CHARACTERIZING PATTERNS OF SEXUAL MIXING AND EGOCENTRIC SEXUAL NETWORK RISK AMONG A POPULATION AT RISK FOR HIV ACQUISITION AND TRANSMISSION IN HO CHI MINH CITY, VIETNAM

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Abstract

Siobhan K. Young, MPH: Characterizing Patterns of Sexual Mixing and Egocentric Sexual Networks among a Population at Risk for HIV Acquisition and Transmission in Ho Chi Minh City, Vietnam
(Under the direction of Sandra L. Martin, PhD)

Heterosexual HIV epidemics are driven by sexual contact between partners (sexual networks), yet little is known about how partnership *patterns* influence HIV transmission dynamics, and individual infection risk, in specific settings. This dissertation describes heterosexual partnership patterns and their potential contributions to the spread of HIV among networks of sexual contacts at elevated HIV risk in Ho Chi Minh City, Vietnam.

The first paper employs within-cluster resampling methods to identify population patterns of heterosexual partnership selection, defined by selected HIV risk factors, within these networks. Nearly one-third (31%) of sexual contacts were HIV-positive. Young and unmarried men and women generally selected other young and unmarried sex partners living within their same districts; a pattern likely allowing HIV to persist within these networks. Men and women injecting drugs and exchanging sex typically chose non-injecting and non-exchanging sex partners; a situation likely to fuel ongoing HIV transmission within these networks. Most importantly, those involved in concurrent partnerships (more than one partnership at the same time) tended to partner with others in concurrent partnerships. This pattern will allow HIV to spread more rapidly through the networks than a pattern of serially monogamous partnerships.

The second paper compares patterns of personal risk-taking and heterosexual partnering among female sex workers and non-sex workers within the networks. Notably, HIV prevalence was more than three times higher among non-sex workers than sex workers. Non-sex workers' own risk taking behavior was low; however, they had a high frequency of unprotected sex with HIV-infected primary partners, likely resulting in their exposure to infection. In comparison, sex workers had a higher frequency of personal risk-taking behavior and a lower frequency of exposure to risky partners,

likely contributing to their exposure to infection. These findings illustrate that different patterns of individual risk-taking and sexual partnering may influence women's HIV risk. In the absence of condom use, these findings imply that women, even those whose own behavior is low risk, may be at increased risk for HIV if they are sexually connected to risky partners, even if they have just one, long-term, primary partner.

To my parents, Dennis and Kathryn Young

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List of Abbreviations

AIDS	Acquired Immunodeficiency Syndrome
ART	Antiretroviral Therapy
BED-FR	BED-False Recent
CCSC	Community Counseling and Support Center
CI	Confidence Interval
ELISA	Enzyme Immunoassay
HCMC	Ho Chi Minh City
HIV	Human Immunodeficiency Virus
HSV-2	Herpes Simples Virus 2
IBBS	Integrated Biological and Behavioral Surveillance Survey
IDU(s)	Injection Drug User(s)
MARPS	Most-at-Risk Populations
MOH	Ministry of Health
MOLISA	Ministry of Labor, Invalids, & Social Affairs
MSM	Men who have Sex with other Men
Non-SWs	Non-Sex Workers
OPC	Outpatient Clinic
STD(s)	Sexually Transmitted Disease(s)
STI(s)	Sexually Transmitted Infection(s)
SW(s)	Sex worker(s)
US	United States
USAID	United States Agency for International Development
VCT	Voluntary Counseling and Testing
VND	Vietnamese Dong

Chapter 1: Introduction

The effective design, targeting, and implementation of HIV prevention interventions are predicated upon delivering the right interventions to the right people. Traditionally, HIV epidemiology has identified the 'right people' by examining isolated individual risk factors for HIV infection.[1] While this approach has contributed to an important literature on individual predictors and outcomes related to HIV, it has also led to a limited and decontextualized understanding of population transmission, and individual risk. By reducing HIV risk to a single characteristic or behavior that increases a person's risk of acquiring infection,[1] this approach neglects how infected and susceptible individuals come into contact with one another to form the connections allowing HIV to spread.[2] The result is a limited understanding of why prevalence rates continue to rise in specific groups, and where an epidemic may spread next, that restricts our ability to effectively prevent future waves of infection.

Recognizing the limitations of this approach, researchers have increasingly begun to analyze how sexual contact between partners (i.e., sexual networks) may influence the spread of HIV.[1, 3-6] As a result, interest in 'sexual networks' and 'sexual network analysis' has increased rapidly; shifting our focus from the individual to the partnerships among individuals.[6] A sexual network approach considers the individual, their partner(s), and overall pattern of partnerships in the population, to understand how these factors interact with biological and social factors to influence the spread of infection.[4, 7] The promise of a sexual network approach is that it will help us to identify who is at risk for both acquiring and transmitting infection in a more complete and refined manner than previously permitted using the traditional epidemiological approach.[1, 8]

A growing body of HIV research has adopted a sexual network approach; however, substantial knowledge gaps remain as the field is still emerging, both theoretically and methodologically.[5] Substantial knowledge gaps remain in terms of how different population and individual sexual network structures (i.e., partnership patterns) may emerge to facilitate, or impede, the spread of HIV in specific settings. The purpose of this dissertation is to begin to address this gap

by examining partnership patterns among networks of sexual contacts in Ho Chi Minh City (HCMC), Vietnam.

1.1. Sexual Networks

Unlike diseases spread via casual contact (e.g., influenza), the sexual transmission of HIV takes place within the unique context of a partnership.[2, 4] Specifically, it requires sexual contact in which one partner is infectious, one partner is susceptible to infection, and condoms are not used to prevent transmission.[2] This suggests that 1) the spread of HIV throughout a population is dependent on the extent to which infected persons are sexually connected to additional partners;[1, 2, 9] 2) partners' characteristics and behaviors are important individual risk determinants;[1,4] and 3) from an intervention approach, preventing transmission is just as important as preventing acquisition.[1, 10]

Sexual contacts, or partnerships, among individuals are commonly referred to as sexual networks.[10] Partnership characteristics emerge within sexual networks to affect their structure.[5] Structural network characteristics, or partnership patterns, have been shown to be critical determinants in the spread of HIV at both the individual and population levels.[11]

Sexual partnership patterns are key determinants in the spread of HIV because people do not chose sexual partners randomly.[12, 13] A person's choice in sexual partner(s) is largely influenced by social and cultural norms regarding the 'appropriate' selection of partners.[12, 14] As a result, sexual partnerships and networks become organized according to the social and demographic attributes, such as age, race/ethnicity, education, geography, injecting drug use, and sexual activity levels, of their members.[12] Normative peer behavior within these social networks (i.e., social groups) may then be diffused and reinforced within sexual partnerships.[15] This process of diffusion and reinforcement has been shown to influence a person's decision to engage in risky behavior, and assuming HIV has already entered the group, their risk of HIV infection.[14, 11, 16 15]

Studies of egocentric sexual networks (defined as a person's direct sexual contacts) have shown that people who have sexual partners that are older,[17] injecting drug users,[18, 19] infected a sexually transmitted disease (STD),[20] and have concurrent partners (i.e., a partner who is involved with more than one partner at given point in time)[21] are at an increased risk for acquiring HIV. Thus, egocentric sexual networks (i.e., personal partnership patterns) have the potential to act as individual-

level risk factors for infection as well as proxies for high-risk sexual networks.[2, 22]

Empirical and modeling studies have demonstrated, however, that the influence of direct sexual partnerships on HIV risk may vary depending on the overall pattern of partnerships,[23, 24] and disease burden, in a population.[2, 25] Thomas et al[26] found that in North Carolina, individuals infected with syphilis had partners that were not only non-monogamous and involved in exchange sex, but were also members of different social networks. As another example, this implies that a man who has sex with other men (MSM) and has multiple MSM partners at the same point in time may have very little risk of infection if these partners are uninfected and not connected to the larger sexual network structure of the population. Alternatively, an MSM with only one partner may have a high risk of infection if that partner is sexually connected to other high risk MSM partners at the same time.

At the population level, partnership patterns (i.e., how and to what extent the sexual network structures of a population are connected) largely determine the epidemic trajectory of sexually transmitted infections (STIs), including HIV.[3, 7, 9, 12, 13, 24, 27] Sexual network partnership patterns can be defined and measured in numerous ways. Ghani and colleagues, for example, found that the component size (the size of the largest subset of people connected together in the same sexual network) and density (the number of connections between individuals) of sexual networks was associated with the establishment and prevalence of gonorrhea.[3, 9] Morris et al. have shown that concurrent partnerships increase network connectivity (i.e., the extent of partners connected at a given time point) and may enhance the spread of HIV throughout a network faster than a series of consecutive partnerships.[28-30]

Studies designed to replicate partnership formation and HIV transmission dynamics have also shown that sexual mixing is a particularly important partnership characteristic that emerges within sexual networks (i.e., networks) to affect their structure.[3, 12, 24, 31, 32] Sexual mixing may enhance the spread of HIV throughout a population depending on the attribute used to define mixing boundaries (i.e., risk groups) and epidemic disease phase.[3, 12, 24, 31, 32] Very little empirical and comparable population data are available, however, to explain the contribution of sexual mixing patterns to the spread of HIV in specific settings.

1.2. Sexual Mixing

Sexual mixing, or simply mixing, refers to sexual partnership selection patterns within and between population groups.[3] The concept of mixing is not new to the study of population disease dynamics.[4] In the late 1970s, studies[33, 34] of sexually transmitted disease (STD) clinic attendees in the United States found that those attendees with repeat gonorrhea infections contributed disproportionately to the total number of cases in the clinics: 3% to 7% of infected attendees accounted for approximately 30% of all clinic cases. This precipitated the formulation of a 'core-group' perspective. The core-group concept has continuously been debated and redefined,[35] but its epidemiological relevance comes from the idea that the core-group acts as a 'reservoir' of infection, allowing infection to persist within a population.[4]

The original core-group concept was based on the basic reproductive rate of sexually transmitted infection (STI), R_0=βcD, where: R_0 is the number of infections generated by one infection; β is the efficacy per contact, or likelihood of infection when a susceptible individual has contact with an infected individual; c is the rate at which contact is made in the population; and D is the duration of infection.[36] In simplified terms, this means that when $R_0 > 1$, most of the population will eventually become infected, or disease will become epidemic. In contrast, when $R_0 < 1$ disease will spread very little, or remain endemic.[27, 37] R_0 is, essentially, a threshold quantity that determines whether a disease will become an epidemic, or die out.

May and Anderson[37] added a corollary to the original R_0 model, stating that the mean rate of partner change is equal to the mean rate of partner change in the population (m) plus the variance of partner change divided by the mean $c = m + \frac{\sigma(2)}{m}$. Basically, this means that the variability of c depends disproportionately on a highly sexually active (i.e., high number of sexual partners) subgroup (i.e., core group) within a population.[3, 6, 10, 37] From an applied public health perspective, the utility of the model is easily grasped. It makes it easy to identify and target high-risk individuals for prevention; they are simply those with the highest numbers of sexual partners.

Within the context of HIV transmission, however, defining the 'core' by the reproductive threshold (i.e., having $R_0 > 1$) is not straightforward.[4, 35] Some core-groups have $R_0 = 0$ (i.e., there is no within group transmission).[4] Female sex workers (SWs), for example, do not infect each other with

HIV; they are infected by their sex partners. Alternatively, if we drop these criteria, and instead, define the core by seroprevalence, it makes defining the core difficult.[4] Should it be defined by a demographic characteristic? A risky behavior? Some combination of these? If the core definition is manipulated to find the necessary seroprevalence, then its' meaning is altered. It provides a description of the infected population, not the population at risk.[4]

In recognition of the need to move beyond core/non-core distinctions, researchers have increasingly advocated examining mixing patterns in "multigroup" populations.[4, 13] In a multigroup population, groups can be, but are not limited to being defined by the reproductive threshold, numbers of sexual partners, or disease prevalence.[4] Rather, groups can be defined with respect to any attribute (e.g., age, marital status, geography, injecting drug use, sex work).[23, 38] In turn, understanding mixing patterns within a multigroup population helps to determine the key attributes identifying "epidemiologically relevant" risk groups involved in HIV transmission dynamics.[4] For example, a recent modeling study by Cohen et al[39] examined the effect of treating HIV serodiscordant (couples with a 'mixing' by HIV status in that one partner is positive and the other is negative) with antiretrovirals (ART) to prevent transmission on the HIV epidemic in four countries. Results showed that the higher the HIV prevalence, and/or the greater the prevalence of serodiscordant couples, the larger the reduction in incidence. However, differences in reductions across countries reflected complex interactions among three factors: HIV prevalence, population size, and the prevalence of serodiscordant couples.

Empirical[12, 24, 32, 40-43] and modeling[13, 23, 31, 36] studies have shown that in a multigroup population, once HIV enters the population, general mixing patterns have an important influence on HIV epidemic trajectory. By convention, mixing is typically classified along a continuum ranging from perfectly assortative to perfectly disassortative.[23] Under assortative mixing conditions, individuals' choose sex partners characteristically similar to themselves[2, 23] which leads to partnering within closed groups (e.g., young women with only young men; IDUs with only other IDUs). Assortative mixing typically restricts HIV to sexually segregated groups, and generally, results in several distinct, rapidly evolving epidemics within a population.[7, 12, 23, 27, 44] In contrast, disassortative mixing refers to individuals choosing sexual partners unlike themselves (e.g., young girls with older men; IDUs with

non-IDUs) which reduces sexual segregation between groups.[12] Under disassortative conditions, disease can be spread directly from high- to low- prevalence groups within a population and often results in a slowly moving, widespread epidemic.[6, 7, 44] Disassortative mixing has also been shown to result in indirect transmission between high- and low- prevalence groups via bridge groups (i.e., bridging).[2] Bridge groups are those linking high- and low- prevalence groups that would otherwise remain unconnected.[2]

Population patterns of partnership selection are not uniform.[12] Studies have demonstrated that assortative and dissortative mixing can be exhibited simultaneously, influencing individual risk of exposure and overall incidence in the population.[2, 12, 13] Moreover, depending on the risk characteristic under examination, the magnitude of assortative and dissortative mixing (i.e., the degree of assortativity) determines the extent to which HIV is restricted to specific risk groups, or spreads into the general population.[2, 13] This makes it important to examine patterns of sexual mixing in multiple settings, or locations, and across multiple groups, defined by relevant HIV risk factors, within these locations.

1.3. Illustrative Example: HIV in Ho Chi Minh City, Vietnam

Vietnam provides a pertinent example of the need to evaluate predominant partnership patterns to better understand HIV epidemic trajectory, and individual risk of infection..

Despite a low prevalence in the general population (0.45%) of adults,[45] Vietnam has one of the fastest growing epidemics in Asia.[46] The number of people living with HIV doubled from 2001 to 2009, from an estimated 140,000 to 280,000 [220,000-350,000].[47] In 2009, there were 15,713 newly reported HIV cases and 2,010 AIDS-related deaths.[47] According to preliminary results of the 2011 Ministry of Health (MOH) Estimation and Projection Study in the period from 2005-2010, Vietnam will have had between 30,000-40,000 new HIV infections annually and the total number of people infected with HIV will have increased to 263,317 by 2015.[45]

Yet, these national estimates do not reflect the HIV epidemics of varying degrees involving different risk groups separated by time, geography, and risk-taking behaviors that have been critical determinants of the spread of HIV in Vietnam. Historically, the country's HIV epidemic has been primarily driven by injecting drug use and commercial sex work, largely insulating the general

population from infection.[48] Current epidemiologic trends suggest that HCMC's HIV epidemic may, once again, be at a critical "inflection point" characterized by a shift in the relative importance of different risk groups on the continued spread and maintenance of the epidemic.[10] Specifically, since heterosexual transmission recently surpassed injecting drug use as the primary mode of transmission, it has been suggested that Vietnam's HIV epidemic is transitioning from an epidemic driven by injecting drug users (IDUs) and commercial sex workers (SWs) to one being driven clients-of-SWs and husband-to-wife transmission.[47, 49] However, the extent to which this transition is occurring, to date, remains unclear.[50]

This pattern is particularly evident in the country's largest city and economic capital, Ho Chi Minh City (HCMC). Since the early 1990s, when Vietnam's first case of HIV was detected in HCMC, the city has served as the epicenter of the national HIV epidemic.[51] HCMC's first sub-epidemic occurred in older male opium injectors and stabilized around 43%.[46] In the late 1990s, a second rapidly expanding sub-epidemic emerged among young, sexually active, heroin IDUs and stabilized around 54%.[46] These young, newly infected IDUs were also sexually active and frequented SWs; consequently, HIV entered commercial sexual networks.[46] Between 1998 and 2000, according to sentinel surveillance data, prevalence among SWs skyrocketed from approximately 2% to 24%.[52] Current estimates of HIV prevalence among IDUs, SWs, and the general population in HCMC are strikingly higher than national averages (55% vs. 29% among IDUs, respectively; 23%, vs. 4% among SWs, respectively; and 2% vs. 4% among the general population, respectively).[52]

Presently, HCMC is home to approximately 30,000 male IDUs and a sizable SW population (unofficial estimates suggest 70,000 women exchanged sex for money and/or drugs in HCMC in the past year);[53] therefore, it is understandable that these two groups have played a critical role in transmission. Prevalence among male IDUs, however, is showing signs of stabilization;[52] primarily resulting from a decline in new infections since most IDUs sharing needles have already been infected.[53] Injecting risk also declined sharply when large numbers of IDUs were sent to government mandated rehabilitation centers.[53] In comparison, prevalence is expected to slowly increase among SWs; especially, as more SWs become IDUs and vice versa.[51, 52]

Available estimates suggest 12% of adult males in HCMC paid for sex in the past year.[53] It is

not surprising then, that the number of new infections among clients of SWs has increased dramatically since 2000.[53] Initially, increases in condom use slowed the rise in new infections, but usage was not consistent enough to prevent all SW- to-client transmission.[51] By 2005, an estimated 4,000 clients a year were contracting HIV.[51] It is estimated that new infections will continue to increase and HIV prevalence among clients will hover around 2% through 2013.[51, 53]

Despite the important implications of these shifting transmission patterns for future prevention efforts, available evidence of this transition is largely limited to national sentinel surveillance data and studies examining individual predictors and outcomes of HIV, such as injecting drug use,[54] condom use,[55] and sexual activity levels.[56, 57] The limitations of examining individual risk factors in isolation were mentioned earlier. Sentinel surveillance estimates also do not account for a number of population and contextual factors that have the potential influence the spread of HIV in HCMC. For example, they do not account for large numbers of IDUs and SWs recently being released from government mandated rehabilitation centers and being added back into the 'risk pool,' nor do they account for shifting demographic trends that may once again give rise to a new, young, injecting population; now, among both men and women. Broad estimates also do not take into account for a potential increase in epidemic trajectory resulting from overlapping sexual networks of male and female injectors. The result is an incomplete view of the extent to which the epidemic is transitioning to one being driven by IDUs and SWs to one being driven by clients-of-SWs and husband-to-wife transmission.

Further complicating our understanding of shifting transmission dynamics in HCMC is a lack of data among women in the general population (defined as women not engaged in injecting drugs and exchanging sex in the past 12 months).[53, 58] Estimates suggest that 81,000 women are currently infected and prevalence among women is increasing in HCMC.[48] Nguyen et al,[59] however, suggest that this estimate may account for a very small percentage of the true number (<20%) of women annually infected in HCMC. Unfortunately, very few empirical HIV studies incorporate women that are not SWs in Vietnam. To the best of our knowledge, no studies have examined sexual contact patterns and their potential influence on HIV risk, or broader transmission dynamics, among women in the general population in Vietnam. The result is an incomplete view of HIV risk among behaviorally

distinct groups of women in HCMC.

Understanding the potential for population and contextual factors to influence the relative importance of various risk groups on the spread and maintenance of the HIV epidemic in HCMC will require characterizing predominant partnership patterns among networks of sexual contacts to identify epidemiologically relevant risk groups. Unfortunately, to date, no studies have examined predominant population, or individual, partnership patterns among networks of sexual contacts in HCMC. Ultimately, the prevention of a widespread national epidemic will require detailed knowledge of predominant partnership patterns in specific settings in HCMC and throughout Vietnam.

Chapter 2: Summary and Significance

Recent evidence suggests that heterosexual sex recently surpassed injecting drug use as the primary mode of HIV transmission in Vietnam.[50] In a heterosexually driven HIV epidemic, understanding epidemic trajectory, and risk, requires understanding patterns of sexual contact between partners. In Vietnam, however, little is known about how sexual partnership patterns influence patterns of population transmission, or individual risk of acquiring and transmitting infection. The paucity of research is particularly apparent among women; especially, among behaviorally distinct groups of women, such as SWs and non-SWs. The result is an incomplete view of the extent to which Vietnam's HIV epidemic is transitioning from one driven by injecting drug use and commercial sex work to an epidemic driven by clients-of-SWs and husband-to-wife transmission.[50]

Identifying various risk groups and their contribution to the continued spread and maintenance of the epidemic, as well as women's risk of infection, will require detailed knowledge of the predominant sexual partnership patterns in specific settings throughout Vietnam. In this dissertation, we describe predominant heterosexual partnership patterns and their potential contribution to the spread of HIV at the population level, as well as women's individual-level risk of acquiring and transmitting infection, among networks[1] of sexual contacts at elevated HIV risk in HCMC, Vietnam. Each dissertation aim described below is addressed in a separate paper, followed by an overall conclusion describing the implications of this research for local public health practice in HCMC, Vietnam as well as the advancement of sexual network research.

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[1] Mathematically, a 'network' can be defined and measured as the sexual contact(s) between two or more individuals. Conceptually, however, the term 'network' may be used to refer to the sexual contacts among any number of individuals in a specific population. This dissertation uses the conceptual definition of the term 'network.' Therefore, in each paper/aim the term 'network' refers to study sample specific to that paper/aim. Since each paper/aim was subset to a different sample of participants in the HCMC Sex Network survey, when discussing both papers/aims we employ the term 'networks.'

Paper 1/Aim 1: To describe heterosexual partnership selection (sexual mixing) patterns among a network of sexual contacts at elevated HIV risk in HCMC, Vietnam.

Paper 2/Aim 2: To compare personal risk-taking and sexual partnership (egocentric sexual network) patterns between female sex workers (SWs) and non-sex workers (non-SWs) among network of sexual contacts at elevated HIV risk in HCMC, Vietnam.

It is important to note that the patterns of sexual contact described in this dissertation are specific to *these* networks of sexual contacts at elevated HIV risk in HCMC, Vietnam. Only to the extent that these networks at elevated risk are similar to other networks at elevated risk in HCMC may our findings be representative of other networks at elevated risk in HCMC. These networks of sexual contacts were evenly distributed throughout HCMC, so our hope is that they are, in fact, similar to other networks of sexual contacts at elevated risk in HCMC. Additionally, identifying the relative importance of risk groups to HIV epidemic trajectory in Vietnam will ultimately require similar analyses of sexual networks in multiple settings across multiple locations in HCMC, and throughout Vietnam; therefore, this dissertation represents an important first step understanding how specific partnership patterns may contribute to the spread of HIV in HCMC, Vietnam.

Chapter 3: Theoretical Framework

3.1. Complex Adaptive System and Emerging Properties Framework

This dissertation situates its use of sexual network analysis within the context of a complex adaptive system and emerging properties theoretical framework (referred to as a complex systems approach) developed by Diez Roux & Aiello and, recently, expanded upon by Blanchard & Aral.[60] Simply defined, a complex system is a system comprised of multiple parts, or components, that have multiple interactions.[60] The system's function is dependent on the interaction of all its parts.[60] Emergent properties are system-wide characteristics integral to the system's operation in that their influence on the relationship(s) among component parts sets into motion a non-linear causal process, allowing every component the potential to affect every other component in the system.[60]

Essentially, a complex system is a dynamic model dependent on understanding how the interactions and interrelations among its component parts contribute to the generation of patterns within a population.[60, 61] With respect to HIV transmission, the underlying principle of this framework is that properties emerging from individual characteristics and behaviors cannot be viewed as isolated variables in determining HIV risk.[62] Rather, it demonstrates that individuals and groups are embedded within a larger social and sexual context, and attempts to analyze how individual and different levels of social and sexual contextual factors interact to influence HIV transmission dynamics, and vice versa.[60, 62, 63]

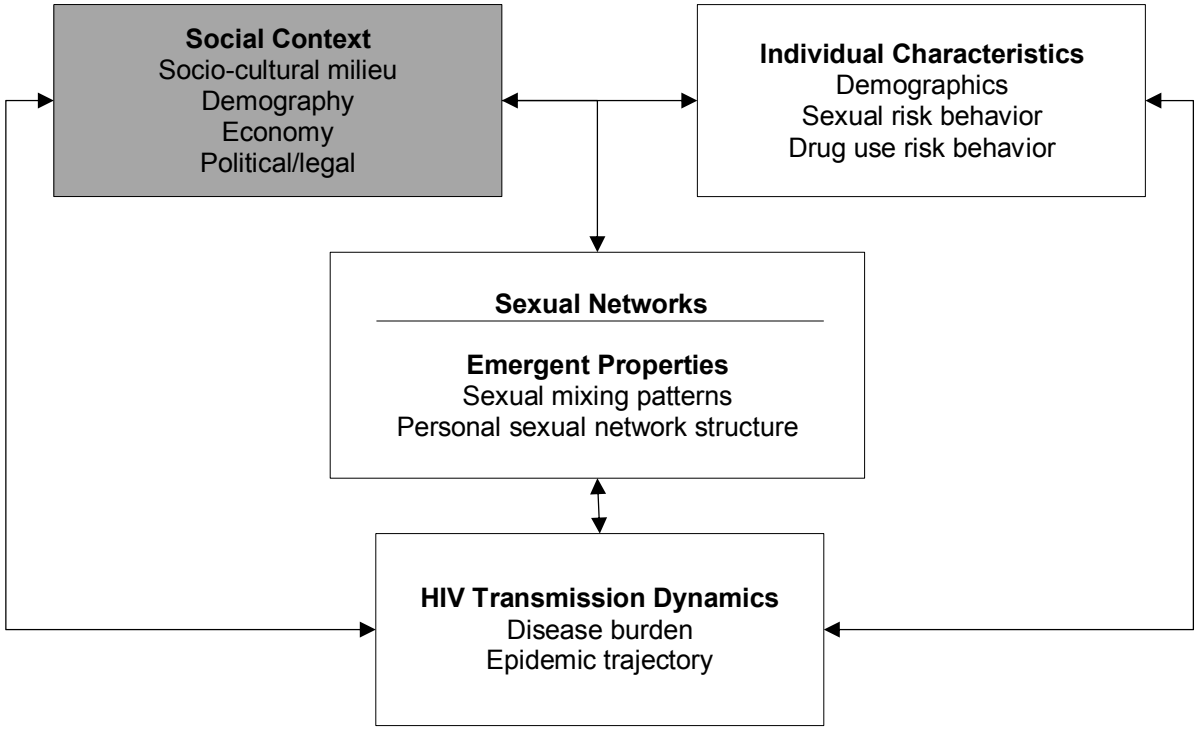
A schematic rendering of a complex systems approach as it relates to the present dissertation is shown in Figure 2.1. From this perspective, the societal context, including the cultural, economic, and political/legal environments, in which people live shapes how they come together to form sexual partnerships (i.e., sexual networks). Interactions among sexual partners generate emerging properties, such as patterns of sexual mixing and personal sexual networks, which determine the sexual network structure of a population. In turn, the sexual network structure of a population influences individual exposure to HIV-infected partners and incidence in the population.

Combined, these elements function as the population's HIV transmission system.[61] Once HIV enters a population, transmission dynamics may, in turn, influence the structure of sexual networks, characteristics and behaviors of individuals and their partners, as well as the societal context in which they live.

The key differences between this framework and others that include individual and population level determinants, such as the proximate-determinants [64] framework, are 1) the identification of structural phenomena (e.g., sexual mixing) as emergent properties influenced by the interaction of multiple components to shape epidemic trajectory, and 2) the emphasis on reciprocal relationships and feedback loops between different elements of the system.[60]

3.2. Figures

Figure 3.1 Conceptual Framework of HIV Transmission Dynamics as a Complex Adaptive System with Emergent Properties



Adapted from: Blanchard & Aral. Sex Transm Infect 2010; 86(Suppl 3):iii4-iii9
Note: Shaded/colored shapes represent variables not measured in this analysis.

Chapter 4: HCMC Sex Network Survey

4.1. Data

For dissertation Aims 1 and 2, analyses were conducted using data from the 2009 *Sexual Behavioral Relationships and HIV Infection in Ho Chi Minh City, Vietnam* (FHI 360 study #10027; referred to as the HCMC Sex Network survey). The HCMC Sex Network survey was embedded in a larger study protocol, the *Combined Cross-Sectional and Prospective Study of HIV Incidence and Detection of Acute HIV Infection among High Risk Populations in Ho Chi Minh City* (FHI 360 study #10018; referred to hereafter as the Incidence study).

The purpose of this chapter is to briefly explain: 1) HCMC Sex Network survey recruitment and data collection procedures; and 2) the rationale for the different subsets of participant data used in dissertation Aims 1 and 2.

4.2. Sampling

4.2.1.Recruitment

There were two types of participants in the HCMC Sex Network survey (n=504), male and female index participants (n=271) and their referred sexual partners (n=233). As shown in Figure 4.1 index participants in the HCMC Sex Network survey with selected HIV risk characteristics, such as biological sex, sexual activity, injecting drug use, and HIV serostatus, were identified, selected, and recruited for survey participation from among a subset of (n=275) participants enrolled in the cross-sectional and BED-false recent (BED-FR) phases of the Incidence study. The Incidence study has previously been described in detail elsewhere.[65] Briefly, Incidence study participants (n=2,015) were recruited in one of two ways depending on study phase:

Index participants

- BED-FR participants (n=403) were recruited from outpatient clinics (OPC).
- Cross-sectional participants (n=1,612) were recruited via chain-referral sampling, starting with a 'seed sample' (n=14) of high-risk individuals identified via targeted peer outreach. Following study completion seeds were given referral coupons to

recruit up to 3 sexual partners for study participation. Referred sexual partners were screened, enrolled, and asked to recruit in a similar manner. Coupons expired after 4 weeks; the ratio of peer and partner referrals varied throughout the study to achieve target sample sizes.

Those participants providing informed consent (n=271) became *index* participants in the HCMC Sex Network survey. Following HCMC Sex Network survey completion, index participants were given four referral coupons to recruit up to four sexual partners for survey participation (note: these 4 coupons were given to indexes in addition to the 3 referral coupons they received during the Incidence study). Referral participants were screened, enrolled and asked to participate in a similar manner. However, these referral participants did not recruit additional partners.

4.2.2. Eligibility Criteria

All eligible *index participants* in the HCMC Sex Network survey were between ages of 18 to 35 years and HCMC residents. In addition, index participants recruited from the

- BED-FR phase (n=62) also had to have a known diagnosis of HIV-positive for greater than 12 months and potential participants could be excluded from the BED-FR if they had ever taken antiretroviral therapy (ART).
- Cross-sectional phase (n=209) also had to have an elevated risk of sexual acquisition of HIV as defined by having greater than three partners in the past month and greater than three sex acts per week, and/or sex with a MSM, IDU, or SW in the past month. Potential participants were excluded from study participation if they were currently receiving antiretroviral therapy (ART) and/or had received a previous diagnosis of HIV-positive/AIDS.

All *referral participants* in the HCMC Sex Network survey were eligible simply based on having been referred by the index participants. Referrals that could not provide the name of the index participant giving them their coupon were excluded from study participation.

4.3. Data Collection

HCMC Sex Network survey data were collected via face-to-face oral interview. Participants were also asked to provide biological specimens for detection of HIV and recent drug use. Plasma samples were tested for HIV using a three-step algorithm, which included the following HIV tests: (1) MUREX Ag/Ab COMBINATION EIA, (2) Greenscreen HIV ½ Enzyme Immunoassay Version 2, and (3) Abbot Determine HIV 1/2 Rapid Test. All three tests had to return a positive result before a positive diagnosis could be made. Urine samples were screened for opiates using the MOP One Step Morphine Test Strip. Participants were paid VND 100,000 (≈ US $6.00) for time spent completing the

survey. Indexes were eligible to receive an additional VND 50,000 (≈ US $3.00) for each enrolled referral. This research was reviewed and approved by the FHI 360 Protection of Human Subjects Committee.

4.4. Dissertation Sample

A total of 504 participants completed the HCMC Network study**.** We will be using two combinations of participants drawn from these 504 data records to complete analyses for the two aims of this dissertation. The rationale for selecting these two subsets of participants is discussed later in this chapter.

In Aim 1, participation is limited to female and male index participants that recruited at least one partner of the opposite sex for participation in the HCMC Sex Network survey; thus our final study sample is comprised of 145 indexes and 222 sexual partners to form 222 heterosexual relationship dyads.

In Aim 2, participation is restricted to 237 female participants in the HCMC Sex Network survey reporting answers in response to two questions on past sex work and from one to five of their nominated egocentric sexual network partners (n=879).

4.4.1. Sample Selection Rationale

The HCMC Sex Network survey collected data from participants at multiple levels. First, individual-level data was provided via participants' self-reports of their own risk characteristics and behaviors. Second, egocentric sexual network data was provided via participants' nomination of from one to five recent personal sexual network contacts from the three months prior to survey interview. Finally, index participants recruited up to four sexual partners for survey participation; linking indexes to their referred sexual partners provided self-reported data from both members of the partnership, or dyad.

The use of each one of these three levels of data in isolation has relative advantages and disadvantages to its use (discussed below). Together, however, they provide a rich context in which to evaluate the distribution of sexual risk characteristics and behaviors in a sexual contact network. Therefore, for these analyses, we decided to take advantage of the unique data available at each level in the HCMC Sex Network survey. However, since participant data with respect to selected HIV

risk factors relevant to this dissertation were not evenly distributed among each level, we were required to subset our data for each Aim.

4.4.1.1. Aim 1 Sample Selection Rationale

In Aim 1, we focus on identifying and quantifying patterns of heterosexual partnership selection (i.e., sexual mixing) to determine how variations in the probability of partnership selection by risk group (defined by selected HIV risk factors, including the virus itself) may influence population-level HIV transmission dynamics with this network of sexual contacts. Analytically, this requires knowledge of the distribution of selected HIV risk characteristics among both members of the sexual partnership (commonly referred to as a dyad in network research).

To date, the majority of research on sexual mixing has been limited to the use of simulation studies and index participants' self-reports of partner data. While some studies [66, 67] have found agreement between heterosexual couples on reports of HIV risk, others have questioned the reliability and validity of such assessments.[68, 69] One study[70] in particular, found agreement on reports of most HIV risk factors with the exceptions of concurrency and drug use behavior. Our earlier literature review indicated that injecting drug use and concurrency are important determinants of HIV transmission and acquisition in HCMC. Misclassification of partners' risk characteristics and behaviors among partners may lead to biased estimates of assortativity, and in doing so, may bias our understanding of the contribution of sexual mixing to HIV transmission dynamics in HCMC.

By linking index participants' self-reported data to data self-reported by their referred sexual partners, dyadic participant data from HCMC Sex Network survey allows us to overcome potential limitations posed by a lack of agreement. Therefore, in Aim 1, we restricted our study sample to index participants recruiting at least one and up to four partners for survey participation; limiting our final sample to 145 indexes and their 222 referred sexual partners (n=222 partnership dyads).

4.4.2. Aim 2 Sample Selection Rationale

The purpose of Aim 2 is to compare personal risk-taking and partnership (egocentric sexual network) patterns among behaviorally distinct groups of women (SWs and non-SWs) in a network of sexual contacts at elevated HIV risk in HCMC, Vietnam.

Existing health behavior models, such as the health belief model and the theory of reasoned

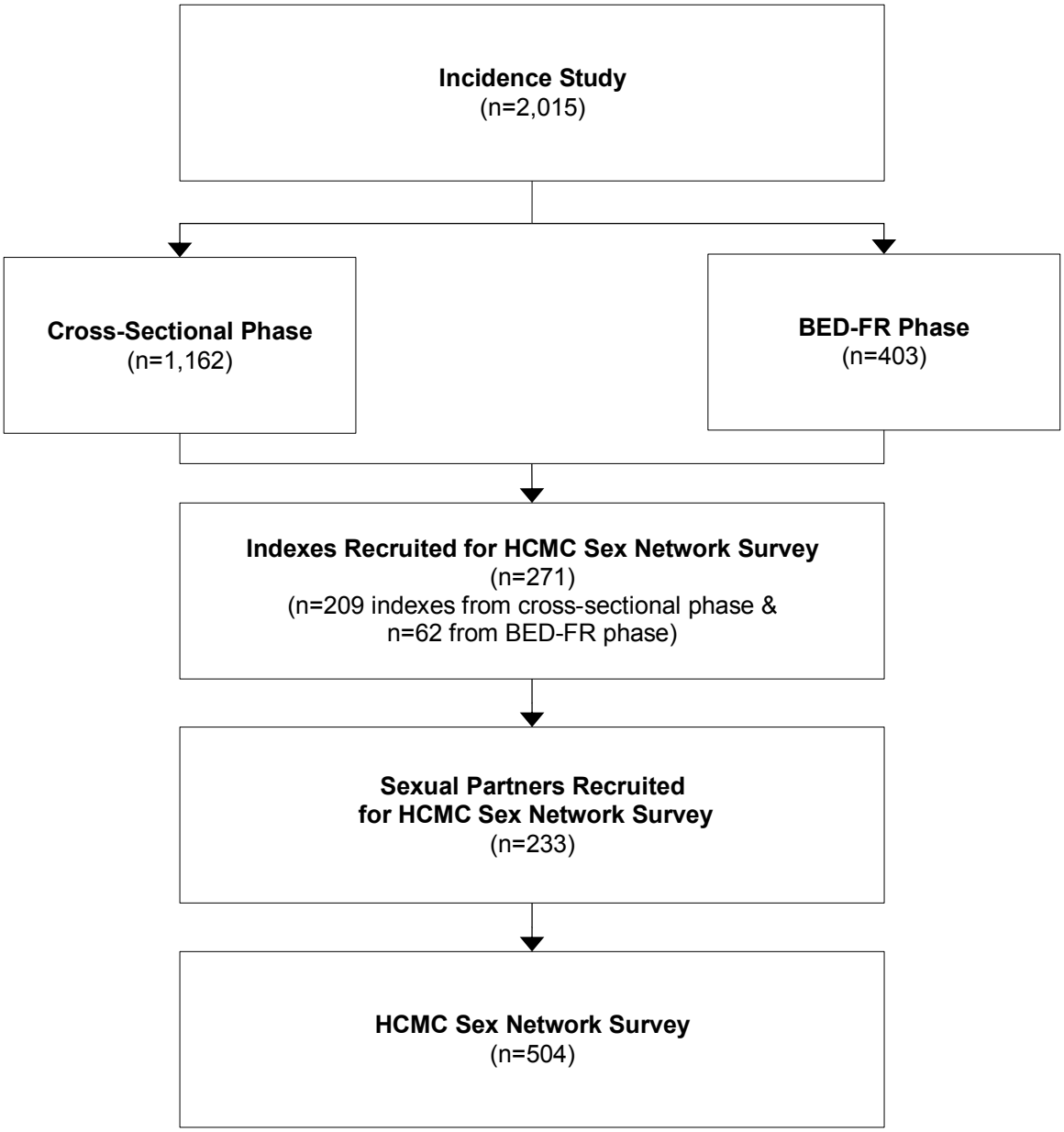
action, have documented the influence of perceived risk on sexual behavior these models do not take into account perceptions of sexual partner risks,[71] or important contextual factors – such as partner type and duration of partnership. As a result, little is known about the extent to which women are aware of their partners' risk and how awareness may differ in accordance with the overall pattern of a woman's partnerships. It is also unlikely that the perception of partner risk is the same for each partner.[71] To account for factors that may vary by partner some researchers have also suggested more precise estimates of individual risk may be derived using event-level data.[71, 72] Therefore, we are particularly interested in SWs' and non-SWs' perceived and event-level partnership risk exposure.

Characterizing partnership risk exposure requires measuring different aspects of personal sexual network structure (i.e., direct sexual contacts). In this case, survey questions regarding perceived and event-level risk exposure were only captured with respect to participants' self-reported nominated egocentric sexual network partners. Therefore, while women's recruited sexual partners (used in Aim 1) could serve as their personal networks; we would not be able to examine perceived and event-level risks that may play a critical role in women's individual risk of infection.

Therefore, our Aim 2 study sample is restricted to women participating in the HCMC Sex Network survey that self-reported answers to two questions on past sex work (n=237) and from one to five of their nominated egocentric sexual network partners (n=879).

4.5. Figures

Figure 4.1 Overview of Targeted Recruitment for HCMC Sex Network Study



Chapter 5: Paper 1, Sexual Mixing Patterns among a Network of Sexual Contacts in Ho Chi Minh City, Vietnam

5.1. Introduction

Once HIV enters a population, epidemic trajectory is largely determined by the underlying patterns of contact between sex partners (commonly referred to as sexual networks). Patterns of sexual partnership selection, or sexual mixing, are an important structural feature of sexual networks, influencing individual exposure to HIV-infected partners and the rate of transmission in the population.[17, 24, 40-42, 73]

Sexual mixing (mixing) patterns can be quantified by estimating the degree of assortativity within a population,[13] or the probability that individuals in a given risk group will form sexual partnerships with individuals in another given risk group. Early mixing research in the context of HIV commonly defined risk groups in terms of age[42, 74] and sexual activity level;[24, 31] however, any risk attribute can be used to define mixing boundaries.[13] Assortativity is typically expressed on a continuum, ranging from perfectly assortative (individuals select only partners from within their risk group) to perfectly disassortative (individuals selecting only partners outside their risk group).[2, 23]

The degree of assortativity within a population largely determines whether HIV remains contained to specific risk groups, or spreads to the general population.[17, 24, 40-42, 73] In groups at elevated risk, assortative mixing typically sustains within group transmission; resulting in a form of sexual segregation between groups that prevents the spread of infection from high- to low- risk groups.[12] Conversely, disassortative mixing decreases sexual segregation between groups.[12] Disassortative mixing is important because it may connect high- to low- prevalence groups directly, and indirectly via bridge populations (individuals who partner with others both like and unlike themselves), facilitating disease transmission across networks and populations.[75]

Existing mixing studies[9, 12, 24, 40, 41, 63] have made substantial contributions to our understanding of its critical role in HIV transmission; several practical and methodological limitations,

however, have made it difficult, to fully develop empirical sexual mixing research. Recently, Young and colleagues[76] illustrated that standard measures for estimating assortativity do not take into account two key factors that may bias estimates, the:1) dependent nature of data reported within partnerships (i.e., dyads); and 2) influence that one dyad member may have on the outcome of another (i.e., the presence of informative cluster size). Research has also been largely dependent on respondents' (referred to as ego, or index, participants) self-reports of partner data which may lead to biased assortativity estimates. For example, studies have shown that participants' self-reports of partner concurrency and condom use may not correspond to actual data.[66, 70] Moreover, many of the assumptions built into estimating assortativity have been shown to vary by population and the attributes used to define risk groups.[2] In a given locale, this means that specific knowledge of sexual partnership selection patterns among a range of possible HIV risk factors is required to understand the course of an epidemic and optimally design prevention interventions.

Despite increasing rates of heterosexual transmission and new infection among women,[47] to date, no studies have examined mixing patterns to examine the extent to which the epidemiological relevance of various risk groups may be shifting in Vietnam. Therefore, using data from a network of sexual contacts at elevated HIV risk in HCMC, Vietnam, the present study describes heterosexual mixing patterns with respect to selected HIV risk factors. Specifically, our objectives are to: 1) estimate and compare the degree of assortativity among dyads overall, and across dyads stratified by index participant gender; and 2) extend prior mixing research, using data self-reported by both dyad members and taking into account the non-independence of dyadic data and presence of informative cluster size.

5.2. Methods

5.2.1. Procedures

We performed a secondary analysis of data collected as part of the HCMC Sex Network survey conducted from March to October 2009 in HCMC, Vietnam. Procedures for Aim 1 have been previously described in Chapter 4. Briefly, two types of participants were recruited for survey participation, index participants and their referred sexual partners. As previously discussed, index participants with selected HIV risk factors, such as age, drug use, and HIV test results, were recruited

directly from a larger study protocol in which the HCMC Sex Network survey was embedded; sexual partners were recruited by index participants. Each index participant was given four unique study recruitment coupons to refer up to four sexual partners for survey participation.

HCMC Sex Network survey protocols and the present study were reviewed and approved by the FHI 360 Institutional Review Board.

5.2.2. Measures

All HCMC Sex Network survey participants were administered a questionnaire designed to elicit information on demographics, STI history and testing, sexual and drug use behavior, and their dates of first and last vaginal sex with up to 5 sexual contacts during the previous three months. All measured defined below were selected because they have established importance for HIV risk, or are commonly used to describe sexual partnerships.

We define a *dyad* as an index participant (labeled *index*) and their one to four referred sexual partners (labeled *partners*).Using this definition, each index could contribute to up to four dyads. All measures were self-reported by both dyad members.

Demographic Characteristics

Age group. Continuous data on age were collapsed to form a categorical indicator variable: (18-20, 21-23, 24-26, 27-29, 30-32, and ≥33 years).

Marital status. Data on current marital status was collected and dichotomized, *currently not married vs. currently married.*

Residential location. Participants were asked to provide the name of the district in which they lived at the time of interview.

Substance Use and Sexual Behavior Characteristics

Injecting drug use (IDU). Participants with a biologically confirmed positive urine test for opiate use and those reporting ever injecting drugs for use other than medicine were considered injecting drug users.

Exchanging sex. Participants reporting ever selling or exchanging sex for money and/or drugs were considered to have exchanged sex.

Concurrency. Concurrency was measured as number of days since last vaginal sex with 2nd

most recent partner minus number of days since first vaginal sex with more recent partner in the three months prior to survey interview.[77] Participants with zero or negative days between partnerships were considered concurrent, while participants with positive gaps between partnerships were considered to have not engaged in a concurrent partnership.

HIV Serostatus and Testing

HIV status. Participants with detectible HIV antibodies on two HIV EIA assays and one rapid test, or those self-reporting HIV-positive serostatus, were considered HIV-positive.

HIV testing. Participants reported whether or not they had ever been tested for HIV.

5.2.3. Statistical Analysis

All analyses were performed using SAS v. 9.2 (SAS Institute, Cary, NC, USA). To compare reports made by both dyad members, we restricted our analysis to indexes referring at least one and up to four partners for survey participation. Dyads were constructed by linking indexes to their one to four partners via unique study recruitment coupon number. Index and partner reports were then compared among two types of dyads: female indexes and their male partners (labeled *female index dyads*) and male indexes and their female partners (labeled *male index dyads*).

Data were analyzed in three stages. First, frequency distributions were calculated to determine the distribution of selected HIV risk characteristics across dyads, stratified by index gender.

Second, for each HIV risk characteristic across dyads stratified by index gender, we calculated the distribution of the indexes' characteristic, stratified by their partners' characteristic.

Next, the mixing matrix, defined as the proportional cross-tabulation of the value of an index's risk characteristic with the corresponding value of their partners' risk characteristics,[13] was calculated for each selected HIV risk characteristic. Mixing matrices are not presented due to space constraints.

Finally, using a measure derived from the mixing matrix, the assortativity coefficient (r),[13] we compared the magnitude and direction of mixing for each HIV risk characteristic across all dyads (n=222) and within female index (n=166) and male index (n=56) dyads.[13, 40, 41, 78] To account for non-independence and informative cluster size (ICS) within dyads, the assortativity coefficient and corresponding 95% confidence interval (CI) for each characteristic was calculated using within-cluster resampling (WCR) methods recently proposed by Young and colleagues[76] (see Appendix A for a

complete description of these methods).

An assortativity coefficient > 0 indicates assortative mixing; when mixing is perfectly assortative, or when partnerships are only formed among similar individuals, $r = +1.0$. When mixing is random, $r \approx 0$ indicates that a characteristic has no influence on partnership formation. A coefficient < 0 indicates disassortative mixing; when mixing is perfectly disassortative, or when only dissimilar individuals partner, $r = -1.0$. A coefficient close to 0 may be interpreted as dissortative mixing because random mixing typically results in partnerships that differ with respect to a given characteristic.[13]

5.3. Results

5.3.1. Study Sample

Of the 209 index participants in the HCMC Sex Network survey, 145 recruited at least one and up to four partners (n=233). Indexes recruiting any partners were more likely than indexes recruiting zero partners to be female ($p<0.05$). Indexes not recruiting any partners (n=64) into the HCMC Sex Network survey were excluded from analysis. Since same-sex dyads may have different characteristics than heterosexual dyads, same sex dyads (n=11) were excluded from analysis.[18, 40, 79] The final sample for the present analysis (n=222 dyads) was comprised of 104 female indexes and 166 male partners (n=166 female index dyads) and 41 male indexes and 56 female partners (n=56 male index dyads).

5.3.2. Distribution of Risk Characteristics

Distributions of the selected HIV risk characteristics used to define risk groups were calculated across dyads, stratified by index gender (Table 5.1). Female indexes were primarily young (<30 years) and unmarried (64%); nearly a quarter (24%) were IDUs, 73% had exchanged sex, 71% had concurrent partnerships, 99% had been tested for HIV, and more than half (51%) were HIV-positive. Nearly half (47%) of their male partners were 30 years of age and older and 74% were unmarried; 30% were IDUs, 5% had exchanged sex, 60% had concurrent partners, 32% had been tested for HIV, and 25% were HIV-positive. Male indexes were primarily under age 30 (68%) and unmarried (83%); 34% were IDUs, 32% had exchanged sex, 71% had concurrent partnerships, 100% had been tested for HIV, and 32% were HIV-positive. The majority of their female partners were

young (equally distributed between 18 to 20 and 27 to 29 year age groups) and unmarried (80%); 16% were IDUs, 84% had exchanged sex, 75% had concurrent partnerships, 38% had been tested for HIV, and 89% were HIV-negative.

5.3.3.Mixing Assessments

Figures 5.1-5.3 display assortativity coefficients and 95% CIs for selected HIV risk characteristics across all dyads (Figure 5.1) and among dyads stratified by index gender (Figures 5.2 and 5.3). To aid in the interpretation of coefficients, Table 5.2 presents distributions of HIV risk characteristics among indexes stratified by sex partners' risk characteristics and gender for dichotomous measures. Distributions of multi-categorical measures (age group and residential location) are not shown due to space constraints.

5.3.4.Mixing Estimates across All Dyads

Demographics. Overall, mixing was assortative with respect to demographic characteristics; reflecting a tendency for participants to select partners similar to themselves with respect to age group ($r = 0.34, 95\%\ CI\ 0.19, 0.50$), marital status ($r = 0.57, 95\%\ CI\ -0.43, 0.71$), and residential location ($r = 0.57, 95\%\ CI\ 0.27, 0.55$).

Substance Use and Sexual Behaviors. Mixing by injecting drug use ($r = 0.07, 95\%\ CI = -0.09, 0.23$) and exchanging sex ($r = -0.19, 95\%\ CI\ -0.32, -0.07$) was disassortative across dyads; demonstrating that indexes involved in injecting drugs and exchanging sex generally chose non-injecting and non-exchanging partners.

In contrast, as a consequence of the high prevalence of concurrency (partnerships that overlap at a given point in time) across all strata of participants, mixing by concurrency was assortative ($r = 0.41, 95\%\ CI\ -0.27, 0.55$) overall.

HIV Testing and Serostatus. Mixing by HIV testing was disassortative ($r = 0.00, 95\%\ CI - 0.00, 0.01$) and assortative by HIV serostatus ($r = 0.44, 95\%\ CI\ 0.31, 0.57$) across dyads. The mixing estimate for HIV testing demonstrates the tendency for indexes, nearly all of whom had ever been tested, to choose partners that had never been tested. The point estimate for mixing by HIV serostatus primarily reflects HIV-negative indexes selecting HIV-negative partners.

5.3.5.Mixing Estimates across Dyads Stratified by Index Gender

Demographics. Demographic mixing differences were more pronounced when stratified by index gender. Female index dyads selected partners more similar to themselves than male index dyads by age group ($r = 0.62\ vs\ r = 0.34, respectively$), marital status ($r = 0.62\ vs\ r = 0.34, respectively$), and residential location ($r = 0.62\ vs\ r = 0.34, respectively$).

Drug Use and Sexual Behaviors. Mixing with respect to injecting drug use and exchanging sex was disassortative among both female and male index dyads. However, female indexes involved in injecting drug use and exchanging sex exhibited a slightly greater tendency to select non-injecting and non-exchanging partners ($r = 0.05$ and $r = 0.03$ among injecting and exchanging female indexes, respectively) than male indexes ($r = 0.10$ and $r = 0.11$ among injecting and exchanging male indexes, respectively). With respect to exchanging sex, however, the underlying partnership patterns differed between dyads stratified by index gender. Within female index dyads, the coefficient reflects the 73% of indexes exchanging sex (Table 5.1); of these, 93% had partners never exchanging sex (Table 5.2). Conversely, among male index dyads, the coefficient reflects the 68% of indexes never exchanging sex (Table 5.1); of these, 78% had partners never exchanging sex (Table 5.2).

Both female and male index dyads exhibited assortative mixing with respect to concurrency; however, mixing was highly assortative among male index dyads ($r = 0.62$) and less assortative among female index dyads ($r = 0.34$). Point estimates for r values suggest important gender differences in mixing by concurrency. Seventy-one percent of both female and male indexes were engaged in concurrent partnerships (Table 5.1); therefore, the difference in estimates likely reflects the higher prevalence of concurrent partnerships among the partners of male (89%) as compared to female (68%) indexes (Table 5.2).

HIV Testing and Serostatus. Mixing by HIV testing was disassortative among female index dyads ($r = 0.00$) and assortative among male index dyads ($r = 0.49$). Nearly all (99%) female and all (100%) male indexes had ever been tested for HIV; therefore, the difference in estimates is likely driven by (1) the higher prevalence of untested partners among female as compared to male indexes and (2) the higher absolute number of female as compared to male dyads.

In contrast, mixing by HIV serostatus was assortative among female $(r = 0.40)$ and male $(r = 0.49)$ index dyads. The small difference in gender-stratified estimates likely results from the 49% of HIV-negative female indexes (Table 5.1); of these, 8% had at least one HIV-positive partner (Table 5.2). By comparison, no HIV-negative male indexes selected an HIV-positive partner (Table 5.2).

5.4. Discussion

This study is the first to describe predominant patterns of heterosexual partnership selection, or mixing, among a network of sexual contacts at elevated HIV risk in HCMC, Vietnam. This network was already at elevated risk for both acquiring and transmitting infection; therefore, it was not particularly surprising to find that approximately one-third (33%) of contacts were HIV-positive, as well as a high prevalence of injecting drug use, exchanging sex, and partnerships overlapping in time (concurrent partnerships) within the network.[80] Using novel WCR methods,[76] however, illustrated multiple, distinct mixing patterns contributing to the spread of HIV within this network and potentially, across networks.

Overall, patterns of highly assortative demographic partnership selection emerged; reflecting the tendency of young and unmarried men and women to select other young and unmarried sexual partners living within their same districts. Simultaneously, we observed overall patterns of disassortative mixing with respect to injecting drug use and exchanging sex; demonstrating that contacts' injecting drugs and exchanging sex generally chose non-injecting and non-exchanging partners. Taken together, these patterns suggest that this is a localized network of young and unmarried men and women at risk for both acquiring and transmitting HIV infection, and among whom infection is likely to persist. Further, injecting and exchanging contacts are likely to remain important reservoirs of infection within this network.

Particularly noteworthy, was the identification of an overall pattern of highly assortative mixing by concurrency, or the tendency for network members with concurrent partnerships to partner with other network members in concurrent partnerships. By eliminating the protective effect of partnership sequencing and reducing the time between sexual contacts, this pattern increases the connectivity of the network (number of partnerships connected at any given point in time), allowing HIV to spread more rapidly than a pattern of serially monogamous partnerships.[28, 81] Consequently, without

increases in harm reduction and protective behavior, an amplified risk of heterosexual transmission exists not only within this network at elevated risk, but potentially, across networks.

Important overall partnering patterns by HIV serostatus and testing also emerged. Assortative mixing by HIV serostatus reveals a limited degree of serosorting (partnering with individuals of similar HIV status) within the network. However, given reportedly high levels of inconsistent and non-existent condom use among IDUs and SWs in HCMC,[47] future transmission risk within the network could only be eliminated under perfectly assortative mixing conditions. While transmission was not directly measured in this analysis, risk is especially apparent among HIV-positive male (43%) and female (56%) indexes reporting at least one HIV-negative partner. These serodiscordant partnerships are particularly concerning given that less than 40% of all partners had never been tested for HIV, suggesting that, if infected, a high risk of secondary transmission exists.

Generally, female index dyads chose partners more like themselves with respect to age group, marital status, residential location, and to a lesser extent, injecting drug use, than male index dyads. In contrast, male index dyads tended select partners more like themselves than female index dyads in terms of exchanging sex, concurrency, HIV testing, and HIV serostatus. With the exception of HIV testing, however, differences in gender stratified point estimates were not statistically significant. Our findings suggest that differences in gender-stratified point estimates were likely driven by the (1) uneven distribution of participants across categories of specific demographic characteristics; and (2) lower absolute participant numbers among male (n=56) as compared to female (n=166) dyads. For example, in the case of mixing by marital status, the lower coefficient among male dyads likely results from the low absolute number of married male indexes (7 total indexes) and their partners, both married (4 partners) and not married (3 partners).

An important avenue for future research will be to investigate differences in partnership selection between men and women as our initial results indicate they may have important implications for disease spread and resource allocation. For example, if the gender-stratified point estimates for residential location reflected a true differential in mixing among women and men it would imply that female indexes' networks were localized, while male indexes were further reaching (i.e., spanned districts). In turn, these patterns would suggest prevention approaches targeting women living in high-

prevalence districts throughout HCMC, and targeting men who travel between districts (perhaps traveling out of necessity for work).[82] Additionally, future research should examine mixing patterns across multiple risk categories simultaneously. Engagement in "compound risk" may increase frequency and type of exposure, increasing cumulative transmission probability.[83]

These results should be interpreted keeping in mind certain limitations. Constructing a network of sexual contacts requires non-random sampling; therefore, mixing patterns among our study population may not be representative of patterns among other networks at elevated risk in HCMC, HCMC's general population, or other parts of Vietnam. However, the sample was relatively evenly distributed throughout HCMC; therefore, it is likely that results are representative of similar groups at elevated risk in HCMC. Data are cross-sectional, so causality between mixing patterns and HIV acquisition and transmission cannot be assessed. Indexes were only asked to recruit up to 4 partners; it is unlikely that partners with weaker ties to index participants were captured (e.g., more casual partners). Research suggests, however, that the majority of risk behaviors take place in relationships resulting from strong ties (i.e., with partners likely to be recruited into our study).[84]

Despite these limitations, our findings describe important aspects of partnership selection and have important implications for understanding HIV transmission dynamics within this network. To the extent that these patterns reflect mixing among similar networks at elevated risk in HCMC, these findings help to identify groups that may be at future risk of both HIV acquisition and transmission in HCMC, Vietnam. These findings also highlight the need for specific prevention interventions discussed in Chapter 7.

5.5. Tables

Table 5.1 Distribution of Selected HIV Risk Characteristics Stratified by Index Gender and Recruitment Status within Dyads, HCMC Sex Network Survey, Vietnam, 2009

	Female Dyads				Male Dyads			
	Index (n=104)		Partner (n=166)†		Index (n=41)		Partner (n=56)†	
HIV risk characteristic	%	n	%	n	%	n	%	n
Age group								
18-20	7.7	8	3.0	5	4.9	2	21.4	12
21-23	15.4	16	11.4	19	14.6	6	12.5	7
24-26	22.1	23	16.3	27	26.8	11	19.6	11
27-29	27.9	29	22.3	37	22.0	9	21.4	12
30-32	16.3	17	19.3	32	17.1	7	17.9	10
≥33	10.6	11	27.7	46	14.6	6	7.1	4
Marital status								
Not married	63.5	66	74.1	123	82.9	34	80.4	45
Married	36.5	38	25.9	43	17.1	7	19.6	11
Injection drug use								
Never	76.0	79	70.5	117	65.9	27	83.9	47
Ever	24.0	25	29.5	49	34.1	14	16.1	9
Exchange sex								
Never	26.9	28	94.6	157	68.3	28	16.1	9
Ever	73.1	76	5.4	9	31.7	13	83.9	47
Concurrent partners (past 3 months)								
No	28.9	30	40.4	67	29.3	12	25.0	14
Yes	71.2	74	59.6	99	70.7	29	75.0	42
HIV testing								
Never	1.0	1	68.1	113	0	0	62.5	35
Ever	99.0	103	31.9	53	100	41	37.5	21
HIV serostatus								
Negative	49.0	51	74.7	124	68.3	28	89.3	50
Positive	51.0	53	25.3	42	31.7	13	10.7	6

†The number of sexual partners is higher than the number of indexes as a result of some indexes recruiting multiple sexual partners (range, 1 to 4).

The distribution of residential location across response categories is not shown due to space constraints.

Table 5.2 Indexes' HIV Risk Characteristics Stratified by Sexual Partners' HIV Risk Characteristics, HCMC Sex Network Survey, 2009

	Female Indexes					Male Indexes			
Male Partners*	%		n		Female Partners*	%		n	
Marital status	**Not married**		**Married**		**Marital status**	**Not married**		**Married**	
Not married	88.2	105	38.3	18	Not married	85.7	42	42.9	3
Married	11.8	14	61.7	29	Married	14.3	7	57.1	4
Injection drug use	**Never**		**Ever**		**Injection drug use**	**Never**		**Ever**	
Never	74.6	94	57.5	23	Never	85.0	34	81.3	13
Ever	25.4	32	42.5	17	Ever	15.0	6	18.7	3
Exchange sex	**Never**		**Ever**		**Exchange sex**	**Never**		**Ever**	
Never	100	30	93.4	127	Never	21.4	9	0	0
Ever	0	0	6.6	9	Ever	78.6	33	100	14
Concurrent partners†	**No**		**Yes**		**Concurrent partners†**	**No**		**Yes**	
No	80.0	24	31.6	43	No	81.8	9	11.1	5
Yes	20.0	6	68.4	93	Yes	18.2	2	88.9	40
HIV testing	**Never**		**Ever**		**HIV testing**	**Never**		**Ever**	
Never	75.0	3	67.9	110	Never	0	0	62.5	35
Ever	25.0	1	32.1	52	Ever	0	0	37.5	21
HIV serostatus	**Negative**		**Positive**		**HIV Serostatus**	**Negative**		**Positive**	
Negative	91.8	78	56.8	46	Negative	100	42	57.1	8
Positive	8.2	7	43.2	35	Positive	0	0	42.9	6

*Partners refer to sexual partners (range, 1 to 4).

†Refers to concurrent partnerships within the 3 months prior to study interview.

Distributions of age group and residential location across response categories are not shown due to space constraints.

5.6. Figures

Figure 5.1 Sexual Mixing Assortativity Coefficients and 95% Confidence Intervals Among All Dyads, HCMC Sex Network Survey, 2009

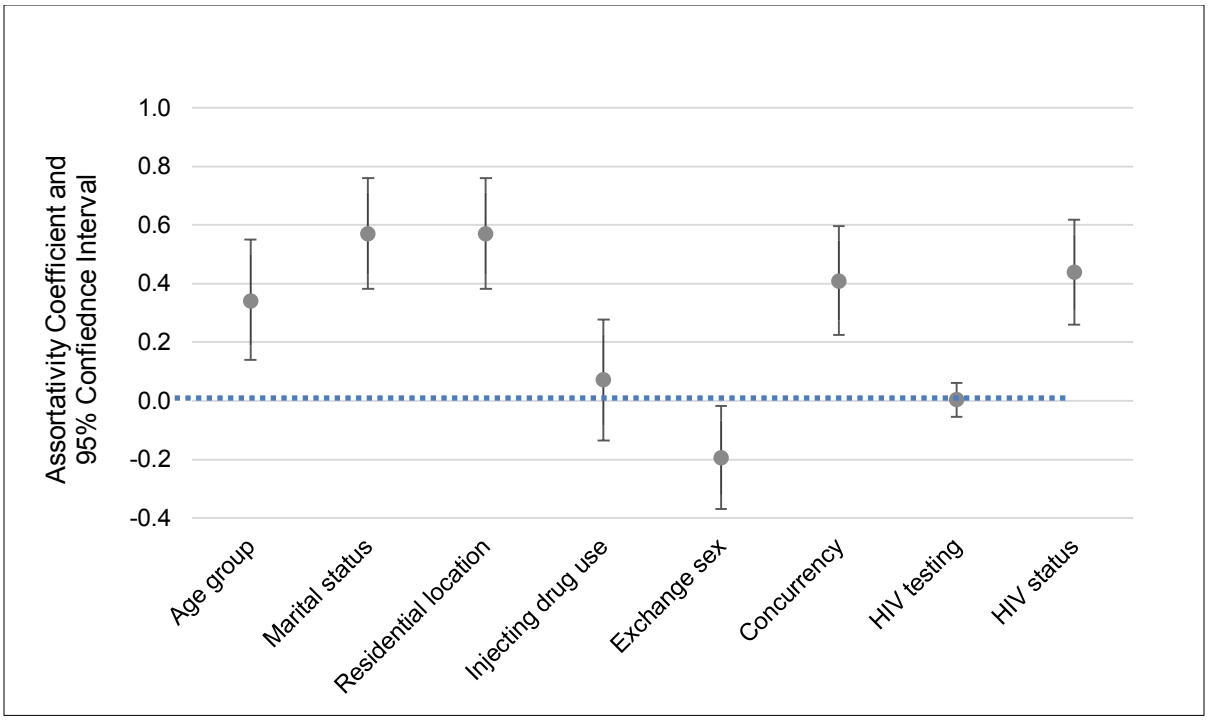


Figure 5.2 Sexual Mixing Assortativity Coefficients and 95% Confidence Intervals Among Female Dyads, HCMC Sex Network Survey, 2009

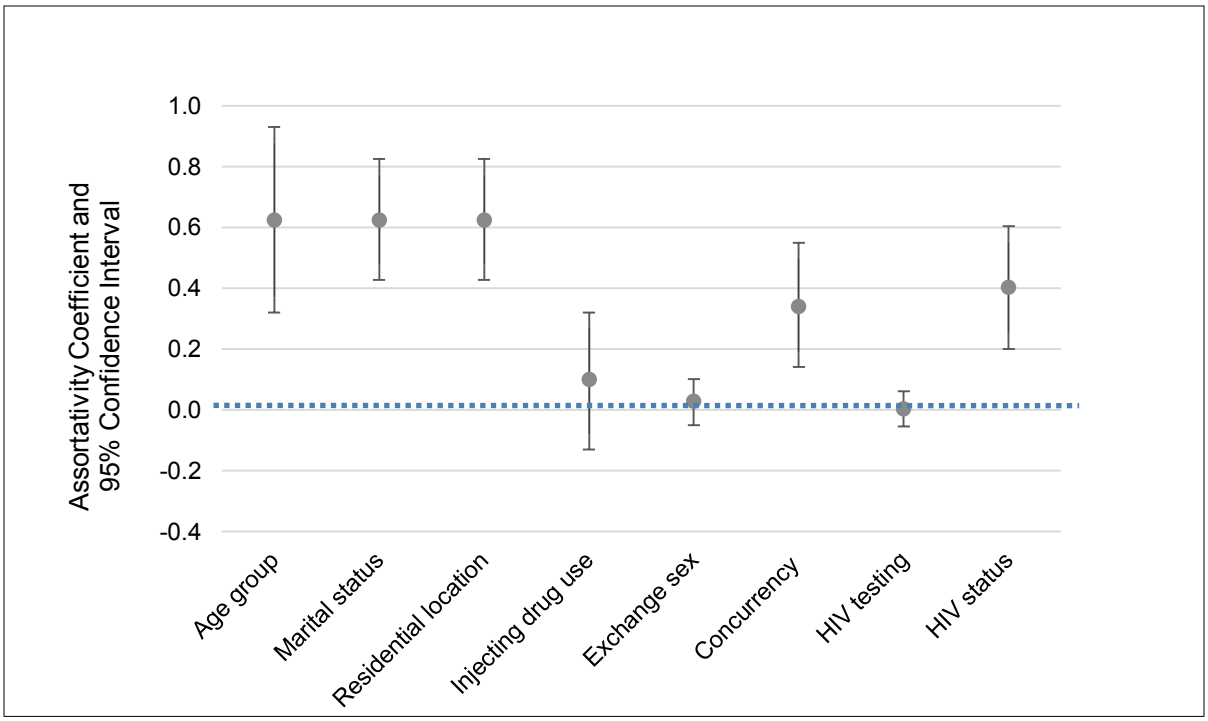
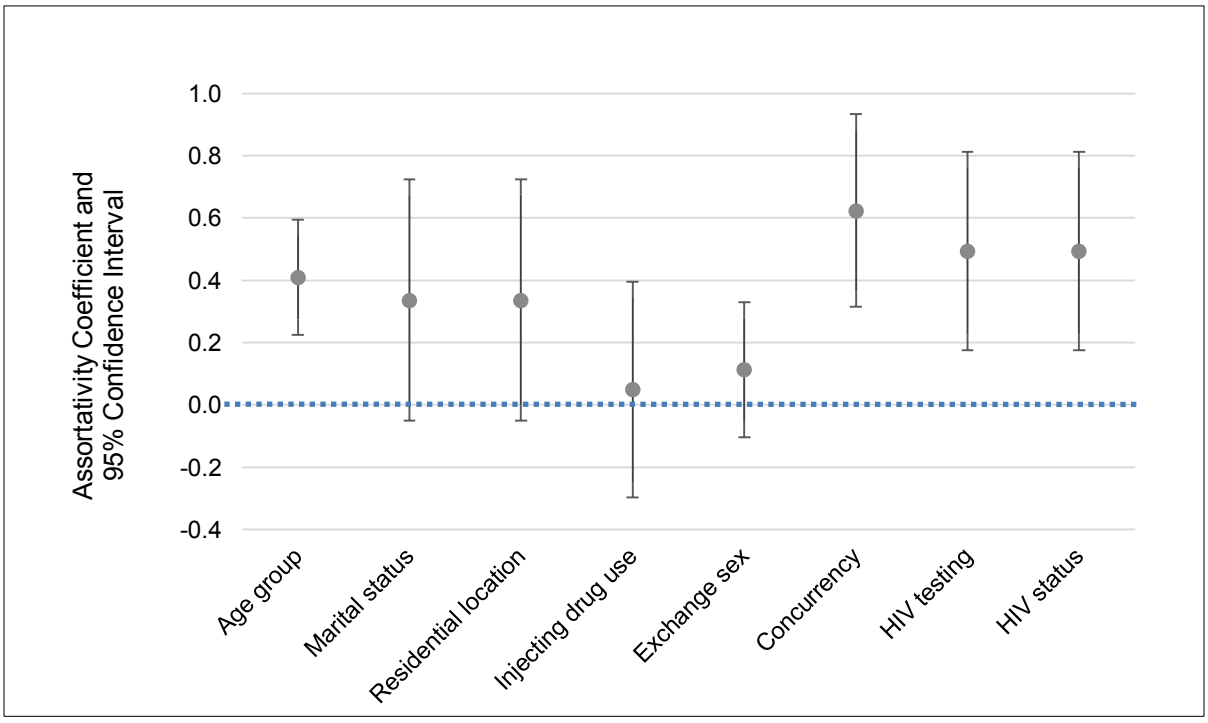


Figure 5.3 Sexual Mixing Assortativity Coefficients and 95% Confidence Intervals Among Male Dyads, HCMC Sex Network Survey, 2009



Chapter 6: Characterizing the Egocentric Sexual Networks of Sex Workers and Non-Sex Workers in Ho Chi Minh City, Vietnam

6.1. Introduction

HIV prevalence is increasing among all women in Vietnam, including those traditionally considered to be at higher (e.g., SWs) and lower risk (e.g., non-SWs) because of their own risk-taking behavior.[49] In Ho Chi Minh City (HCMC), according to an estimation and projection study by the country's Ministry of Health (MOH), from 2000 to 2010, HIV prevalence increased 59% among higher-risk women and 700% among lower-risk women; resulting in an increase in prevalence from 0.10% to 0.80% among all women.[49,53] This increase in transmission among women raises important questions about women, their partners, and their broader HIV risk environment in Vietnam.

HIV is largely a behaviorally transmitted disease subject to relative risk and population-level variations in characteristics and behaviors.[16] An accumulating body of research suggests that an individual's proximity to risk, perception of risk, and subsequently, their probability of engaging in risky behavior that results in HIV exposure is not only a result of their own characteristics and behavior.[4, 31, 85-87] Rather, it is also a function of their social and sexual contacts (i.e., social and sexual networks) and HIV prevalence within these networks. [4, 25, 31, 85-87]

An individual's personal (i.e., egocentric) sexual network is defined by those partners with whom they have direct sexual contact.[11] Characterizing egocentric sexual networks enhances our understanding of who may be at risk of infection, and behavior that may be considered risky, by identifying who has a high probability of coming into contact with an HIV infected partner.[11, 20] Studies have demonstrated that measuring individual's sexual network composition (e.g., number and type of partners)[4, 11] and risk exposure (defined as the degree of partner's engagement in a specific risk behavior, such as injecting drug use), may illustrate potential network influences on individual decision-making in response to risk.[11]

Despite the established link between an individual's HIV risk and the 'riskiness' of their partners, there is a paucity of research describing women's risk and the context in which this risk occurs; especially, among behaviorally distinct groups of women (e.g., SWs and non-SWs).[59] Given that unsafe heterosexual sex recently surpassed injecting drug use as the primary mode of HIV transmission and increasing prevalence among all women in Vietnam, to better inform intervention approaches it is important to understand how their personal risk-taking and partnership patterns may be contributing to their HIV risk.

Using data from a network of sexual contacts at elevated HIV risk in HCMC, Vietnam, the purpose of this paper is to describe and compare personal risk-taking and partnership patterns among behaviorally distinct groups of women. Specifically, we examine differences in personal risk-taking and recent egocentric sexual network partners between SWs and non-SWs.

6.2. Methods

6.2.1. Current Study Sample

Two hundred and forty women participated in the HCMC Sex Network survey (Figure 6.1). The present analysis is limited to women participating in the HCMC Sex Network survey who provided responses to two questions assessing past 30 day and lifetime sex work (n=237).

In addition to recruiting sexual partners for survey participation, participants identified and self-reported data on at least one and up to five nominated egocentric sexual network partners (n=886). Since same-sex partnerships may have different characteristics than heterosexual partnerships,[18, 40, 79] same-sex partners (n=7) were excluded. The final sample for the present analysis comprised 237 women and their 879 nominated, male, and egocentric sexual network partners (labeled 'partners').

6.2.2. Recruitment and Procedures

Recruitment and procedures for the HCMC Sex Network survey have been described in Chapter 4. Briefly, all women participating in the HCMC Sex Network survey were eligible as either: 1) participants at elevated risk for the sexual acquisition and transmission of HIV recruited from the Incidence study (i.e., index participants); or 2) having been recruited as a sexual partner of an index participant in the HCMC Sex Network survey (i.e., referral participants).

6.2.3. Measures

Survey information, including demographics, STI history and testing, sexual and drug use behavior, and egocentric sexual network data, was reported by participants about themselves and, about their one to five nominated partners. Individual and egocentric sexual network characteristics that may influence HIV risk were considered for this analysis and are described below.

6.2.4.Sex Worker Status

Sex Worker status. Participants who reported ever selling or exchanging sex for money and/or drugs were classified as SWs. All other participants were classified as non-SWs. Recognizing that women engaged in commercial sex work may be different than women engaged in more episodic transactional sex,[88] we conducted two sensitivity analyses; first, restricting the SW definition to women reporting selling or exchanging sex in the past 30 days and second, restricting the definition to women identifying their occupations as SWs. Results did not differ based on definition.

6.2.5.Individual-Level Risk Characteristics

Demographics. Participants provided data on *age*, *education level* (dichotomized as less than secondary school vs. secondary school or higher), *current marital status* (dichotomized as married vs not married), and *personal weekly income* (collapsed by quartile).

Injecting risk behavior. Participants with a biologically confirmed positive urine test for opiate use, or ever injecting drugs for use other than medicine, were considered injection drug users (IDUs).

Sexual risk behaviors. Two measures assessed sexual risk behaviors, including: *number of sex partners* (past month) and having engaged in *concurrent partnerships* (past three months). Concurrency was measured as the number of days since last sex with 2nd most recent partner minus the number of days since first sex with more recent partner in the three months prior to survey interview.[77] Participants with zero or negative days between partnerships were considered concurrent, while participants with positive gaps between partnerships were considered to have not engaged in a concurrent partnership.

HIV status and *STI symptoms*. Participants with detectible HIV antibodies on two HIV EIA assays and one rapid test were considered HIV-positive. Participants answering “yes” to the question, “Are you HIV positive?”, were also considered HIV-positive. Participants answering “yes” to at least

one of the following questions: “Have you had…1) vaginal discharge?; 2) painful urination?; 3) vaginal itching or burning?; and/or 4) a sore on your vagina?” were considered to have had past year STI symptoms.

6.2.6.Egocentric Sexual Network-Level Risk Characteristics

A sexual network inventory (detailed series of questions about each partner and the relationship between the respondent and each partner) was used to collect data on participants’ recent egocentric sexual networks. For the purposes of this study, participants’ recent *egocentric sexual networks* (labeled ‘networks’) are defined as their one to five nominated sexual partners from the three months prior to interview. Questions elicited information from participants regarding their network composition (e.g., partner age, partner type), as well as perceived and event-level risk exposure. Event-level risk exposure questions elicited information on last sex between participant and partners (e.g., dates of first and last sex and whether or not a condom was used). All network measures defined below refer to these one to five partners.

Composition. Three measures assessed network composition, including: (1) *partner age* (defined as average age of all partners of a participant); (2) *partner type* (defined as number of partners considered husbands/live-in, boyfriends/non-live-in, casual, regular clients, or one-time clients); and (3) *partner time-in-network* (defined as number of one time partners and partners known for ≤ 6 months, 6 months to < 1 year, or ≥ 1 year).

Perceived and event-level risk exposure. Perceived risk exposure was measured by asking participants whether partner(s): (1) had ever injected drugs; (2) had ever had sex with a man; (3) had had other (concurrent) sexual partners (in addition to the participant) in the past three months; and (4) was HIV-positive.

Event-level risk exposure was determined by *condom use* and was measured as the number of partners with whom a participant used a condom at last vaginal sex, and then dichotomized for analysis (no vs. yes).

6.2.7.Analysis

Data were analyzed in three stages. First, to compare SWs and non-SWs, a series of descriptive statistics were calculated. To test for bivariate differences in individual-level risk

characteristics between groups, comparisons were made using Pearson's X^2 test for categorical variables and two-sample Wilcoxon rank-sum (Mann-Whitney) tests ranks for continuous variables.

Next, SWs' and non-SWs' network compositions were compared. Means and standard deviations (SD) were reported for continuous measures, and number and frequency are reported for categorical measures. For highly skewed continuous measures, medians and ranges are included to aid with interpretation. Some continuous measures (e.g., average partner age) were taken across up to five partners making it necessary to account for within-participant variability. This was done by first, calculating each participant's average partner age (within-participant average), followed by calculating an average partner age across all participants (between-participant average) using within-participant averages weighted by the reciprocal of their respective variances.

Finally, summary profiles (i.e., number and frequency of total number of partners) were generated to compare SWs' and non-SWs' networks in terms of perceived and event-level risk exposure.

6.3. Results

6.3.1. Sample Characteristics

Of the 237 female participants, 192 (81%) were SWs and 45 (29%) were non-SWs (Table 6.2). Among SWs, 67% nominated the maximum of five partners, for a total of 833 partners. In contrast, only one non-SW nominated more than one partner, for a total of 46 nominated partners.

6.3.2. Individual-Level Risk Characteristics

SWs' and non-SWs' individual-level risk characteristics and behaviors are compared in Table 6.3. On average, SWs were similar in age to non-SWs (26 vs. 27 years, respectively). SWs were significantly less likely than non-SWs to have completed secondary school (20% vs. 40%, respectively; $p=0.001$) and be currently married (19% vs. 87%, respectively; $p<0.0001$). However, non-SWs were three and a half times more likely than their counterparts to be very poor, or have personal weekly income below the poverty line at less than 500,000 VND (≈ $24 USD).

While SWs and non-SWs were similar in terms of injecting risk (24% vs. 18% were IDUs, respectively), there was significant heterogeneity between them across sexual risk taking behaviors and STI history. SWs were significantly more likely to have a higher average number of past month

partners (mean=21 vs. 1 partner(s); p<0.0001) and to have concurrent partners (92% vs. 6%, respectively; p<0.001). STI prevalence was significantly higher among SWs than non-SWs (77% vs. 51%, respectively; p<0.001). However, HIV prevalence was more than three times higher among non-SWs compared to SWs (84% vs. 25%, respectively; p<0.0001).

6.3.3. Network-Level Risk Characteristics

Network composition and risk exposure differed between the two groups (Tables 6.4 and 6.5). On average, SWs' partners were older than those of non-SWs (34 vs. 31 years; respectively). SWs' networks predominately consisted of clients (75%); of these, 25% were one-time clients. SWs reported knowing 38% of partners from one week to six months. In contrast, non-SWs' networks consisted of long-term, primary partners, including husbands (96%) and boyfriends (2%), and partners known for one year or more (96%).

SWs did not know if at least one-third of partners were exposing them to risk, across all perceived risk categories. However, SWs did believe 48% of partners had concurrent partners. In contrast, non-SWs believed they knew of their risk exposure from the majority of partners, across all perceived risk categories. Non-SWs believed 59% of partners were IDUs; 8% had concurrent partners, and 4% had ever had sex with another man.

Partners' perceived HIV serostatus provided the largest difference in perceived risk exposure between groups. SWs did not know the HIV status of 93% of partners. In contrast, non-SWs believed they knew 98% of partners' HIV status; of these, they believed 87% were HIV-positive.

Despite mixed perceptions of network risk exposure, the proportion of last vaginal sexual encounters where a condom was not used was high among both groups (45% and 35%, respectively among SWs and non-SWs).

6.4. Discussion

Our study is the first to demonstrate SWs' and non-SWs' predominate patterns of personal risk-taking and sexual partnering in HCMC, Vietnam. In addition, it contributes to a limited body of sexual network research illustrating the potential for partnership patterns to influence the risk of both acquiring and, transmitting, HIV infection. This study sample involved SWs and non-SWs from a network of sexual contacts already at elevated HIV risk; therefore, it was not particularly surprising to

find a high proportion of HIV-positive SWs. It was quite surprising however, to discover that the proportion of HIV positive non-SWs was more than three times higher than SWs. Notably, we observed non-SWs' own risk taking behavior was low; however, non-SWs' had a high frequency of exposure to HIV-infected primary partners via unprotected sex likely resulting in their HIV infection. In comparison, SWs demonstrated a lower frequency of exposure to HIV infected partners and a higher frequency of individual risk-taking behavior likely resulting in their HIV infection. Together, these findings demonstrate that different personal risk-taking and sexual partnering patterns may influence HIV risk among behaviorally distinct groups of women. In the absence of condom use, these findings imply that women, even those whose own behavior is low risk, may be at increased risk if they are sexually connected to risky partners, even if they have just one, trusted, long-term, primary partner.

Both SWs and non-SWs were poor. However, non-SWs were significantly more likely to be very poor and married women than SWs. It is well established that, among women, both poverty and marriage[21, 71] are correlated with increased risk of HIV infection.[85, 89] The association between poverty and HIV is complex, but appears to result from the manifestation of structural (e.g., political, social, cultural, economic, and gender) inequalities within the sexual partnership.[89]

Qualitative research in Vietnam, for example, argues that national policies have declared sex work a "social evil" and linked both the country's economic prosperity, as well as women's socio-economic survival, to the existence of "happy, wealthy, and stable families".[59, 82, 90-92] These policies are diffused and reinforced within partnerships by traditional Confucian socio-cultural norms that legitimize men's control over the timing, nature, and frequency of sexual contact, as well as the decision to use condoms and have multiple sex partners.[59, 82, 90-93] This dynamic restricts communication between partners and limits women's abilities to negotiate safer sex; particularly among married women. [89, 91, 94]

Intertwining inequalities have created a marital ideal in Vietnam that defines fidelity by financial stability[97, 99] and emphasizes protecting men's social risk (i.e., threats to their reputation), rather than preventing their physical risk of acquiring HIV and transmitting infection to their primary partners.[94] For women, and married women in particular, failure to conform to socio-cultural and sexual partnership norms is commonly met with coercion, physical and sexual violence, loss of

financial support, and threats of familial abandonment.[82, 91] Therefore, to serve the larger goal of publically appearing to be a "happy, wealthy, stable" family, married women have prioritized the appearance of fidelity above acknowledging that their partners may be placing them at risk.[94] In turn, these inequalities reinforce monogamous and married women's economic dependence and decrease their ability to negotiate condom use and to leave risky sexual relationships.[89]

Paradoxically, the same patterns increasing non-SWs' HIV risk also provide the structure and opportunity for men to seek extramarital partners, and in turn, heighten SWs' economic potential.[91, 94, 95] Stigmatization and marginalization notwithstanding, this may enhance (albeit only slightly) SWs control over their choice in sexual partners and behavior within partnerships.[89]

SWs' and non-SWs' partnering patterns illustrate the differing influence of entrenched structural inequalities on their exposure to risky partners. SWs' had a high number of partners; of whom the majority, were clients (75%) and short-term partners (64% known for less than six months). Each of these factors is correlated with an increased risk of HIV infection. However, SWs believed only 2% were HIV-positive, 11% were IDUs, and 3% were MSM. This suggests that, despite high sexual activity, SWs' direct exposure to HIV, IDU, and MSM (i.e., risky) partners was low. SWs' did believe nearly half (48%) of partners had concurrent partners which implies direct and indirect exposure to risky partners. Awareness of this risk, however, may have encouraged SWs' condom use with these 'risky' partners, resulting in their lower risk of infection from risky partners.

In contrast, non-SWs', with one exception, had a single, long-term, primary partner. Despite low sexual activity levels, however, non-SWs' believed that 59% of partners were IDUs and 87% were HIV-positive which demonstrates direct connections to risky partners. Moreover, non-SWs' believed that very low proportions of partners had concurrent (<9%) and MSM (<3%) partners, both well-established risk factors for acquiring infection.[28, 96] These figures likely underestimate the true frequency of non-SWs' concurrent and MSM partners and subsequently, their risk of exposure to infection given 1) the high-risk nature (e.g., high frequency of HIV, injecting drug use, and exchanging sex) of the larger network of sexual contacts from which this sample was drawn; 2) cultural norms dictating a "compulsory heterosexuality"[94] that compels men with same-sex desires to marry women and not disclose their MSM partnerships; and 3) SWs' belief that more than a third of their partners

(i.e., clients) had concurrent partners. Overlap between SWs' and non-SWs' partners was not directly measured in this analysis; however, it is not only possible, but probable given the larger network's high-risk nature. Taken together, these findings are consistent with research showing that having a partner from a high-risk group is associated with a greater risk of infection than a higher number of partners.[12, 29, 75]

Despite the risk from HIV-positive, injecting, and other, potentially risky partners, our findings suggest that non-SWs did not perceive their primary partners to be particularly risky. This may help to explain non-SWs' continued engagement in unsafe sex with their partners. Feelings of intimacy may interfere with rational risk perception, preventing a partner from being seen as risky, or as a source of infection.[97, 71] Research has also shown that people, particularly those in long-term partnerships, are often unable to introduce condoms into relationships without violating shared norms and trust.[5] Therefore, non-SWs' low frequency (65%) of condom use at last vaginal sex was with partners was not unexpected. Nevertheless, it is concerning; especially, given non-SWs' awareness of partners' HIV-positive serostatus and injecting risk. This figure is also likely to be an overestimate as it is much higher than estimates traditionally found in committed partnerships in Vietnam (range, 9% to 8%) and aligns with the importance of social desirability among poor, marginalized, married women.[94] Yet, overestimation only reinforces our concern, as it means actual condom use among non-SWs is even lower. Our findings are consistent with the limited research on influence of partner risk on individual behavior showing that economically disadvantaged women do not change their sexual behavior in response to being made aware of exposure to risky partners.[71]

These patterns demonstrate that poor, monogamous, and married women in HCMC may be at very high risk of acquiring HIV as a result of their sexual connections to high-risk primary partners. This result parallels the larger trend in HCMC, and Vietnam, of increasing prevalence among women traditionally considered lower risk (non-SWs and non-IDUs) and husband-to-wife transmission; underscoring the importance of targeting non-SWs (i.e., married women) for future prevention efforts in HCMC. Specifically, these results reveal an extremely urgent need for interventions that go beyond making women aware of their partners' risk (e.g., know your partner interventions) to focus on women's empowerment[93] and couples-based prevention efforts.

In comparison, SWs' patterns of individual risk-taking and sexual partnering illustrate their risk for not only acquiring, but transmitting infection. SWs' acquisition risk is primarily illustrated by their own high levels of injecting drug use and sexual activity.[86, 89] SWs' were largely unaware of their partners' injecting- and HIV-status, also likely contributing their risk of exposure to infection.[22] Mizuno et al[98] recently showed that HIV-positive IDUs with partners of 'unknown' HIV status, in comparison to those with HIV-negative and HIV-positive partners, consistently demonstrated the riskier behaviors and felt less empowered to disclose their HIV status and use condoms at last vaginal sex. In combination with SWs' low frequency of condom use at last vaginal sex with partners, having partners of unknown HIV status puts 75% of HIV-negative SWs at risk of acquiring infection from potentially infected partners and 25% of HIV-positive SWs at risk of transmitting infection to potentially uninfected partners.

SWs' transmission is risk further exhibited by their high frequency of concurrent[28] and short-duration[19] partnerships. Moreover, SWs believed that 48% of their partners also had concurrent partners. This pattern suggests that not only is the effect of concurrency likely to be amplified within SWs' networks, but that a high-risk of secondary transmission exists. [28]

The results of this analysis should be interpreted keeping in mind certain limitations. First, this was not a random sample; therefore, it may not be representative of all women at elevated HIV risk in HCMC. The cross-sectional nature of this study does not allow us to identify the temporal relationship between SW status and individual- or partner-specific risk. With the exception of biological test results, data were based on participants' self-reports. Validity and reliability of self-reported data may be compromised due to social desirability bias. All network data were egocentric and thus, derived from participants without partner corroboration. Finally, participants were only asked about one to five recent partners and may have had more than five partners.

These findings enhance our understanding of different patterns of individual risk-taking and sexual partnering and their potential influence on the risk of HIV acquisition and transmission among SWs and non-SWs. Most importantly, these patterns reflect an urgent need for intervention efforts tailored to the unique needs of behaviorally distinct women and their partners to prevent future waves of infection in HCMC, Vietnam.

6.5. Tables

Table 6.1 Number of Nominated Egocentric Sexual Network Partners Reported by SWs and Non-SWs, HCMC Sex Network Study, Vietnam, 2009

	SWs (n=192)		Non-SWs (n=45)	
	%	n	%	n
Number of partners* (range, 1 to 5)				
1	4.2	8	97.8	44
2	3.1	6	2.2	1
3	13.0	25	0	0
4	12.5	24	0	0
5	67.2	129	0	0

SWs indicates sex workers; Non-SWs indicates non-sex workers

*Refers to the number of nominated egocentric sexual network partners.

Table 6.2 Demographic and Risk Characteristics Reported by SWs and Non-SWs, HCMC Sex Network Study, Vietnam, 2009 (n=237)

	SWs (n=192)		Non-SWs (n=45)		*p*-value*
	%	n	%	n	
Demographics					
Age					
Mean (SD)	(4.6)	26.2	(3.3)	27.1	0.146
Range		17-37		20-35	
Median		26.5		27.0	
Education level					
< Secondary school	80.2	154	60.0	27	0.01**
≥ Secondary school	19.8	38	40.0	18	
Current marital status					
Not married	81.2	156	13.3	6	<0.0001***
Married	18.8	36	86.7	39	
Personal weekly income (quartiles), VND					
≤ 500,000	19.2	37	82.2	37	<0.0001***
500,001-1,000,000	34.4	66	11.1	5	
1,000,001-1,500,000	18.8	36	6.7	3	
≥ 1,500,001	27.6	53	0	0	
Injecting risk behavior					
Injection drug use					
Never	76.0	146	82.2	37	0.374
Ever	24.0	46	17.8	8	
Sexual risk behaviors					
No. of sex partners (past month)					
Mean (SD)	(16.7)	20.8	(0.30)	1.0	<0.0001***
Range		1-100		1-3	
Median		16.0		1.0	
Concurrent partners (past 3 months)					
No	7.7	15	93.6	44	<0.001**
Yes	92.3	177	6.4	3	
STI infection history					
Any STI symptoms (past year)¥					
No	23.0	44	48.9	22	<0.001**
Yes	77.0	147	51.1	23	
HIV serostatus					
Negative	74.5	143	15.6	7	<0.0001***
Positive	25.5	49	84.4	38	

SW indicates female sex worker; Non-SW indicates female non-sex worker; SD indicates standard

deviation; VND indicates Vietnamese Dong ($1 U.S. = 21,070 VND at the time of this publication); IDU indicates injection drug user; and MSM indicates men who have sex with men.

*Pearson's chi-square statistic was used to compare the distribution of categorical variables; Kruskal-Wallis chi-square statistic was used to compare the distribution of continuous variables; significance: **p≤0.001, ***p<0.0001.

¥Due to missing values for the characteristic among SWs, n=191.

Table 6.3 Egocentric Sexual Network Composition Reported by SWs and Non-SWs, HCMC Sex Network Study, Vietnam, 2009 (n=879)*

	SWs' Networks† (n=833)		Non-SWs' Networks† (n=46)	
Network† composition	%	n	%	n
Partner age				
Mean (SD)	(9.5)	33.9	(5.3)	30.5
Range		18-77		21-48
Partner type(s) included in network				
Husband/live-in partner	6.6	55	95.6	44
Boyfriend	13.2	110	2.2	1
Casual partner	5.6	47	2.2	1
Regular client	42.9	357	0	0
One-time client	31.7	264	0	0
Partner time-in-network				
One time	25.2	210	0	0
1 week to 6 months	38.4	320	0	0
> 6 months, but < 1 year	12.1	101	4.4	2
≥ 1 year	24.3	202	95.6	44

SW indicates female sex worker; Non-SW indicates female non-sex worker

† Networks refer to participants' 1 to 5 nominated egocentric sexual network partners.

*n is higher than the number of participants due to participants reporting on multiple partners (n=the number of nominated sexual partners, range 1 to 5).

Table 6.4 Perceived and Event-Level Egocentric Sexual Network Risk Characteristics Reported by SWs and Non-SWs, HCMC Sex Network Study, Vietnam, 2009 (n=879)*

	SWs' Networks† (n=833)		Non-SWs' Networks† (n=46)	
	%	n	%	n
Perceived risk characteristic				
Perceived injection drug use				
Partner has never used injection drugs	55.3	461	41.3	19
Partner has ever used injection drugs	11.4	95	58.7	27
Do not know if partner has ever used injection drugs	33.3	277	0	0
Missing	0	0	0	0
Perceived concurrency				
Partner does not have concurrent partners	12.4	103	78.3	36
Partner has concurrent partners	47.9	399	8.7	4
Do not know if partner has concurrent partners	39.6	330	13.0	6
Missing	0.10	1	0	0
Perceived has had sex with another man				
Partner has never had sex with another man	60.0	500	87.0	40
Partner has ever had sex with another man	2.8	23	4.4	2
Do not know if partner has ever had sex with another man	36.8	306	8.6	4
Missing	0.40	4	0	0
Perceived HIV serostatus				
Partner is HIV negative	5.5	46	10.8	5
Partner is HIV positive	1.7	14	87.0	40
Do not know partner's HIV status	92.7	772	2.2	1
Missing	0.10	1	0	0
Event-level risk characteristics				
Condom use during vaginal sex at last sexual encounter				
No	45.3	377	34.8	16
Yes	53.4	445	65.2	30
Missing	1.3	11	0	0

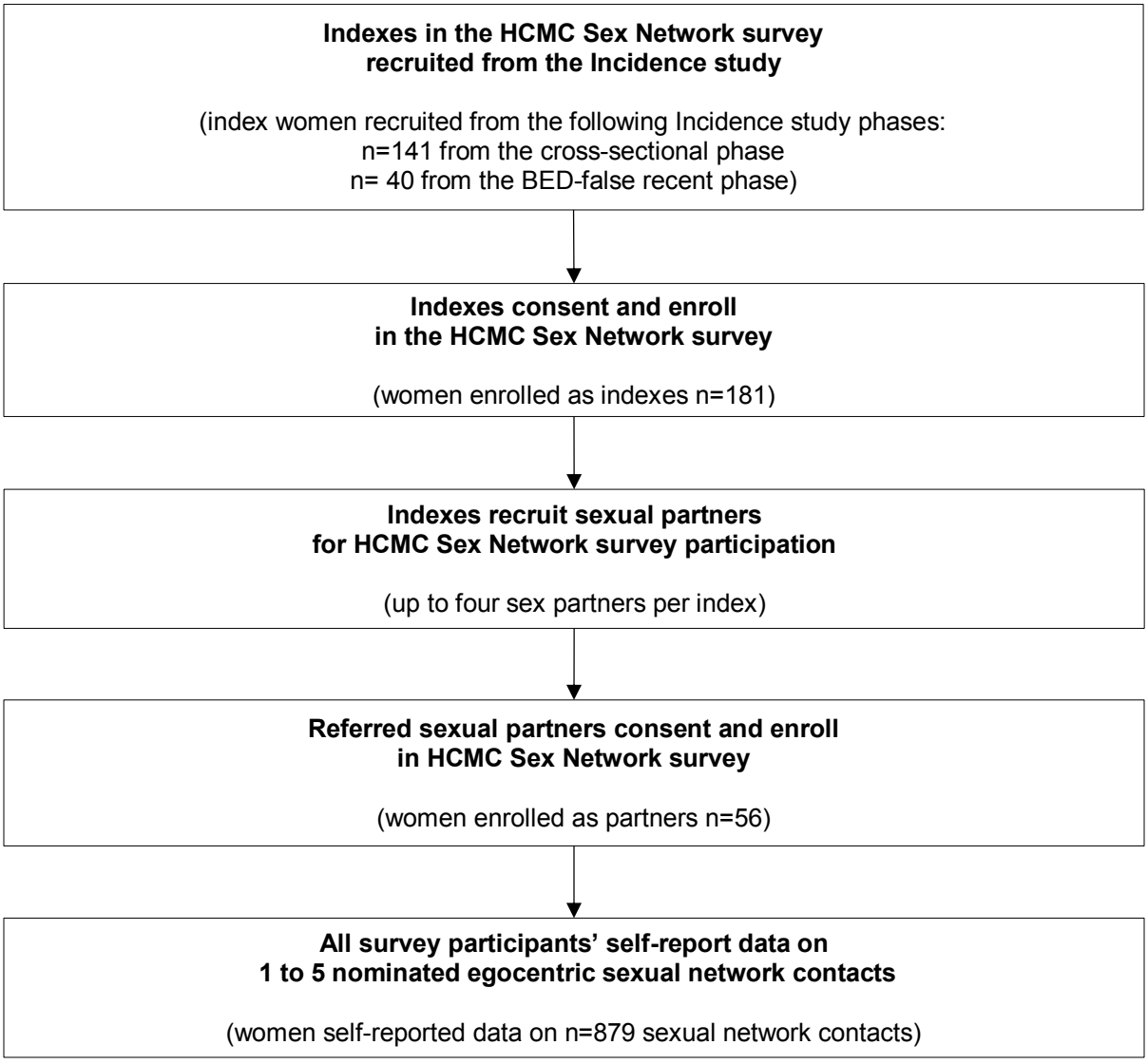
SW indicates female sex worker; Non-SW indicates female non-sex worker.

†Networks refer to participants' 1 to 5 nominated egocentric sexual network partners.

*n is higher than the number of participants due to participants reporting on multiple sexual partners (n=the number of nominated sexual partners, range 1 to 5).

6.6. Figures

Figure 6.1 Overview of Targeted HCMC Sex Network Survey Recruitment for Aim 2 Participants, (n=237 Women and n=879 Sexual Network Contacts)



Chapter 7: Conclusion

7.1. Conclusion

The purpose of this dissertation was to describe predominant heterosexual partnership patterns and their potential implications for population HIV transmission, as well as individual risk of infection, among networks of sexual contacts at elevated risk in HCMC, Vietnam. To date, studies examining isolated individual predictors of acquiring infection - such as number of sexual partners and condom use - comprise the bulk of epidemiological HIV research. There is a limited focus on how different aspects of the HIV transmission system - such as sexual partnership patterns and disease burden within networks - interact to influence the spread of infection. Subsequently, our view of population HIV transmission dynamics has been largely divorced from the context in which it occurs. The result is a limited understanding of why prevalence rates continue to rise in specific groups, and where an epidemic may spread next, that restricts the effective design, targeting, and implementation of initiatives to prevent future waves of infection.

In Vietnam, for example, this narrow focus has hampered efforts to identify the relative importance of various risk groups on the continued spread and maintenance of the epidemic, as well as women's risk of both acquiring and transmitting HIV infection. Therefore, using sexual network analysis, this dissertation describes predominant partnership patterns among networks of sexual contacts at elevated HIV risk in HCMC, Vietnam. The following section summarizes key findings and implications of these analyses.

7.2. Key Findings and Implications

In the first paper, we employ within-cluster resampling methods to describe patterns of heterosexual partnership selection (mixing) with respect to selected HIV risk factors among a network of sexual contacts at elevated HIV risk in HCMC, Vietnam. We observed that approximately one third of the network was HIV-positive and distinct patterns of assortative and disassortative partnership

selection patterns. Generally, we found that young and unmarried men and women selected other young and unmarried sex partners living within their same districts; assortative mixing patterns likely allowing HIV to persist within this network. Men and women injecting drugs and exchanging sex typically chose non-injecting and non-exchanging sex partners; disassortative mixing patterns likely fueling ongoing transmission and allowing IDUs and SWs to remain important reservoirs of infection within this network. Most importantly, those involved in more than one partnership at a given point in time (i.e., concurrent partnerships) tended to partner with others in concurrent partnerships. This pattern will allow HIV to spread more rapidly through the network than a pattern of serially monogamous partnerships. To a limited degree, we also observed partnering among contacts of similar HIV-serostatus (i.e., serosorting). However, given the tendency for contacts that had been tested for HIV to choose partners that had not been tested, this serosorting appears to be unintentional. Together, these patterns suggest an urgent need for improvements in counseling and testing initiatives.

In the second paper, we describe and compare personal risk-taking and recent partnership (egocentric sexual network) patterns among SWs and non-SWs in a network of sexual contacts at elevated HIV risk in HCMC, Vietnam. Notably, we observed that HIV prevalence was more than three times higher among non-SWs than SWs. Non-SWs' own risk-taking behavior was low; however, non-SWs' had a high frequency of unprotected sex with HIV-infected primary partners, likely resulting in their exposure to HIV infection. In comparison, a lower frequency of exposure to risky partners and a higher frequency of individual risk-taking behavior likely contributed to SWs' exposure to HIV infection. These findings illustrate that different patterns of personal risk-taking and recent sexual contact may influence women's exposure to HIV infection. In the absence of condom use, these findings imply that women, even those whose own behavior is low risk, may be at increased risk for HIV if they are sexually connected to risky partners, even if they have just one, long-term primary partner.

Several important themes emerged relevant to HIV transmission dynamics within these networks. First, we observed that partnership patterns differed not only among individuals, but across partnerships, and episodes of sex within these networks. Few studies[72, 96, 99] have been able to

provide this comprehensive view of HIV risk, largely as a result of the difficulty of collecting network data. These findings support our use of sexual network analysis and a complex systems approach to develop a more nuanced view of population HIV transmission, and individual risk, among networks of sexual contacts at elevated risk in HCMC, Vietnam.

Second, differences in partnership patterns have important implications for identifying which groups and individuals are at risk of not only acquiring, but transmitting HIV infection. In the first paper, we observed a highly connected network with a high prevalence of HIV and risky behavior (e.g., injecting drug use and sex work). Demographic partnership patterns within this network indicated that the network was localized (lived within the same districts) and was primarily contained to young and unmarried men and women. This pattern suggests that HIV may remain contained within this network at elevated risk. However, we also observed partnering between IDUs and non-IDUs and SWs and non-SWs, as well as partnering between mutually concurrent partners. Specifically, index participants tended to be IDUs and SWs choosing non-IDUs and non-SWs as partners. Additionally, while nearly all index participants had been tested for HIV, the majority of their partners had not. Without increases in harm reduction and protective behaviors, these patterns suggest that IDUs and SWs are at high-risk for transmitting HIV, while their non-IDU and non-SW partners are at high-risk of acquiring infection. Moreover, both indexes and their partners reported extremely high levels of concurrent partnerships. Together, these patterns indicate that IDUs and SWs are likely to continue to fuel ongoing transmission within this network. Concurrency has the potential to amplify transmission not only within this network, but across networks (i.e., into the general population). This makes it important to continue to deliver treatment and prevention efforts to IDUs and SWs, as well as the general population.

In the first paper, a few noteworthy gender-based differences in partnership selection did emerge. Male indexes tended to choose partners slightly more unlike themselves in terms of age, injecting drug use, and geography than female indexes. Male indexes tended to be young men (<25 years of age) partnering with both older and younger women; of these women, the majority were SWs. In addition, injecting male indexes also tended to select non-injecting partners. This suggests that young male IDUs may be an important bridging group between higher- and lower- risk women.

Perhaps most importantly, male indexes exhibited a tendency to partner with women living outside their districts of residence; illustrating their potential to spread HIV from high- to low- prevalence districts in HCMC. These patterns parallel those, discussed in Chapter 1, between young male IDUs and SWs that led to the second wave of HIV transmission and the explosive growth of the epidemic in HCMC in the 1990s. It should be noted that these gender-based partnership selection differences were not statistically significant; primarily as a result of an imbalanced gender ratio in our sample. An important avenue for future research will be to investigate these gender-based mixing differences to help further refine our identification of those groups at risk.

These findings are reinforced by the results of the second paper. For instance, we observed that the frequency of HIV infection was three times higher among non-SWs than SWs. Non-SWs had lower levels of personal risk taking behavior than SWs; however, they also reported a higher frequency of injecting and HIV-positive partners. These findings underscore the importance of young male IDUs acting as an important transmission bridge within these networks. Non-SWs' partners, with one exception, were also all primary partners with whom non-SWs had unprotected sex. Research has shown long-term, as compared to short-term, partnerships increase the duration of exposure to HIV infection.[28] In primary partnerships, where emotional bonds are formed, feelings of safety and trust often serve as barriers to condom use.[5] In contrast, SWs had higher levels of personal risk-taking behavior (e.g., higher frequency of injecting drug use, partners, concurrency, and short-duration partnerships). Clearly, both SWs and non-SWs are at risk in this network; yet, for different reasons that will require interventions uniquely tailored to the context in which both groups must negotiate risk.

Despite their high-risk of acquiring infection, it is unlikely that monogamous and married women (i.e., non-SWs) will transmit infection to other partners within this network. In contrast, SWs exhibited a high-risk of not only acquiring, but transmitting infection. Most importantly, SWs' reported their own high levels of concurrency, as well as a high number of partners in concurrent partnerships. In the absence of condom use, this suggests that SWs are at high risk of transmitting infection not only within this network, but across networks, making them a crucial link in the transmission system.

Finally, in contrast to reports suggesting that Vietnam's HIV epidemic is transitioning from

one driven by IDUs and commercial SWs to one being predominantly driven by clients-of-SWs and husband-to-wife transmission, we found that IDUs and SWs were likely critically important drivers of transmission within these networks. At the same time, the significantly higher frequency of HIV among non-SWs, as compared to SWs, does support the larger trend of increasing prevalence among women in HCMC's general population. Non-SWs' infection likely resulted from high-levels of unprotected sex with high-risk primary partners, paralleling the larger trend in HCMC of husband-to-wife transmission. Together, these results suggest an urgent need for interventions designed to meet the needs of women (non-IDUs and non-SWs) and men (clients-of-SWs) in the general population. However, as prevention efforts as increasingly directed toward the general population, it will remain critically important to include IDUs and SWs as both groups are key to the transmission system.

It is important to note that the patterns of sexual contact described in this dissertation are specific to *these* networks of sexual contacts at elevated HIV risk in HCMC, Vietnam. Only to the extent that these networks at elevated risk are similar to other networks at elevated risk in HCMC may our findings be representative of other networks at elevated risk in HCMC. These networks of sexual contacts were evenly distributed throughout HCMC, so our hope is that they are, in fact, similar to other networks of sexual contacts at elevated risk in HCMC. Additionally, identifying the relative importance of risk groups to HIV epidemic trajectory in Vietnam will ultimately require similar analyses of sexual networks in multiple settings across multiple locations in HCMC and throughout Vietnam; therefore, this dissertation represents an important first step understanding how specific partnership patterns may contribute to the spread of HIV in HCMC, Vietnam.

7.2.1.Intervention Implications

Together, our results demonstrate that knowledge of the predominant partnership patterns within networks may aid in the design of individual- and partnership- level risk assessment, population-level prevention strategies, and the prioritization of programmatic resource allocation.[32] Serodiscordant mixing patterns found in paper one, for example, revealed that despite a high HIV prevalence among indexes, their partners' prevalence was still relatively low. This implies that 1) partner characteristics (such as partners' contact patterns with others and risky behavior) are important components of individual-risk assessment; 2) network characteristics (such as type and

extent of mixing) are key factors in determining which populations may be at elevated risk; and, most importantly, 3) significant opportunities for prevention remain within these networks at elevated risk, and in HCMC.

At the population-level, our findings demonstrate an urgent need in HCMC for interventions addressing concurrent and serodiscordant partnerships as well as HIV testing, particularly, in the context of injecting drug use and exchanging sex. The high prevalence of injecting drug use and exchanging sex, as well as overlapping injecting and sexual networks, reflect the insufficiency of the current intervention paradigm in HCMC focused on changing individual risk behavior in isolation. Critically, our results show that core group interventions alone will be inadequate to prevent future waves of infection; however, as IDUs and SWs will remain important infection reservoirs, our findings simultaneously demand that IDUs and SWs must be included in future efforts designed to reduce transmission.

For example, the discordant patterns of HIV testing across partnerships reveal a critical need to target partners of core group members for testing interventions. Rapid testing methods are known to be effective, but are not widely diffused.[100] Implementing rapid testing in, or close to, settings where sex and drugs are known to be exchanged in HCMC (e.g., parks, karaoke bars, and cafes) may be particularly effective at reducing transmission in this context. Further, the patterns of assortative mixing by residential location found among network members means those at highest risk generally live in the same districts which indicates that significant reductions in incidence may come from implementing interventions and directing resources to high prevalence districts. This same data could be used to target STI screening and syndromic management as well as voluntary counseling and testing (VCT) to SWs in high prevalence areas to prevent transmission.

Keeping these circumstances in mind, as well as HIVs long duration of infection and relative lack of symptoms, a shift in normative behavior – for example, establishing mandatory condom use across the board, or normative condom use when involved with concurrent partners - will be required to effectively reduce HIV incidence in HCMC.[8] A campaign similar to neighboring Thailand's 100% Condom Use Program may effectively reduce incidence given the similar epidemiologic context of HIV both countries.[101]

Interventions leveraging existing social and sexual networks to promote reductions in concurrent partnerships and condom use with all partners may be effective in reducing primary and secondary transmission among those exchanging sex and their partners in HCMC. Research suggests that social network-based prevention programs have led to substantial risk reduction among vulnerable populations, including at-risk women,[102] drug users,[78, 103] and MSM.[104, 105] Approaches are varied, but typically involve advancing traditional peer health promotion models by incorporating existing social networks and using conversation to generate a continuing process of normative influence and social support.[15] Changing the risk environment in which existing social and sexual networks exist, via diffusion and reinforcement, may also lead to more sustainable interventions.[15, 106] In HCMC, for example, men's proclivity for group male social activity often results in "going out for sex,"[82, 91] and a substantial number of men solicit sex as a result of pressure from peers and co-workers.[82, 91] This may provide a unique opportunity to implement place-based network interventions addressing concurrency and condom use[105, 107, 108] to reduce secondary transmission among HIV-positive men.

Most importantly, there is an urgent need to include women and their primary partners in couples–based, or partnership-level, risk reduction programs. While there are multiple areas of risk reduction to be addressed within primary partnerships, our results indicate a critical need to increase consistent condom use. Studies among heterosexual couples[109, 110] and serodiscordant heterosexual couples[111, 112] have shown couples-based interventions to be effective in increasing condom use between women and their primary partners. One study[112] conducted among married couples in the Democratic Republic of Congo found couples-based VCT to be associated with an uptake in condom use and a reduced rate of seroconversion.

Further, because the reasons for inconsistent and non-condom use within partnerships are numerous (ranging from trust and intimacy issues to a fear of violence), often resulting from cultural- and gender- based power imbalances,[113] there is a need to build upon existing strategies in recognition of the unique social and structural contexts of stigma and discrimination in which many women in HCMC live; including, SWs and non-SWs. Promoting culturally sensitive interventions may include taking steps to ensure that appropriate language is used and addressing normative behavior

and beliefs (e.g., those surrounding masculinity, motherhood, sexuality).[114] Gender-specific interventions, or intervention components, may include offering differing programs and materials for men and women. Considering context may mean, for example, ensuring that interventions and services are not only available, but accessible to those who need them (e.g., married women).

In addition to addressing the broader cultural and gender inequalities and normative beliefs, interventions should also strive to enhance women's abilities to navigate the broader risk environment via a focus on women's empowerment. Efforts to enhance women's empowerment, if not the sole focus intervention, must be included at every level of prevention. Empowering women means strengthening their capacity to make choices and transform those choices into the actions and outcomes they desire.[89] In India, a community mobilization and women's empowerment intervention, implemented among 1,750 SWs demonstrated significant improvement in self-efficacy, self-esteem, reduced violence and coercion, condom use, and treatment seeking.[115] Given the role poverty likely plays in increasing HIV risk among women in HCMC, interventions targeting women's empowerment via microfinance may be particularly beneficial in reducing risk. Microfinance programs provide women with access to small-scale credit and savings opportunities.[89] These programs have generally been found to result in increased self-esteem, self-confidence, household decision-making power, conflict resolution skills, and access to supportive social networks.[89]

7.3. Future Research

A particularly important avenue for future research will be to examine the mechanisms leading to the emergent patterns described in these analyses by answering questions, such as: why do people mix in observed patterns? why do these patterns have different implications both within and between distinct groups?; and how does disease burden influence these patterns and their epidemiological consequences? Network research being conducted in the US has begun to examine these mechanisms in relationship to race and HIV transmission.[12, 30, 40, 43, 116] Promising research among African American women, for instance, has shed light on the influence of large subsets of African American males being incarcerated on patterns of partnership selection.[30, 40, 117]

Clearly, sexual network analysis is a developing field both analytically and methodologically. Our mixing analysis is the first to use a newly recommended approach to calculating assortativity

estimates and standard errors, in hopes of refining assortativity estimates. However, even with respect to assortativity estimates many important avenues of development remain. For example, Doherty et al[40], raise an important issue regarding the contextualization of mixing estimates. Using mixing estimates derived from the US general population, they create a scale that classifies estimates from minimally to highly assortative and use that scale as a means of contextualizing their estimates from a US-based study sample. To the best of our knowledge no other international studies have quantified assortativity levels within populations; thus, providing no broader context for our estimates. Future research would benefit from mixing research conducted in different locations and among different populations, with varying levels of disease burden, as well as the development of standardized classifications of assortativity within populations.

Finally, incorporating mixing point estimates into models to provide direct estimates of the potential for HIV acquisition and transmission may also provide local policy makers and program planners with key insights to prevent future waves of infection in HCMC, Vietnam.

Appendix

To calculate the assortativity coefficient $(r)$and corresponding 95% CI we used the within cluster sampling (WCR) methods proposed by Young and colleagues (2013) in a manuscript that is currently under review. This method expands upon the work of Newman by taking into account the non-independent nature of dyadic data.

Briefly, each index subject and his or her up to four partners may be considered a cluster, C, where the dyads in each cluster are correlated. To implement WCR, we randomly sampled *with replacement* one dyad from each of the C clusters. This resampled data set then involves C mutually independent dyads so we can use standard methods for computing a kappa-type statistic (like r) and its estimated variance based on a multinomial distribution assumption for a $k \times k$ table. We then generated Q resampled data sets (each of size C), where $Q = 1{,}000$. For each dataset, we computed an assortativity coefficient and its corresponding 95% confidence interval (CI). Now, for the q-th resampled data set, $q = 1, 2, ..., Q$, suppose that we obtain k^2 cell entries $\{e_{qij}\}$, the k row totals $\{a_{qi}\}$ and the k column totals $\{b_{qj}\}$. Using these data, we calculated the assortativity coefficient

$$r_q = \frac{\sum_{i=1}^{k} e_{qii} - \sum_{i=1}^{k} a_{qi} b_{qi}}{1 - \sum_{i=1}^{k} a_{qi} b_{qi}}.$$

Since the Q resampled data sets contain overlapping observations, the estimated variance of $\bar{r}$, $\hat{V}(\bar{r})$, was calculated as

$$\hat{V}(r_q) = \frac{1}{C\left(1 - \sum_{i=1}^{k} a_{qi} b_{qi}\right)^2} \left\{ \sum_{i=1}^{k} e_{qii} \left[1 - (a_{qi} + b_{qi})(1 - r_q)\right]^2 \right.$$

$$\left. + (1 - r_q)^2 \times \sum_{\text{all } i \neq j} e_{qij} (b_{qi} + a_{qj})^2 - \left[r_q - \left(\sum_{i=1}^{k} a_{qi} b_{qi} \right)(1 - r_q) \right]^2 \right\}$$

Then, the WCR estimator of the true population value of the assortativity coefficient is simply the mean of these Q r_q values, namely,

$$\bar{r} = \frac{1}{Q}\sum_{q=1}^{Q} r_q \ .$$

And, since the Q resampled data sets contain overlapping observations, the estimated variance $\hat{V}(\bar{r})$ of $\bar{r}$ was determined using the following expression

$$\hat{V}(\bar{r}) = \frac{1}{Q}\sum_{q=1}^{Q} \hat{V}(r_q) - \left(\frac{Q-1}{Q}\right) S_r^2 ,$$

where

$$S_r^2 = \frac{1}{(Q-1)}\sum_{q=1}^{Q} (r_q - \bar{r})^2$$

is the sample variance of the Q r_q values.

The 95% CI for the true population value of the assortativity coefficient is

$$\bar{r} \pm 1.96\sqrt{\hat{V}(\bar{r})} \ .$$

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