather than to the general population.

Future research could include collecting data for both frequency of injection and frequency of sharing injection equipment and then comparing results for the generated exponents. If comparable, the ability to use frequency of injection to identify network structure would reduce the amount of data required to asses the structure of a network. This would reduce costs and the length of the questionnaire. As a result smaller NEPs would be more likely to be able to afford to collect the data needed to assess local network structure and then tailor their interventions based on the results. In addition, testing different generative mechanisms that generate power laws such as the Barabási and Albert (BA), Yule, Reed-Hughes or Copy model against empirical data is an essential next step to validate the existence of scale-free networks among IDUs.

Results from the multivariate analysis revealed the potential for existing NEP program staff to identify high frequency injectors or those located in the tail end of the distribution. High frequency injectors in Winnipeg, Canada were significantly more likely to have injected cocaine, Talwin & Ritalin (T&Rs) and to have obtained their needles from a dealer. These results have yielded additional interventions that could be introduced by the NEP to help reduce the transmission of HIV and HCV among this network of individuals who inject drugs in Winnipeg, Canada.

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Appendix 1

Ethical Approval

The study design was approved by the Health Research Ethics Board of the University of Manitoba and the Winnipeg Regional Health Authority Research Review Committee. The analysis specific to this paper was also approved by the Ottawa Hospital Research Ethics Board.

THE UNIVERSITY OF MANITOBA

BANNATYNE CAMPUS
Research Ethics Boards

A112 - 753 McDermot Avenue
Winnipeg, Manitoba
Canada R3E 0W3

Tel: (204) 789-3255
Fax: (204) 789-3942

APPROVAL FORM

Principal Investigator: **Dr. J. Wylie**

Protocol Reference Number: H2000:065
Date: July 17, 2000

Protocol Title: **Social Networks of Injection Drug Users**

The following are approved for use:

- **Protocol**
- **Questionnaire and Interview guide**
- **Informed Consent Form for Questionnaires and Hepatitis C Typing dated 00-07-12**
- **Informed Consent Form for Interviews 00-07-12**
- **Informed Consent Form for Key Informants dated 00-07-12**
- **Informed Consent Form for Focus Group dated 00-07-12**

The above was approved by Dr. A. Katz, Chair, Health Research Ethics Board, Bannatyne Campus, University of Manitoba on behalf of the committee per your letter dated July 12, 2000. The Research Ethics Board is organized and operates according to Health Canada/ICH Good Clinical Practices, Tri-Council Policy Statement, and the applicable laws and regulations of Manitoba.

This approval is valid for one year only. A study status report must be submitted annually and must accompany your request for reapproval. Any significant changes of the protocol and informed consent form should be reported to the Chair for consideration in advance of implementation of such changes. The REB must be notified regarding discontinuation or study closure.

This approval is for the ethics of human use only. For the logistics of performing the study, approval should be sought from the relevant institution, if required.

Sincerely yours,

Alan Katz, MB., Ch.B., MSc., CCFP, FCFP.
Chair,
Health Research Ethics Board
Bannatyne Campus

Please quote the above protocol reference number on all correspondence.
Inquiries should be directed to the REB Secretary
Telephone: (204) 789-3255 / Fax: (204)789-3942

UNIVERSITY
of MANITOBA

BANNATYNE CAMPUS
Research Ethics Boards

[illegible] Bannatyne Avenue
Winnipeg, Manitoba
Canada R3E 0W3
Tel: (204) 789-3255
Fax: (204) 789-3414

APPROVAL FORM

Principal Investigator: Dr. John Wylie
Sponsor: CIHR

Protocol Reference Number: H2003:016
Date: March 19, 2003

Protocol Title: **"Networks and infectious disease: social and molecular factors affecting transmission of hepatitis C and HIV among injection drug users"**

The following is/are approved for use:

- **Protocol submitted February 3, 2003**
- **Questionnaire submitted February 3, 2003**
- **Informed Consent Form (dated 03/03/12)**
- **Revised Ad submitted March 19, 2003**

The above was approved by Dr. K. Brown, MD, MBA, Chair, Health Research Ethics Board, Bannatyne Campus, University of Manitoba on behalf of the committee per your letter dated March 12, 2003 and facsimile dated March 19, 2003. The Research Ethics Board is organized and operates according to Health Canada/ICH Good Clinical Practices, Tri-Council Policy Statement, and the applicable laws and regulations of Manitoba. The membership of this Research Ethics Board complies with the membership requirements for Research Ethics Boards defined in Division 5 of the *Food and Drug Regulations*.

This approval is valid for one year only. A study status report must be submitted annually and must accompany your request for re-approval. Any significant changes of the protocol and informed consent form should be reported to the Chair for consideration in advance of implementation of such changes. The REB must be notified regarding discontinuation or study closure.

This approval is for the ethics of human use only. For the logistics of performing the study, approval should be sought from the relevant institution, if required

Sincerely yours,

Kefi Brown, MD, MBA
Chair, Health Research Ethics Board
Bannatyne Campus

Please quote the above protocol reference number on all correspondence.
Inquiries should be directed to the REB Secretary
Telephone: (204) 789-3255/ Fax: (204) 789-3414

The Ottawa Hospital | L'Hôpital d'Ottawa

Research Ethics Board
Conseil d'éthique en recherches
798-5555 ext 14146, 14902 or 15072
Fax No. - 761-4311
http://www.ohri.ca/ohreb/

Friday, September 23, 2005

Ms. Linda Pelude
University of Ottawa
Epidemiology and Community Medicine
451 Smyth Road
Ottawa, ON
K1H 8M5

Dear Ms. Pelude:

Re: Protocol # 2005587-01H **Injection Drug Users' Injection Equipment Sharing Networks: Random or Scale-Free?**

Protocol approval valid until - Friday, September 22, 2006

Thank you for your letter dated September 12, 2005. I am pleased to inform you that your study (listed above) and the Thesis Proposal were given expedited review by the Ottawa Hospital Research Ethics Board (OHREB) and are approved. No changes, amendments or addenda may be made in the protocol without the OHREB review and approval.

Approximately two months prior to the expiration date listed above, a single renewal form should be sent to the OHREB office.

The Tri-Council Policy Statement requires a greater involvement of the OHREB in studies over the course of their execution. You must inform the Board of adverse events encountered during the study, here or elsewhere, or of significant new information which becomes available after the Board review, either of which may impinge on the ethics of continuing the study. The OHREB will review the new information to determine if the protocol should be modified, discontinued, or should continue as originally approved.

Yours sincerely,

Raphael Saginur, M.D.
Chairman
Ottawa Hospital Research Ethics Board

/cb

Appendix 2

Questionnaires

The questionnaires used in network analysis are lengthy by nature of the information required relating to contact networks.

Both the pilot and main study questionnaires have been modified for inclusion to this appendix. Questions relevant to these analyses have been included.

The pilot study questionnaire is first, followed by the main study questionnaire.

Egocentric questionnaire (Pilot study 2001)

A. **DEMOGRAPHICS:**

Read: "The first set of questions are general questions about yourself".

Inquire as to whether the person knows if they are HCV positive and record on answer sheet.

A1. What is your date of birth? (dd/mm/yyyy).

A2. What gender do you identify yourself as? (Only ask about gender if necessary to clarify):

A. Male
B. Female
C. Biologically female but transgender
D. Biologically male, but transgender
E. Refused to answer

A4. What is the highest level of education you have completed?

A. Primary school (to grade 6)
B. Secondary school (to grade 9)
C. Secondary school (to grade 12)
D. Trade school
E. University
F. College
G. Other
H. Unsure
I. Refused to answer

A5. Over the last year how did you get money to live on (check all sources and identify main one)?

A. social welfare
B. employment insurance
C. occasional work(small contracts every now and then)
D. regular work(part or full time)
E. money from my family
F. money from friends
G. prostitution
H. stealing
I. dealing or doing drug runs
J. panhandling
K. money from a social worker
L. squeegee
M. other (specify)
N. Unsure
O. Refused to answer

A6. Over the last year what was your average annual income?

A. < $5000
B. $5000-10000
C. $10000-20000
D. $20000-30000
E. $30000-40000
F. $40000-50000
G. $50000
H. Unsure
I. Refused to answer

A7. What ethnic group or family background do you most identify yourself with:
Do not read choices

A. Caucasian/White
B. Chinese
C. Filipino
D. South-Asian (e.g. Indian, Pakistani)
E. Other Asian (e.g. Vietnamese, Japanese)
F. Latin American, specify country
G. Middle Eastern, specify:
H. Black-African
I. Black-Caribbean
J. Other black, specify
K. First Nations (treaty)
L. First Nations (non-treaty)
M. Metis
N. Inuit
O. Other, specify
P. Unsure
Q. Refused to answer

A8. What type of residence do you currently live in?

A. Empty House
B. Hostel/Shelter
C. Hotel
D. At family member's house or apartment
E. At your own house or apartment
F. At a friend's house house or apartment
G. Shooting gallery
H. Rooming/ boarding house
I. Recovery house/treatment centre
J. On the street
K. Vehicle (trailer, van, car)
L. Other (specify)
M. Unsure
N. Refused to answer

B. INDIVIDUAL DRUG BEHAVIOURS

Read: "Now I would like to ask you about your drug use. All of the answers that you give me are confidential".

B1. The first time you fixed (injected/shot up), how old were you?

A. Record answer in years.
B. Unsure **Probe: "About how old were you?"**
C. Refused to answer

B2. Have you ever sold drugs?

A. Yes B. No C. Unsure D. Refused

B3. Have you ever sold syringes?

A. Yes B. No C. Unsure D. Refused

B4. Have you ever given syringes to someone else?

1. Yes 2. No 3. Unsure 4. Refused

B5. Have you ever been paid (money or in kind) by someone to help them inject drugs?

A. Yes B. No C. Unsure D. Refused

B6. Have you ever bought drugs for someone else?

A. Yes B. No C. Unsure D. Refused

B7. In the past year, which of the following drugs have you used without injecting?

A. Alcohol
B. Acid
C. Painkillers (e.g. dilaudid)
D. Amphetamines
E. Barbiturates
F. Cocaine
G. Crack
H. Demerol/morphine/opium
I. Downers/tranquilizers
J. Ecstasy
K. Gasoline/solvents
L. Marijuana
M. PCP/Angel dust
N. T3's
O. None
P. Other (specify)
Q. Unsure
R. Refused to answer

B9. What drug do you most frequently inject?

A. Heroin and cocaine (speedball)
B. Talwin and Ritalin (speedball)
C. Heroin mixed with another drug
D. Cocaine (uptown)
E. Amphetamines (speed, uppers)
F. Methadone
G. Heroin (dust,horse, junk, smack, downtown)
H. Other (specify)
I. Unsure
J. Refused to answer

B10. When was the last time you injected any drug?

A. In the past week
B. In the past month
C. In the past 6 months
D. More than 6 months ago (specify a time)
E. Unsure
F. Refused to answer

B11. If B10 = A or B; How many <u>days</u> in the past month did you shoot up?
If B10 = C or D; How many <u>days</u> in the past year did you shoot up?
Enter answer as number of days or; **A.** unsure
B refused to answer.

B12. If B10 = A or B; How many <u>times</u> in the past month did you shoot up?
If B10 = C or D; How many <u>times</u> in the past year did you shoot up?
Enter answer as number of times or; **A.** unsure
B refused to answer.

B13. Over the last year what type of places have you injected drugs? Indicate which location was the most recent injection site. (**Ask the individual to provide postal code, nearest intersection, neighborhood, or block for each category. Their most recent injection at that location could be used as a frame of reference if they have shot up multiple times at different locations for the various categories**).

A. Empty House
B. Hostel/Shelter
C. Hotel
D. At your own house or apartment
E. At a friend's house or apartment
F. Shooting gallery
G. Rooming/ boarding house
H. Detention centre/youth camp
I. On the street
J. Vehicle (trailer, van, car)
K. Jail or prison
L. Other
M. Unsure
N. Refused to answer

B14. Have you ever used a needle that someone else has already used or may have already used?

A. Yes
B. No
C. Unsure (**Probe**: ever get a rig mixed up?)
D. Refused

If B14 is No, go to B18.
If B14 is yes, go to question B15.

B15. When was the last time you fixed (injected/shot up) with a needle (rig) that had already been used by someone else (or might have been used by someone else)?

A. Less than 1 week ago
B. Between 1 week and 1 month ago
C. Between 1 month and 6 months ago
D. Between 6 months and 1 year ago
E. Over 1 year ago
F. Refused
G. Unsure

B16. How frequently would you say that you fix with a needle that someone else has already used:

A. Rarely
B. Some of the time
C. Most of the time
D. All of the time
E. Used to fix with used needles, but now always use a clean needle

B18. Have you ever used a cooker, rinse water, or cotton that someone else has already used, or may have already used?
A. Yes
B. No
C. Refused
D. Unsure

SOCIAL NETWORKS (Pilot study)

1.) Network members: We are interested in the relationship between close personal contact and infectious diseases that are transmissible through used syringes, like hepatitis. We would like to ask you some questions about the people you normally associate with. We will not ask you for any information that could be used to identify those individuals and any information you provide to us will be confidential.

First, please think back over the last 30 days about the people with whom you have had more than casual contact. These would be people that you have seen or have spoken to on a regular basis. Most of these close contacts would be people such as friends, family, sex partners, people you inject drugs with, or people you live with. Lets make a list of these people.

Interviewer: use the following prompts as needed, to help clients recall their associates.

People that you used drugs with in the last 30 days.
People who you had sex with during the last 30 days.
For subjects who are sex workers: list a maximum of 10 sex partners. If the name of a client is not known, they can be listed as unknown1, unknown2, etc. If they have a regular sex partner(s) try to ensure that they are included on the list)
Friends, relatives or other individuals that you feel close to?
People you live with.
People you hang out with.

2.) Type of contact: Once names are listed, please ask the participant the following questions and circle the letter by a name for the specific type of interaction the participant has with the network member. Each network member can have more than one letter circled.

1. Please tell me which of the individuals on the list injects drugs or has injected drugs in the past?
2. Which of these individuals are people that you have had sex with?
3. Which of these people could you go to if you needed advice on a personal problem or if you needed to request a favor such as helping you move or lending you money?

3.) Interaction of network members: Transfer the names of the network members to the interaction circle. For each person listed ask the subject to indicate which of the other individuals on the list that particular person knows.

4.) Choose members: Now transfer up to 10 names to the answer guide. Enter them in the order that they appear on the network member list.

D) Network questions re each contact:
Now I will ask you some questions about the contacts that we have listed on the sheet. Please answer each question to the best of your knowledge.

Interviewer: record the answers on the answer sheet.

C. Contact information

C1. What sex is [person]?

A. Male
B. Female
C. Transgender, male
D. Transgender, female
E. Unsure
F. Refused to answer

C2. To the best of your knowledge, how old is [person] (enter as years)?

C3. What ethnic group would you identify [person] as?

Do not read choices

A. Caucasian/White
B. Chinese
C. Filipino
D. South-Asian (e.g. Indian, Pakistani)
E. Other Asian (e.g. Vietnamese, Japanese)
F. Latin American, specify country
G. Middle Eastern, specify:
H. Black-African
I. Black-Caribbean
J. Other black, specify
K. First Nations (Treaty)
L. Aboriginal (non-treaty)
M. Aboriginal (treaty status unknown)
N. Metis
O. Inuit
P. Other, specify
Q. Unsure
R. Refused to answer

C4. What is [person]'s relationship to you?

A. Mother
B. Father
C. Brother
D. Sister
E. Ex-lover
F. Spouse
G. Girl/Boyfriend (lover)
H. Ex-spouse
I. Son
J. Daughter
K. Cousin
L. In-laws
M. Niece, Nephew
N. Uncle
O. Aunt
P. Other relative
Q. Friend
R. Acquaintance
S. Injection buddy
T. Stranger
U. Dealer
V. Trick
W. Other
X. Unsure
Y. Refused to answer

C6. How frequently would you say you have contact with this person?

A. Daily
B. Once a week
C. 1-2 times per month
D. Less than once per month
E. Unsure
F. Refused to answer

E. Contact injection drug risk (ask these questions for those contacts listed as IDU)

E4. Have you ever injected drugs with [person]?
A. Yes B. No C. Unsure D. Refused

If yes, go to question E5. If No, go to question E9.

E6. Have you ever injected with a syringe after this person injected with it first?
A. Yes B. No C. Unsure D. Refused

E7. When did you first begin injecting drugs with [person]? (Record as date or time span)

E8. When did you last inject drugs with this person

E9. Has [person] ever fixed with a needle after someone else had already used it?
A. Yes B. No C. Unsure D. Refused

Individual and egocentric questions (Main study 2004)

DEMOGRAPHICS:

Read: "The first set of questions is general questions about yourself".

DEM1. What is your date of birth? (yyyy/mm/dd)

DEM2. What gender do you identify yourself as? *(Interviewer: Only ask about gender if necessary to clarify)*
0 Male
1 Female
2 Transgender female
3 Transgender male
55 Unsure
66 Not applicable
99 Refused to answer

DEM3. Were you born in Canada?
0 No
1 Yes
55 Unsure
66 Not applicable
99 Refused to answer

DEM6. What is the highest level of education you have completed?
0 Graduated grade 12
1 In grade school now (grade _____)
2 Dropped out before grade 12 (grade_____)
3 Trade school
4 University
5 College
6 Other, (specify_____)
55 Unsure
66 Not applicable
99 Refused to answer

DEM7. Over the last year what was the main way you got money to live on? ***(circle only one)***
0 Regular work (full, part time or contract)
1 Welfare, EI, pension or other government support
2 Money from family/friends
3 Sex trade/prostitution
4 Dealing or doing drug runs
5 Panhandling
6 Stealing
7 Boosting
8 Other, (specify_____)
55 Unsure
66 Not applicable
99 Refused to answer

DEM9. What ethnic group or family background do you most identify yourself with:
Do not read choices
0 Caucasian/White
1 Chinese
2 Filipino
3 South-Asian (e.g. Indian, Pakistani)
4 other Asian (e.g. Vietnamese, Japanese)
5 Latin American
6 Middle Eastern
7 Black-African
8 Black-Caribbean
9 Other black
10 First Nations (treaty)
11 First Nations (non-treaty)
12 Metis
13 Inuit
14 Other, (specify_____)
55 Unsure
66 Not applicable
99 Refused to answer

DEM10. What type of residence do you currently live in?
0 At your own house or apartment
1 At family member's house or apartment
2 At a friend's house or apartment
3 Empty House
4 Hostel/Shelter
5 Hotel
6 Shooting gallery
7 Rooming/ boarding house
8 Recovery house/treatment centre
9 On the street
10 Vehicle (trailer, van, car)
11 Detention centre/ Youth camp
12 Jail or prison
13 Other, (specify_____)
55 Unsure
66 Not applicable
99 Refused to answer

DEM11. Including your current residence, how many different places have you lived in the past year?

INDIVIDUAL DRUG BEHAVIOURS

Read: "Now I would like to ask you about your drug use. All of the answers that you give me are confidential".

ED1. The first time you fixed (injected/shot up), how old were you?

ED2. In the past 6 months, which of the following drugs have you used without injecting? ***(circle all that apply)***

0 Alcohol
1 Acid
2 Painkillers (e.g. dilaudid)
3 Amphetamines
4 Barbiturates
5 Cocaine
6 Crack
7 Demerol/morphine/opium
8 Downers/tranquilizers
9 Ecstasy
10 Gasoline/solvents
11 Marijuana
12 PCP/Angel dust
13 Tylenol 3
14 Heroin
15 Mushrooms
16 Ruffies (Rohypnol)
17 GHB (gamma-hydroxybutyrate)
18 Methadone prescribed
19 Methadone unprescribed
20 None
21 Other, (specify_____)
55 Unsure
66 Not applicable
99 Refused to answer

ED4. What drug do you most frequently inject? ***(circle only one)***

0 Cocaine (uptown)
1 Talwin and ritalin (speedball)
2 Morphine
3 Heroin (horse, junk, smack, downtown)
4 Heroin and cocaine (speedball)
5 Heroin mixed with another drug
6 Amphetamines (speed, uppers)
7 Methadone
8 Crack/rock cocaine
9 Methamphetamine (crystal meth)
10 PCP (angel dust)
11 Dilaudid
12 Barbiturates (downers)
13 Ritalin alone
14 Other, (specify_____)
55 Unsure

66 Not applicable
99 Refused to answer

ED5.Which drugs have you injected in the last 6 months? ***(circle all that apply)***
0 Cocaine (uptown)
1 Talwin and Ritalin (speedball)
2 Morphine
3 Heroin (horse, junk, smack, downtown)
4 Heroin and cocaine (speedball)
5 Heroin mixed with another drug
6 Amphetamines (speed, uppers)
7 Methadone
8 Crack/rock cocaine
9 Methamphetamine (crystal meth)
10 PCP (angel dust)
11 Dilaudid
12 Barbiturates (downers)
13 Ritalin alone
14 Other, (specify_____)
55 Unsure
66 Not applicable
99 Refused to answer

ED6. In the past month, how often did you inject (shoot up)?
0 Not at all
1 Once in a while, not every week
2 Regularly, once or twice a week
3 Regularly, three or more times a week
4 Every day
55 Unsure
66 Not applicable
99 Refused to answer

ED7. Over the past 6 months, what types of places have you injected drugs? ***(circle all that apply)***
0 At your own house or apartment
1 At family member's house or apartment
2 At a friend's house or apartment
3 Empty House
4 Hostel/Shelter
5 Hotel
6 Shooting gallery
7 Rooming/ boarding house
8 Recovery house/treatment centre
9 On the street
10 Vehicle (trailer, van, car)
11 Detention centre/ Youth camp
12 Jail or prison
13 Other, (specify_____)
55 Unsure

66 Not applicable
99 Refused to answer

Individual Drug Behaviours (Continued)

ED8. How many different hotels have you injected at in the past 6 months?

ED9. Over the past 6 months, on how many different days did you inject at each of these hotels **(to a maximum of 6 hotels - if more than 6 ask the person to think about the hotels at which they most frequently inject)**

ED10. Over the past 6 months, what type of place did you inject at most frequently?***(circle only one)***
0 At your own house or apartment
1 At family member's house or apartment
2 At a friend's house or apartment
3 Empty House
4 Hostel/Shelter
5 Hotel
6 Shooting gallery
7 Rooming/ boarding house
8 Recovery house/treatment centre
9 On the street
10 Vehicle (trailer, van, car)
11 Detention centre/ Youth camp
12 Jail or prison
13 Other, (specify_____)
55 Unsure
66 Not applicable
99 Refused to answer

ED12. In the past 6 months, how often have you given away one of your used needles to someone who needed it to inject drugs?
0 Never
1 Occasionally
2 Sometimes
3 Usually
4 Always
55 Unsure
66 Not applicable
99 Refused to answer

ED13. In the past 6 months, how often have you used someone else's cooker, rinse water, or cotton that someone else has already used, or may have already used?
0 Never
1 Occasionally
2 Sometimes
3 Usually
4 Always
55 Unsure

66 Not applicable
99 Refused to answer

ED14. In the past 6 months, how often did you inject drugs after someone transferred (frontloading, backloading, or piggybacking) drugs into your syringe from their syringe?
0 Never
1 Occasionally
2 Sometimes
3 Usually
4 Always
55 Unsure
66 Not applicable
99 Refused to answer

ED15. In the past 6 months, how often have you used a needle that someone else has already used or may have already used?
0 Never
1 Occasionally
2 Sometimes
3 Usually
4 Always
55 Unsure
66 Not applicable
99 Refused to answer
If "never", go to ED19

ED16. In the last **6 MONTHS**, have you used a needle that had been previously used by someone you suspected or knew was HIV (AIDS virus) and/or HCV (hepatitis C) positive?
0 No
1 Yes
55 Unsure
66 Not applicable
99 Refused to answer

ED19. Do you think that you can be infected with hepatitis C by injecting drugs after someone has squirted drugs into your syringe from a syringe that they already injected with?
0 No
1 Yes
55 Unsure
66 Not applicable
99 Refused to answer

ED20. Do you think that you can be infected with HIV by injecting drugs after someone has squirted drugs into your syringe from a syringe that they had already injected with?
0 No
1 Yes
55 Unsure
66 Not applicable
99 Refused to answer

ED21. Do you think that you can be infected with hepatitis C by using someone else's cooker, rinse water, or cotton?
0 No
1 Yes
55 Unsure
66 Not applicable
99Refused to answer

ED22. Do you think that you can be infected with HIV by using someone else's cooker, rinse water, or cotton?
0 No
1 Yes
55Unsure
66 Not applicable
99Refused to answer

ED27. In the past 6 months, how many times have you injected someone else with drugs as a service in return for drugs, money or other goods?
0 time
1 time
2-4 times
5-9 times
10-24 times
25-49 times
50-99 times
100 times or more
55 Unsure
66 Not applicable
99 Refused to answer

ED28. In the past 6 months, how many time have you injected someone else with drugs as a favour to help them out (i.e. you weren't expecting anything in return)?
0 time
1 time
2-4 times
5-9 times
10-24 times
25-49 times
50-99 times
100 times or more
55 Unsure
66 Not applicable
99 Refused to answer

NEEDLE SOURCES

NS1. In the last 6 months, have you exchanged needles or gotten new needles at a needle exchange?

0 No
1 Yes
55 Unsure
66 Not applicable
99 Refused to answer

NS4. In the last 6 months, where did you get your new needles from.? (***Circle all that apply)***

0 Nurse/doctor/hospital
1 Pharmacy/drugstore
2 Street Connections
3 Other needle exchanges, (specify_____)
4 Someone on the street
5 Dealer
6 Shooting Gallery Owner
7 Friends/partners/family
8 Found on the street
55 Unsure
66 Not Applicable (don't ever use new syringes)
99 Refused to answer

NS6. In the last 6 months how easy was it for you to obtain a brand new needle/syringe when you needed one?

0 Very easy
1 Somewhat easy
2 Somewhat difficult
3 Very difficult
55 Unsure
66 Not applicable
99 Refused to answer

BINGES

Read: Binges are "when you fixed more often than your usual drug use for a short period of time
and then you went cold or back to usual use"

BN1 Over the last 6 months, did you go on runs or binges of injection drugs?
If No go to SIS1, otherwise BN2

0 No
1 Yes
55 Unsure
66 Not applicable
99 Refused to answer

BN2 How often did you binge over the last **6 months**?

0 At least once a week
1 Every couple of weeks
2 About once a month (about 6 times)
3 Once every 2-3 months (about 2-3 times)
4 Once every 3-6 months (about 1-2 times)
5 Less than once every 6 months
6 Never
55 Unsure
66 Not applicable
99 Refused to answer

BN3 In the last **6 months**, on average, how long were your binges/drug runs (of injection drugs)?

# of days: _____

# of injections per day: _____

Total/binge (#days x # injections per day): _____

What injection drug(s) do you normally binge on? ***(list in order of most frequent)***

SMOKING, INHALING OR SNORTING DRUGS

SIS1. Have you smoked, inhaled or snorted any drugs in the last 6 months?
If No, go to SEB1 (page 10), otherwise SIS2
0 No
1 Yes
55 Unsure
66 Not applicable
99 Refused to answer

SIS2. What drugs have you smoked/inhaled/snorted? ***(circle all that apply)***
0 Acid
1 Barbiturates
2 Cocaine (uptown)
3 Crack/rock cocaine
4 Demerol/morphine/opium
5 Downers/tranquilizers
6 Ecstasy
7 Gasoline/solvents
8 Marijuana
9 PCP/Angel dust
10 Tylenol 3
11 Ruffies (Rohypnol)
12 GHB (gamma-hydroxybutyrate)
13 Methadone prescribed
14 Methadone unprescribed
15 Talwin and Ritalin (speedball)

16 Morphine
17 Heroin (horse, junk, smack, downtown)
18 Heroin and cocaine (speedball)
19 Heroin mixed with another drug
20 Amphetamines (speed, uppers)
21 Methamphetamine (crystal meth)
22 Dilaudid
23 Ritalin alone
24 Other, (specify_____)
55 Unsure
66 Not applicable
99 Refused to answer

HEALTH AND SUPPORT
Social support

SS1. Are there people who would loan you $50 if you needed it?
0 No
1 Yes
55 Unsure
66 Not applicable
99 Refused to answer

HEALTH AND SUPPORT
Social diversity

Read: In the past two weeks have you spoken in person or on the phone with:
SD1. A spouse (girl/boyfriend)
0 No
1 Yes
55 Unsure
66 Not applicable
99 Refused to answer

HEALTH AND SUPPORT
Drug dependency

DD1. Do you think your use of injection drugs is out of control?
0 Never/almost never
1 Sometimes
2 Often
3 Always/nearly always
55 Unsure
66 Not applicable
99 Refused to answer

DD2. Does the prospect of missing a fix make you anxious or worried?
0 Never/almost never
1 Sometimes
2 Often
3 Always/nearly always
55 Unsure
66 Not applicable
99 Refused to answer

DD3. Do you worry about your use of injection drugs?
0 Never/almost never
1 Sometimes
2 Often
3 Always/nearly always
55 Unsure
66 Not applicable
99 Refused to answer

DD4. Do you wish you could stop?
0 Never/almost never
1 Sometimes
2 Often
3 Always/nearly always
55 Unsure
66 Not applicable
99 Refused to answer

DD5. How difficult do you find it to go without using injection drugs?
0 Not difficult
1 Quite difficult
2 Very difficult
3 Impossible
55 Unsure
66 Not applicable
99 Refused to answer

HEALTH AND SUPPORT

Depression

DEP1. Have you recently been feeling unhappy and depressed?
0 Not at all
1 No more than usual
2 More than usual
3 Much more than usual
55 Unsure
66 Not applicable
99 Refused to answer

Extraversion
Read: How would you describe yourself for the following list of common human characteristics. Using the first trait (adventurous) as an example, you can choose numbers from 1-9 with 1 being very unadventurous, 3 is moderately unadventurous, 7 is moderately adventurous, and 9 is very adventurous.

EV1. Unadventurous 1 2 3 4 5 6 7 8 9 Adventurous

HEALTH AND SUPPORT
Infection information for study participant

INF1. Have you ever been tested for hepatitis C? **If No, go to INF2, otherwise INF3.**
0 No
1 Yes
55 Unsure
66 Not applicable
99 Refused to answer

INF5. Have you ever been tested for HIV (AIDS virus)? **If No, go to INF 6, otherwise INF7.**
0 No
1 Yes
55 Unsure
66 Not applicable
99 Refused to answer

HEALTH AND SUPPORT
Overall group norms

GN1.How many of your close friends talk about harm reduction and safe injection?
0 None
1 Very little/few
2 Less than half
3 About half
4 More than half
5 Almost all
6 All
55 Unsure
66 Not applicable
99 Refused to answer.

SOCIAL NETWORKS

1) Network members:

Read: We are interested in the relationship between close personal contact and infectious diseases that are transmissible through used syringes, like hepatitis. We would like to ask you some questions about the people you normally associate with. We will not ask you for any information that could be used to identify those individuals and any information you provide to us will be confidential.

First, please think back over the last 30 days about the people with whom you have had more than casual contact. These would be people that you have seen or have spoken to on a regular basis. Most of these close contacts would be people such as friends, family, sex partners, people you inject drugs with, or people you live with.

Let's make a list of these people *(Interviewer - the maximum allowed on the list is 20 people. If the individual reaches 20 people ask them how many additional people they would be able to nominate and note their response on the answer sheet).* **Please use only initials, or some other identifier that will make sense to you such as a made up name. Please do not use their last names. We will use this list to make sure we know which individuals we are talking about. Remember that we are interested in people that you've had contact with in the last 30 days.**

Interviewer: use the following prompts as needed, to help clients recall their associates.
People that you used drugs with in the last 30 days.
People who you had sex with during the last 30 days.
For subjects who are sex workers: list a maximum of 10 sex partners. If the name of a client is not known they can be listed as unknown1, unknown2, etc. If they have a regular sex partner(s) try to ensure that they are included on the list)
Friends, relatives or other individuals that you feel close to?
People you live with.
People you hang out with.

2.) Type of contact: *Interviewer: Once names are listed, please ask the participant the questions listed below and circle the appropriate letter by each name on the following page.*

Questions to ask regarding each of the network members listed on the following page:

Which of these people has injected drugs in the last 6 months: Enter **Y** (Yes) or **N** (No) or **U** (Unsure)

Not including marijuana use, which of these people has smoked/snorted/inhaled drugs in the last 6 months: Enter **Y** (Yes) or **N** (No) or **U** (Unsure)

Which of these people has been a sex partner of yours in the last 6 months: Enter **Y** (Yes) or **N** (No)

What is the gender of each of these people? Enter **M** Male, **F** female, **TM** transgender male, **TF** transgender female.

What is the age of each of these people?

What is this person's relationship to you: Enter **F** (family member), **L** (lover, spouse, girl/boyfriend), **R** (Friend), **C** (Acquaintance/Stranger).

What is this person's ethnic group: Enter the appropriate letter response

A. Caucasian/White;
B. Chinese;
C. Filipino;
D. South-Asian
E. Other Asian
F. Latin American
G. Middle Eastern
H. Black-African
I. Black-Caribbean
J. Other black
K. First Nations (treaty)
L. First Nations (non-treaty)
M. Metis
N. Inuit
O. Other
P. Unsure
Q. Refused to answer

CONTACT INJECTION DRUG RISK

CDR1. To the best of your knowledge, in the past month, how often did [person] shoot up?

Network Member #

CDR2. To the best of your knowledge, what drug does [person] most frequently inject? ***(Check only one)***

Network Member #

CDR7. In the past 6 months, how often did you inject with [person]?

CDR8. Have you ever injected with a needle after [person] used it first?

CDR9. In the past 6 months, how often have you injected with a needle after [person] used it first?

CDR11. In the past 6 months, how often has [person] injected with a needle after you used it first?

Appendix 3

Bootstrapping program for maximum likelihood estimation of exponent.

Bootstrapping with Newman's MLE Method; Mathcad program from Liljeros, F., Stockholm University, Stockholm, Sweden, 2005.

This function uses Bootstrapping to estimate confidence intervals around the slope of a set of data generated from a power law distribution. The function takes three values:

INData (data): a vector of all data points (Data points from the tail end of distribution imported from SPSS: 100% of respondents injected at least 63 times during binge drug use; 70% at least 90 times, 62% at least 100 times and so on).

min: the minimum value of the tail end of the distribution = 63 injections

max: the maximum value for the tail end of the distribution = 1200 injections

p: the probability that the true value is within the 95% confidence interval

Output

The function generates a vector with three values. The first one is the estimate of the slope alpha (α). The second and third values are the upper and lower limits of the 95% confidence interval

Bootstrap (INData , min, max, p) :=

$r \leftarrow 0$

for $i \in 0..\text{rows}(\text{INData}) - 1$

This part removes input data that are smaller than the minimum value

if $\text{INData}_{i,0} \geq \text{min} \wedge \text{INData}_{i,0} \leq \text{max}$

$\text{Data}_{r,0} \leftarrow \text{INData}_{i,0}$

$r \leftarrow r + 1$

This part generates 10,000 estimates by using bootstrapping

for $i \in 0..9999$

for $j \in 0..\text{rows}(\text{Data}) - 1$

$\text{slask}_{j,0} \leftarrow \text{Data}_{\text{floor}(\text{rnd}(\text{rows}(\text{Data}))),0}$

$\text{estimates}_{i,0} \leftarrow 1 + \text{rows}(\text{Data}) \left(\sum \ln\left(\frac{\text{slask}}{\text{min}} \right) \right)^{-1}$

This part estimates the slope for the bootstrapped data.

$\text{estimates} \leftarrow \text{csort}(\text{estimates} , 0)$

This line sorts the 10,000 estimates in order

$$\begin{bmatrix} 1 + \text{rows}(\text{Data}) \left(\sum \ln\left(\frac{\text{Data}}{\text{min}} \right) \right)^{-1} \\ \text{estimates}_{\text{ceil}\left(\text{rows}(\text{estimates}) \cdot \frac{p}{2} \right)} \\ \text{estimates}_{\text{floor}\left[\text{rows}(\text{estimates}) \cdot \left(1 - \frac{p}{2} \right) \right]} \end{bmatrix}$$

This part estimates the slope for the original data

The last two lines select the upper and lower estimates for the 95%confidence interval

minx := 63

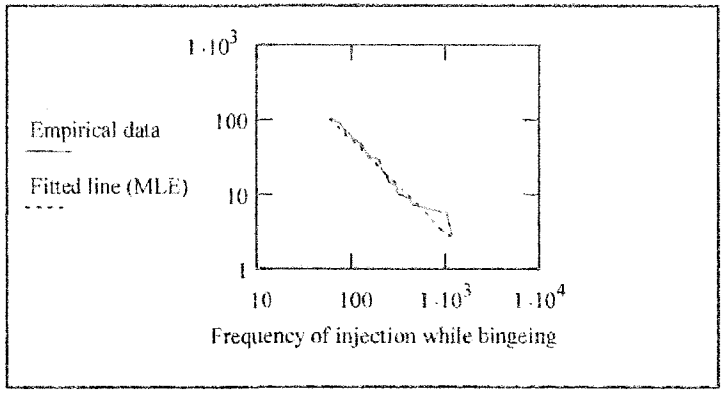
maxx := 1200

Estimates := Bootstrap (data , minx, maxx, 0.05)

$$\text{Estimates} = \begin{pmatrix} 2.261 \\ 2.042 \\ 2.567 \end{pmatrix}$$

$$\text{p\_estimate}(x) := \frac{100}{\text{minx}^{-\text{Estimates}_{0,0}+1}} \cdot x^{-\text{Estimates}_{0,0}+1}$$

This function makes it possible to fit the line to the observed data below



Appendix 4

Additional descriptive results for chapter 3, manuscript 3: Scale free networks among injection drug users in Winnipeg, Canada

Variable	N = 242 n (%)
Age groups	
15-19 yrs	13 (5.4)
20-24 yrs	29 (12.0)
25-29 yrs	27 (11.2)
30-34 yrs	37 (15.3)
35-40 yrs	49 (20.2)
41-44 yrs	49 (20.2)
45-49 yrs	23 (9.5)
≥ 50 yrs	15 (6.2)
Age ≥ 35 yrs	
No	106 (43.8)
Yes	136 (56.2)
Age ≥ 25 yrs	
No	42 (17.4)
Yes	200 (82.6)
Current housing	
Own house/apt	117 (48.3)
Family members house/apt	30 (12.4)
Friend's house/apt	27 (11.2)
Shelter/Rooming house/Treatment Centre	27 (11.2)
Hotel	25 (10.3)
On the street/vehicle	16 (6.6)
HCV genotype [†]	
1a	44 (57.9)
1b	4 (5.3)
2b	2 (2.6)
3a	26 (34.2)
HBV vaccination [†]	
No	163 (79.1)
Yes	43 (20.9)
Drugs not injected in past 6 months [§]	
Alcohol	221 (91.3)
Marijuana (smoked)	189 (78.1)
Crack (smoked)	187 (77.3)
Cocaine (snorted)	177 (73.1)
Downers/tranquilizers	172 (71.1)
Demerol/morphine/opium	116 (47.9)
Methadone (non-prescribed)	63 (26.0)
Methadone (prescribed)	35 (14.5)
Crystal meth (smoked)	47 (19.4)
Heroin (smoked)	30 (12.4)
Gas/solvents	25 (10.3)
Ecstasy	23 (9.5)
Drugs injected in past 6 months [§]	
Dilaudid	48 (19.8)
Methamphetamine	34 (14.0)
Heroin	32 (13.2)
Methadone	18 (7.4)
Ritalin	16 (6.6)
Oxycodone	12 (5.0)
Amphetamines	11 (4.5)
Heroin with another drug	3 (1.2)
Barbiturates	2 (0.8)
PCP	1 (0.4)
Other drugs	24 (9.9)

Drug most frequently injected in past 6 months [†]	
Crystal meth	17 (7.1)
Crack	14 (5.8)
Heroin	8 (3.3)
Dilaudid	6 (2.5)
Oxycodone	3 (1.3)
Other drugs	11 (4.6)
Drugs most frequently injected during binge drug use in past 6 months [†]	
Crack	18 (7.5)
Crystal meth	17 (7.1)
Heroin	9 (3.7)
Oxycodone	5 (2.1)
Other drugs	12 (5.0)
Number of different drugs injected in past 6 months [†]	
1-3 drugs	168 (79.6)
4-9drugs	43 (20.4)
Place most frequently injected in past 6 months [†]	
Own house/apt	98 (40.7)
Friend's house/apt	79 (32.8)
Hotel	17 (7.1)
On the street	17 (7.1)
Shooting gallery	13 (5.4)
Family member's house/apt	9 (3.7)
Empty house	1 (0.4)
Rooming house	1 (0.4)
Other	6 (2.5)

[†] Does not add up to 242 due to missing values [§] For each drug N = 242

Appendix 5

Additional univariate results for chapter 3, manuscript 3: Scale free networks among injection drug users in Winnipeg, Canada

Variable	Injects ≥ 63 times while bingeing N = 71 n (%)	Injects < 63 times while bingeing N = 171 n (%)	X^2 (df = 1)	*p*
Injected methadone in the past 6 months				
No	61 (85.9)	163 (95.3)	6.447	0.011
Yes	10 (14.1)	8 (12.7)		
Injected Ritalin in the past 6 months				
No	61 (85.9)	165 (96.5)		0.008*
Yes	10 (14.1)	6 (3.5)		
Injected at family member's house/apt in the past 6 months				
No	54 (76.1)	150 (87.7)	5.156	0.023
Yes	17 (23.9)	21 (12.3)		
Injected at a shooting gallery in the past 6 months				
No	49 (69.0)	140 (81.9)	4.849	0.028
Yes	22 (31.0)	31 (18.1)		
Has injected at a rooming house in the past 6 months				
No	33 (46.5)	119 (69.6)	11.472	0.001
Yes	38 (53.5)	52 (30.4)		
Has injected in a vehicle in the past 6 months				
No	39 (54.9)	124 (72.5)	7.056	0.008
Yes	32 (45.1)	47 (27.5)		
Has injected in a public washroom in the past 6 months				
No	39 (54.9)	135 (78.9)	14.324	<0.001
Yes	32 (45.1)	36 (21.1)		
Obtained needles from a NEP in the past 6 months				
No	16 (22.5)	64 (37.4)	5.028	0.025
Yes	55 (77.5)	107 (62.6)		
Injected multiple drugs in the past 6 months				
1-3 drugs	47 (71.2)	121 (83.4)	4.185	0.041
4-9 drugs	19 (28.8)	24 (16.6)		
Injected after someone transferred drugs from their syringe into participant's syringe				
No	50 (70.4)	144 (86.7)	8.923	0.003
Yes	21 (29.6)	22 (13.3)		

Appendix 6

Chapter 3: Logistic Regression methods, examination of residuals and variables for multicollinearity

Dependent variable: ≥63 times during binge drug use.
Four independent variables included: type of drug injected (cocaine and T&Rs), injected at a hotel, needles obtained from a dealer.
Logistic regression was conducted using the stepwise backward method. Removal criterion for the variables entered was assessed using the likelihood ratio test.

Case Processing Summary

Unweighted Cases		N	Percent
Selected Cases	Included in Analysis	242	100.0
	Missing Cases	0	.0
	Total	242	100.0
Unselected Cases		0	.0
Total		242	100.0

Dependent Variable Encoding

Original Value	Internal Value
no	0
yes	1

Categorical Variables Codings

			Paramete
		Frequency	(1)
got needles from dealer in past 6 months	no	192	.000
	yes	50	1.000
has injected T & Rs in the past 6 months	no	159	.000
	yes	83	1.000
injected at hotel in past 6 months	no	130	.000
	yes	112	1.000
has injected cocaine in the past 6 months	no	74	.000
	yes	168	1.000

Block 0: Beginning Block

Iteration History[a,b,c]

Iteration		-2 Log likelihood	Coefficients Constant
Step 0	1	293.036	-.826
	2	292.896	-.878
	3	292.896	-.879

a. Constant is included in the model.

b. Initial -2 Log Likelihood: 292.896

c. Estimation terminated at iteration number 3 because parameter estimates changed by less than .001.

Classification Table[a,b]

Observed			Predicted: injected > or = to 63 inj during a binge (use for logistic regression) no	Predicted: injected > or = to 63 inj during a binge (use for logistic regression) yes	Percentage Correct
Step 0	injected > or = to 63 inj during a binge (use for logistic regression)	no	171	0	100.0
		yes	71	0	.0
	Overall Percentage				70.7

a. Constant is included in the model.

b. The cut value is .500

Variables in the Equation

		B	S.E.	Wald	df	Sig.	Exp(B)
Step 0	Constant	-.879	.141	38.762	1	.000	.415

Variables not in the Equation

			Score	df	Sig.
Step 0	Variables	inj_cocaine(1)	10.772	1	.001
		inj_TandRs(1)	3.910	1	.048
		inj_hotel(1)	8.244	1	.004
		dealer(1)	18.488	1	.000
	Overall Statistics		34.667	4	.000

Omnibus Tests of Model Coefficients

		Chi-square	df	Sig.
Step 1	Step	35.445	4	.000
	Block	35.445	4	.000
	Model	35.445	4	.000
Step 2[a]	Step	-.404	1	.525
	Block	35.042	3	.000
	Model	35.042	3	.000

a. A negative Chi-squares value indicates that the Chi-squares value has decreased from the previous step.

Model Summary

Step	-2 Log likelihood	Cox & Snell R Square	Nagelkerke R Square
1	257.451[a]	.136	.194
2	257.855[a]	.135	.192

a. Estimation terminated at iteration number 5 because parameter estimates changed by less than .001.

Hosmer and Lemeshow Test

Step	Chi-square	df	Sig.
1	7.892	6	.246
2	8.952	5	.111

Classification Table[a]

			Predicted		
			injected > or = to 63 inj during a binge (use for logistic regression)		Percentage Correct
	Observed		no	yes	
Step 1	injected > or = to 63 inj during a binge (use for logistic regression)	no	161	10	94.2
		yes	47	24	33.8
	Overall Percentage				76.4
Step 2	injected > or = to 63 inj during a binge (use for logistic regression)	no	157	14	91.8
		yes	46	25	35.2
	Overall Percentage				75.2

a. The cut value is .500

Variables in the Equation

		B	S.E.	Wald	df	Sig.	Exp(B)	95.0% C.I.for EXP(B)	
								Lower	Upper
Step 1[a]	inj_cocaine(1)	1.362	.414	10.842	1	.001	3.905	1.736	8.786
	inj_TandRs(1)	.901	.345	6.820	1	.009	2.463	1.252	4.846
	inj_hotel(1)	.209	.328	.405	1	.524	1.232	.648	2.341
	dealer(1)	1.206	.361	11.160	1	.001	3.341	1.646	6.780
	Constant	-2.616	.420	38.815	1	.000	.073		
Step 2[a]	inj_cocaine(1)	1.427	.402	12.591	1	.000	4.165	1.894	9.158
	inj_TandRs(1)	.947	.338	7.859	1	.005	2.578	1.330	4.998
	dealer(1)	1.266	.349	13.147	1	.000	3.545	1.789	7.026
	Constant	-2.591	.418	38.470	1	.000	.075		

a. Variable(s) entered on step 1: inj_cocaine, inj_TandRs, inj_hotel, dealer.

Model if Term Removed

Variable		Model Log Likelihood	Change in -2 Log Likelihood	df	Sig. of the Change
Step 1	inj_cocaine	-134.924	12.396	1	.000
	inj_TandRs	-132.195	6.939	1	.008
	inj_hotel	-128.927	.404	1	.525
	dealer	-134.308	11.166	1	.001
Step 2	inj_cocaine	-136.285	14.716	1	.000
	inj_TandRs	-132.938	8.022	1	.005
	dealer	-135.515	13.175	1	.000

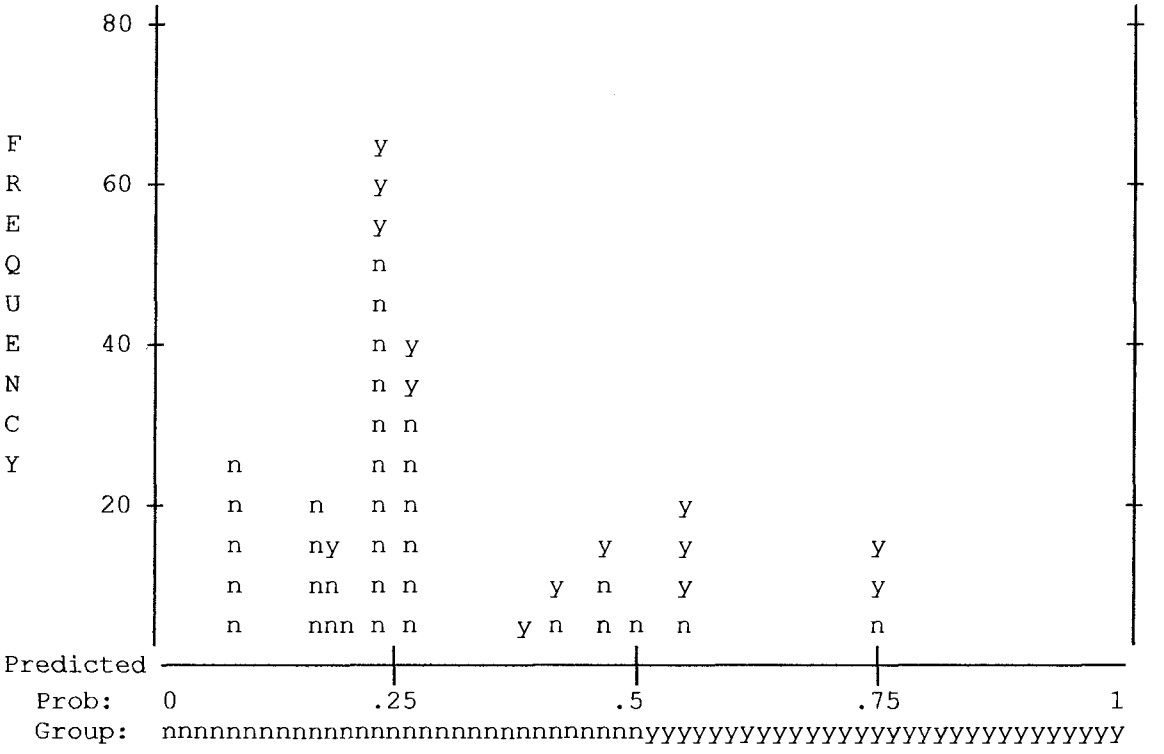
Variables not in the Equation

			Score	df	Sig.
Step 2[a]	Variables	inj_hotel(1)	.406	1	.524
	Overall Statistics		.406	1	.524

a. Variable(s) removed on step 2: inj_hotel.

Step number: 1

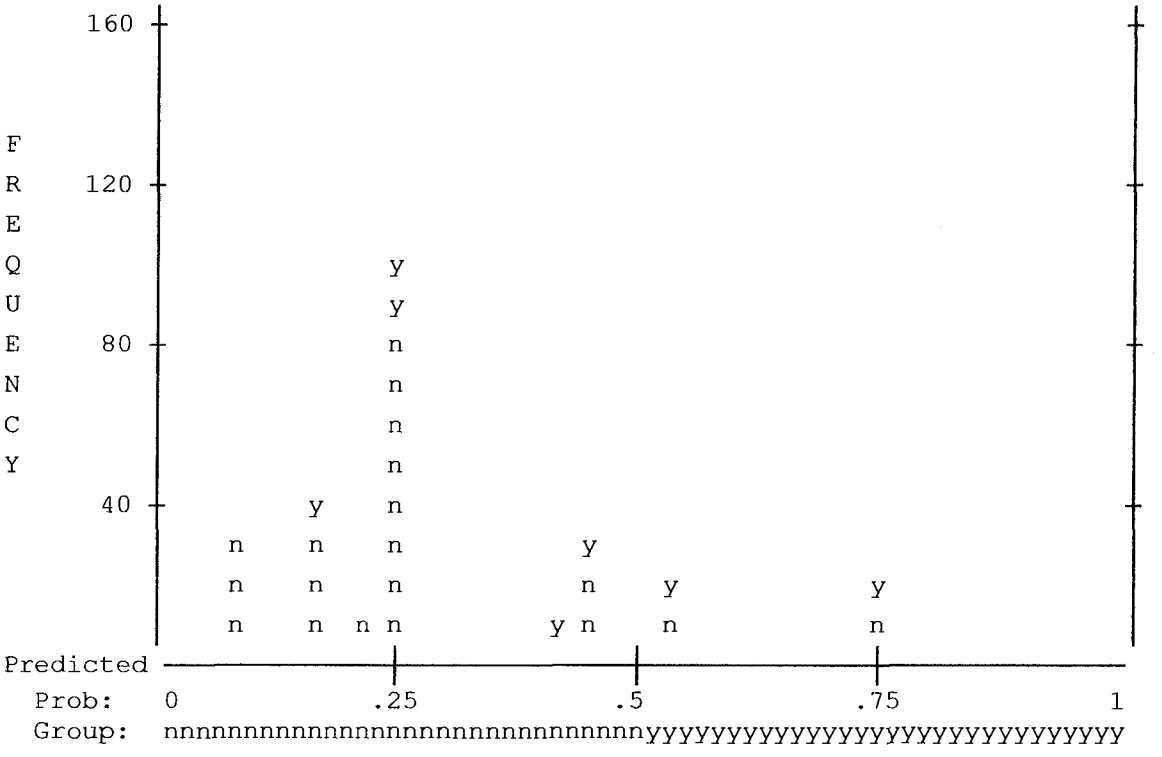
Observed Groups and Predicted Probabilities



Predicted Probability is of Membership for yes
The Cut Value is .50
Symbols: n - no
y - yes
Each Symbol Represents 5 Cases.

Step number: 2

Observed Groups and Predicted Probabilities



Predicted Probability is of Membership for yes
The Cut Value is .50
Symbols: n - no
y - yes
Each Symbol Represents 10 Cases.

Casewise List[a]

a. The casewise plot is not produced because no outliers were found.

Residuals

Examination of the residuals indicates that when an individual who binges on injection drug use does not inject cocaine or T&RS and does not obtain their needles form a dealer there is approximately a 7% chance (a probability of 0.06969) that they will be in the tail end of the distribution (high frequency injector during binge drug use). However, this increases to a 24% chance (0.23780) if they inject cocaine, a 44.6% chance (0.44577) if they inject cocaine & T&Rs and a 74% chance (0.7403) if they if they inject cocaine & T&Rs and obtain their needles from a dealer. These values provide evidence for the role of 3 independent variables in identifying individuals who are high frequency injectors and consequently at greater risk of transmitting or acquiring HIV and HCV infection.

There are no unusually high values of Cook's distance (all < 1), Some of the leverage values (number of predictors +1/sample size) are a little high (> 0.0165) however nothing extreme (minimum value: 0.00843, maximum value: 0.03934). None of the standardized residuals are > ± 2.5 and the DFBetas for the constant and the predictors are all < 1.

Multicollinearity

All the tolerance values are < 1 and no VIF value is > 10.

Coefficients[a]

Model		Collinearity Statistics	
		Tolerance	VIF
1	has injected cocaine in the past 6 months	.839	1.192
	has injected T & Rs in the past 6 months	.863	1.159
	injected at hotel in past 6 months	.851	1.175
	got needles from dealer in past 6 months	.928	1.078
2	has injected cocaine in the past 6 months	.900	1.111
	has injected T & Rs in the past 6 months	.905	1.105
	got needles from dealer in past 6 months	.982	1.018

a. Dependent Variable: injected > or = to 63 inj during a binge (use for logistic regression)

The eigenvalues are similar and the final condition index (4.511) is not too large. There are no predictors which have high variance proportions on the same small eigenvalue. Overall, it appears that the logistic regression model is not affected by multicollinearity.

Collinearity Diagnostics[a]

Model	Dimension	Eigenvalue	Condition Index	Variance Proportions				
				(Constant)	has injected cocaine in the past 6 months	has injected T & Rs in the past 6 months	injected at hotel in past 6 months	got needles from dealer in past 6 months
1	1	3.154	1.000	.02	.02	.03	.03	.03
	2	.708	2.111	.00	.01	.40	.00	.48
	3	.648	2.206	.02	.11	.24	.00	.42
	4	.366	2.935	.06	.05	.02	.95	.06
	5	.123	5.059	.90	.81	.31	.01	.00
2	1	2.522	1.000	.03	.03	.04		.05
	2	.707	1.888	.00	.01	.40		.54
	3	.646	1.975	.02	.13	.25		.41
	4	.124	4.511	.94	.83	.31		.00

a. Dependent Variable: injected > or = to 63 inj during a binge (use for logistic regression)