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HIV Vaccination among High-risk Drug Users in Appalachia: Insights from Social Network Analysis on Feasibility, Consequences, and Dissemination Strategies

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HIV Vaccination among High-risk Drug Users in Appalachia: Insights from Social Network Analysis on Feasibility, Consequences, and Dissemination Strategies

By

April Marie Young

Bachelor of Arts, Transylvania University, 2003

Master of Public Health, University of Kentucky, 2010

Advisor: Ralph J. DiClemente, PhD

An abstract of
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Abstract

HIV Vaccination among High-risk Drug Users in Appalachia: Insights from Social Network Analysis on Feasibility, Consequences, and Dissemination Strategies

By
April Marie Young

A preventive HIV vaccine could substantially impact the epidemic, but high uptake, effective dissemination, and continued promotion of behavioral risk reduction will be necessary. Research suggests that low vaccine uptake and risk compensation (e.g. increased risk behavior after vaccination) are possible. However, there are notable gaps in the literature. Rural, drug-using populations have been significantly underrepresented and risk compensation related to syringe sharing has been under-studied. Moreover, no research to date has examined the potential impact of risk compensation on risk network structure. Thus, the secondary analyses for this dissertation address important gaps in the extant literature, as they provide a comprehensive individual- and network-level examination of HIV vaccine acceptability, risk compensation, and peer-based vaccine promotion among a sample of high-risk drug users from rural Appalachia. Study 1 examined demographic, behavioral, and psychosocial correlates to HIV vaccine acceptability. Findings indicated that vaccine acceptability was lower among men, but higher among those who believed they were susceptible to HIV, that a vaccine could benefit them, and who had positive perceived social norms. Study 2 explored network-level correlates to willingness to encourage HIV vaccination among risk network members. The study showed that vaccine promotion was more likely when the partner was perceived to be at high-risk for HIV, willing to accept the vaccine, and likely to reciprocate the encouragement. Encouragement was also more common in relationships involving intended risk compensation. In Study 3, network-level correlates to and consequences of risk compensation were explored. Intent to engage in risk compensation was rare, but was more common in relationships of shorter duration. A risk network constructed based on intended risk compensation revealed that risk network structure would increase in connectivity, although only minimally. These analyses demonstrate that HIV vaccine acceptability is high among this sample of rural drug users and that peer-based vaccine promotion may be feasible. However, peer-based strategies should be approached cautiously, as promotion may be associated with intent to engage in risk compensation. Further research in this and other populations is needed to explore the role that drug users' social networks could play in vaccine uptake, dissemination, and risk compensation.

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Chapter 1 : Introductory Literature Review

HIV Vaccination

Since 1987, the scientific community has been in pursuit of an effective HIV vaccine (Girard, Osmanov, Assossou, & Kieny, 2011). To date, more than 30 vaccines have been tested in Phase I/II clinical trials and four have been tested in Phase III/IIb trials (Girard et al., 2011; Ross, Bråve, Scarlatti, Manrique, & Buonaguro, 2010). HIV vaccine development has proved daunting (Chhatbar, Mishra, Kumar, & Singh, 2011), and after various setbacks, the utility of continuing to pursue an HIV vaccine has been debated (Gallo, 2005; Horton, 2004). However, recent breakthroughs, such as the modest efficacy achieved by the RV144 vaccine in Thailand (Haynes et al., 2012; Rerks-Ngarm et al., 2009), have resulted in renewed optimism in the possibility of developing a safe and effective HIV vaccine. In fact, global investments increased by US$2 million from 2011 to 2012, totaling more than microbicides, pre-exposure prophylaxis, male circumcision, and treatment-as-prevention combined (HIV Vaccines and Microbicides Resource Tracking Working Group, 2013). Several candidate vaccines are currently being tested in Phase I trials and plans are underway to initiate a large-scale trial of the Pox-Protein Public-Private Partnership (P5) within the next few years (HIV Vaccines and Microbicides Resource Tracking Working Group, 2013).

While various new prevention technologies hold promise, a vaccine is considered the "holy grail" of HIV prevention (Newman, Lee, et al., 2009). Even with modest efficacy, a preventive HIV vaccine could make a substantial impact

on the epidemic (Andersson et al., 2007; Fonseca et al., 2010; Stover, Bollinger, Hecht, Williams, & Roca, 2007). In the US, an HIV vaccine with modest efficacy could prevent over 300,000 cases over the next 20 years, and many of the averted infections would be among *unvaccinated* individuals. The long term economic impact is also substantial; a vaccine with modest efficacy, even at a vaccine price of up to $1000, could save $30 billion in US healthcare expenditures over the next 20 years (Long, Brandeau, & Owens, 2009). However, to achieve maximal cost-effectiveness and impact with a partially effective vaccine, high levels of vaccine uptake will be necessary among men who have sex with men (MSM), people who inject drugs (PWID), and high-risk heterosexual populations (Fonseca et al., 2010; Long et al., 2009).

HIV Vaccine Acceptability

In response to the possibility that an HIV vaccine is on the horizon, researchers have mobilized to examine the feasibility of achieving adequate vaccine coverage. Since the early 1990's, numerous studies on individuals' willingness to accept an HIV vaccine, or '*HIV vaccine acceptability*', have been conducted. A meta-analysis published in 2010 revealed that the average level of HIV vaccine acceptability across studies was moderate (66 on a 100-point scale) and that acceptability varied widely across studies (range: 37 - 94). The average acceptability of a high-efficacy vaccine was rated a 74 compared to 40 for a low-efficacy vaccine (Newman & Logie, 2010). A panel of experts convened in 2001 by the World Health Organization and the Joint United Nations Program on

HIV/AIDS (UNAIDS) estimated that the probable uptake for a vaccine of high efficacy (80 to 90%) would only be 38% of the estimated need. Moreover, the probable uptake for a low (30 to 50%) efficacy vaccine was only 19% of the estimated need (Esparza et al., 2003).

As the target of many early HIV vaccine clinical trials, populations in Thailand have been the focus of several vaccine acceptability studies (Newman, Roungprakhon, Tepjan, & Yim, 2010; Newman, Roungprakhon, Tepjan, Yim, & Walisser, 2012; Suraratdecha, Ainsworth, Tangcharoensathien, & Whittington, 2005; Whittington et al., 2008), as have countries in Southern and East Africa (Bishai, Pariyo, Ainsworth, & Hill, 2004; Sayles, Macphail, Newman, & Cunningham, 2010). These studies have primarily involved household surveys (Bishai et al., 2004; Suraratdecha et al., 2005; Whittington et al., 2008) or qualitative data collection from young adults (Sayles et al., 2010); few have focused on those at highest risk for HIV, such as MSM, PWID, sex workers, and transgender persons (Newman et al., 2010; Newman, Roungprakhon, et al., 2012).

In North America, the uptake of a high-efficacy HIV vaccine is anticipated to be only 32% of the projected need (Esparza et al., 2003), yet vaccine acceptability research among high-risk populations in North America is generally lacking. In the US and in Canada, many quantitative HIV vaccine acceptability studies have been conducted among undergraduate students (Gagnon & Godin, 2000; Liau & Zimet, 2000; Liau, Zimet, & Fortenberry, 1998; Zimet, Liau, & Fortenberry, 1997) or adolescents (Webb, Zimet, Mays, & Fortenberry, 1999;

Zimet, Fortenberry, & Blythe, 1999). In these studies, vaccine acceptability has generally been high, exceeding 80% in some studies (Gagnon & Godin, 2000; Webb et al., 1999) and 70% in another (Zimet et al., 1997). Fewer quantitative studies of HIV vaccine acceptability conducted in the US have involved representatives from groups at high risk for HIV (Allen et al., 2005; Crosby & Holtgrave, 2006; Crosby, Holtgrave, Bryant, & Frew, 2004; Kakinami, Newman, Lee, & Duan, 2008; Lally et al., 2006; Newman, Duan, Lee, et al., 2006; Salazar, Holtgrave, Crosby, Frew, & Peterson, 2005), and some have focused on acceptance of a vaccine that prevents progression from HIV to AIDS rather than prevention (Crosby & Holtgrave, 2006; Crosby et al., 2004; Salazar et al., 2005).

In quantitative studies of HIV vaccine acceptability in high-risk groups in the US, acceptability has generally been high. For example, in a study conducted among inmates in Rhode Island, over 90% reported they would accept an HIV vaccine (Lally et al., 2006). Similarly, a study involving PWID from San Francisco, found that 86% they would accept an HIV vaccine (Seal et al., 2003). However, other studies have found more moderate levels of acceptability. In a study of high risk adults recruited from syringe exchange programs (SEPs), gay and lesbian centers, and Latino primary care clinics in Los Angeles, the average rating of acceptability was 61 on a 100-point scale (with higher numbers indicating higher likelihood of accepting an HIV vaccine) (Kakinami et al., 2008). A study conducted in a similar population that examined acceptability of eight hypothetical vaccines of varying efficacy, duration, dosing, side effects, and cost found that acceptability varied from 32 to 82 on a 100-point scale, with an

average of 60. Acceptability for what was considered the "best possible vaccine" (a one dose, oral vaccine that had 95% efficacy, no side effects, and provided 10 years of cross-clade protection at a cost of $50) had an acceptability rating of 88 (Newman, Duan, Lee, et al., 2006).

Much of what is known about HIV vaccine acceptability among high risk groups in the US comes from qualitative research. The majority of qualitative studies on HIV vaccine acceptability have been conducted among adults recruited from SEPs, gay and lesbian centers, sexually transmitted disease (STD) clinics, and Latino primary care clinics in Los Angeles (Newman, Duan, Kakinami, & Roberts, 2008; Newman, Duan, Rudy, Roberts, & Swendeman, 2004; Newman, Lee, et al., 2009; Newman, Seiden, Roberts, Kakinami, & Duan, 2009; Roberts, Newman, Duan, & Rudy, 2005; Rudy et al., 2005). Qualitative studies have been particularly valuable in revealing factors that could impede uptake. Participants have expressed concerns that an HIV vaccine would cause HIV or false positive results to occur on future HIV tests. Many also reported worry about costs, fear of side effects, and anxiety regarding negative impacts on social relationships (the latter is described in detail below). Some participants believed that HIV and HIV vaccination were part of a US government conspiracy, in which an HIV vaccine was already available but was being withheld in an attempt to increase drug company profits for antiretroviral medications (Roberts et al., 2005).

Psychosocial correlates to HIV vaccine acceptability.

Given the complexity of mental models surrounding HIV vaccine acceptability, it is surprising that few HIV vaccine acceptability studies to date have been grounded in behavioral theory. The lack of theory-grounded research related to HIV vaccination has been noted as an area in need of further research (Lau, Stansbury, Gust, & Kafaar, 2009). While vaccine-related characteristics (e.g., efficacy, duration of protection, side effects, cost) will likely play an important role in determining uptake, so too will psychosocial factors such as risk perception and perceived benefits of vaccination (Newman & Logie, 2010). The most well-established psychosocial correlate to vaccine acceptability is perceived risk or susceptibility to HIV infection (Bishai et al., 2004; Liau & Zimet, 2000; Newman, Duan, Rudy, Roberts, et al., 2004; Suraratdecha et al., 2005; Zimet et al., 1999; Zimet et al., 1997). Perceived benefits of HIV vaccination (Liau & Zimet, 2000; Zimet et al., 1999), anticipated barriers to vaccine acceptance (Liau & Zimet, 2000; Zimet et al., 1997), and perceived behavioral control over HIV vaccination (Gagnon & Godin, 2000) also play an important role.

These constructs are germane to value-expectancy theories, such as the Health Belief Model (HBM) (Becker, 1974; Rosenstock, 1974), Theory of Reasoned Action (TRA) (Ajzen & Fishbein, 1980; Fishbein, 1980), and Theory of Planned Behavior (TPB) (Ajzen, 1991), which are commonly used in health behavior research (DiClemente, Salazar, & Crosby, 2013; Glanz & Bishop, 2010). Briefly, the HBM suggests that perceived threat (i.e., perceived susceptibility and severity of HIV) and expected net gain (i.e. benefits of HIV

vaccination) affect individuals' intent to perform behavior (i.e. vaccine acceptability). Demographic factors and cues to action (i.e., exposure to reminders to be vaccinated, knowing others who are HIV positive, etc.) affect individuals' perceived threat and benefits, and therefore, indirectly affect intention (Becker, 1974; Rosenstock, 1974). The TRA and TPB also suggest that similar attitudes affect behavioral intention, but expand upon the HBM by also positing that social influences, or *subjective norms*, affect intent (Ajzen, 1991; Ajzen & Fishbein, 1980; Fishbein, 1980). The TRA and TPB are similar with the exception that the TPB also includes the construct of perceived behavioral control and suggest that it influences behavior both directly and indirectly (via intention) (Ajzen, 1991).

Previous studies on HIV vaccine clinical trial participation have used the TRA (Frew et al., 2010; Frew, Archibald, Hixson, & del Rio, 2011; Frew, Archibald, Martinez, del Rio, & Mulligan, 2007), and others examining HIV vaccine acceptability have used the TPB (Gagnon & Godin, 2000) and HBM (Liau et al., 1998; Zimet et al., 1999; Zimet et al., 1997). Gagnon and colleagues (2000) found that attitudes and perceived behavioral control were significantly associated with HIV vaccine acceptability in a sample of college students in Canada. Studies conducted by Zimet and colleagues (1997, 1999) based in the HBM found that perceived susceptibility to HIV and perceived barriers to HIV vaccination were associated with vaccine acceptability among college students and adolescents in an urban setting in the Midwest (Zimet et al., 1999; Zimet et al., 1997). More comprehensive tests of theory have been conducted by Frew

and colleagues (2007, 2011) in relation to HIV vaccine clinical trial participation. A study grounded in the TRA found that behavioral beliefs, but not subjective norms, were associated with African American adults' willingness to engage in community involvement activities associated with HIV vaccine research (Frew et al., 2007). A more recent study by Frew and colleagues (2011) conducted in a similar setting revealed that attitudes and subjective norms were associated with individuals' willingness to involve others in HIV vaccine research (Frew et al., 2011).

While these theory-grounded studies have provided important insight into the psychosocial factors that may affect HIV vaccine uptake and clinical trial participation, notable gaps remain. The traditional, individual-level theories on which these studies are based do not capture the complexity of social influences on HIV vaccine acceptability. These studies have generally used a conglomerate concept of “social norms” which fails to make a distinction between two types of normative influence: injunctive and descriptive (Cialdini, Reno, & Kallgren, 1990; Manning, 2009). *Injunctive norms* are one's beliefs that focus on whether others think he/she should perform the given behavior. *Descriptive norms* refer to a person's perceptions about how others are behaving (Cialdini et al., 1990; Fishbein, 2009). While combining these two constructs during analysis is not an invalid approach to evaluating the theory (Bleakley & Hennessy, 2012), the distinction between injunctive and descriptive norms has not been explored in relation to HIV vaccination and is deserving of investigation. Several studies have found that descriptive norms can independently contribute to the prediction of

intent (Rivis & Sheeran, 2003) and others have found that the relative influence of descriptive and injunctive norms on intent varies depending on the target behavior (Smith-McLallen & Fishbein, 2008).

Integrative Model of Behavioral Prediction

The Integrative Model of Behavioral Prediction (IM) (Fishbein, 2008) addresses some of the limitations of the theories previously used in HIV vaccine acceptability research. The IM is an individual-level theory (DiClemente et al., 2013; Glanz, Rimer, & Viswanath, 2008) built upon the frameworks of the TRA (Ajzen & Fishbein, 1980; Fishbein, 1980), TPB (Ajzen, 1991), HBM (Becker, 1974; Rosenstock, 1974), and Social Cognitive Theory (Bandura, 1998, 2001). According to the model, behavior is directly affected by behavioral intention, which is in turn influenced by attitudes, perceived norms, and personal agency. Thus, the IM framework offers an advantage over many individual-level theories in that it provides a unified structure integrating theoretical constructs that would otherwise be pulled from various individual theories. Moreover, the model has successfully been applied to the study of other types of vaccine uptake (Dillard, 2011; Painter et al., 2010; Painter et al., 2011), as well as to examinations of risk reduction intention and behavior in high-risk populations (e.g., (Bleakley, Hennessy, Fishbein, & Jordan, 2011; Hennessy et al., 2010; Kasprzyk, Montaño, & Fishbein, 1998).

The IM makes a distinction between injunctive and descriptive norms (described above) and between experiential and instrumental attitudes (Fishbein,

2009). Experiential attitude is an individual's emotional response to the idea of performing a behavior, while instrumental attitude is the individual's cognitive appraisal of performing the behavior based on outcome beliefs (Fishbein, 2007). While measures of experiential attitude have been used in previous research on HIV vaccine acceptability (Gagnon & Godin, 2000), the distinction and relative importance of the two attitudinal constructs applied to vaccine acceptability remains unclear.

The IM also distinguishes between perceived behavioral control and self-efficacy. Self-efficacy is the belief in one's capabilities to exercise control over his/her behavior (Bandura, 1991), while perceived behavioral control focuses on one's abilities to perform a behavior in light of various barriers (Ajzen, 2011). While the distinctiveness and methods of operationalizing these constructs have been debated (e.g., (McCaul, Sandgren, O'Neill, & Hinsz, 1993; Sparks, Guthrie, & Shepherd, 1997; Terry & O'Leary, 1995), there is some evidence that the two constructs are indeed dissimilar applied to protective health behaviors and that they add to models' predictive ability (McCaul et al., 1993; Povey, Conner, Sparks, James, & Shepherd, 2000).

Limitations of the Integrative Model of Behavioral Prediction

The main criticism of the IM is its proposition that intent is the primary influence on behavior. Many argue that intent is a poor predictor of behavior (Gollwitzer, 1999). Meta-analyses have found that the average correlation between intention and behavior is moderate (0.47 - 0.62) (Armitage & Conner, 2001; Randall & Wolff, 1994; Sheppard, Hartwick, & Warshaw, 1988). A more

recent meta-analysis of 47 experimental studies found a medium to large effect size for intent (d=0.66), but only a small to medium effect size (d=0.36) for the association between intent and behavior. The analysis also revealed that the association between beliefs and behavior was not fully mediated by intent (Webb & Sheeran, 2006). Studies, including a review of randomized control trials (Hardeman et al., 2002), also found that propositions of intent being a mediator were not supported (Godin, Gagne, & Sheeran, 2004; Hardeman et al., 2002). Some evidence from research on vaccine uptake, including that of the HPV and flu vaccines, has demonstrated that intent is an important predictor of vaccine uptake (Liao, Cowling, Wendy Wing Tak, & Richard, 2011; Painter et al., 2011; Patel et al., 2012).

Several other measurement factors have been found to modify the association between intent and behavior, including *correspondence* (i.e. degree of match between elements of the behavior defined in the intent items and that of the actual behavioral outcome), time elapsed between measurement of intention and observation of behavior (McEachan, Conner, Taylor, & Lawton, 2011), discrepancies between participants' affect at measurement and time of behavior (Ajzen, 2011), and differences in the physical context in which measurement is completed and behavior is performed (Cooke & French, 2011). The latter two factors are difficult to address in cross-sectional studies. Issues of correspondence and time-elapsed between measurement and performance of the behavior are especially difficult to address in HIV vaccine acceptability

research given that the exact characteristics of the forthcoming vaccine are yet to be known, as is the timeline for approval.

Despite these limitations, the use of behavioral theory in HIV vaccine acceptability research can contribute to the development of more thorough studies of the psychosocial mechanisms involved. To date, relatively few HIV vaccine acceptability studies have grounded their measures in a theoretical framework, presenting a limitation not only to their generalizability but also to the establishment of measures for which construct validity can be determined. The IM offers a comprehensive and detailed framework for the examination of vaccine acceptability in future research and could possibly illuminate the complexity of normative influence on vaccine uptake.

Social Influences on HIV Vaccine Acceptability

Several qualitative studies have revealed that social influences, particularly those regarding concerns about stigmatization and negative peer reactions, may impede vaccine uptake (Milford, Barsdorf, & Kafaar, 2007; Newman, Duan, Rudy, & Anton, 2004). In fact, recent conceptual models of HIV vaccine uptake and clinical trial participation include social networks, norms, and peer influence among the key determinants of attitudes toward HIV vaccination (Lau et al., 2011; Sayles et al., 2010). The diversity of settings in which social stigma has been mentioned as a barrier to vaccine acceptability is striking. Concerns about negative social implications of accepting an HIV vaccine have been reported in the Dominican Republic (Barrington, Moreno, & Kerrigan, 2007),

US (Kakinami et al., 2008; Liau & Zimet, 2000; Newman, Duan, et al., 2008; Newman, Duan, Rudy, Roberts, et al., 2004; Rudy et al., 2005), Canada (Newman, Woodford, & Logie, 2012), and South Africa (Sayles et al., 2010). Similar concerns about HIV vaccine clinical trial participation are equally widespread, reported by participants in the US (Brooks, Newman, Duan, & Ortiz, 2007; Fuchs et al., 2007; Koblin et al., 1998; Moutsiakis & Chin, 2007; Newman, Duan, Roberts, et al., 2006; Strauss et al., 2001), Canada (Newman, Daley, Halpenny, & Loutfy, 2008), South Africa (Fincham, Kagee, & Swartz, 2010; Jaspan et al., 2006; Lesch, Kafaar, Kagee, & Swartz, 2006; Smit et al., 2006), Thailand (Jenkins, Temoshok, & Virochsiri, 1995; Jenkins et al., 2000), Italy (Starace et al., 2006), China (Yin et al., 2008), and Kenya (Nyblade, Singh, Ashburn, Brady, & Olenja, 2011).

Social concerns about HIV vaccine acceptance include fear of negative reaction amongst family members and peers (Kakinami et al., 2008; Newman, Duan, Rudy, Roberts, et al., 2004), specifically regarding being perceived as promiscuous (Newman, Roungprakhon, et al., 2012; Rudy et al., 2005; Sayles et al., 2010), gay (Newman, Daley, et al., 2008; Rudy et al., 2005), or HIV positive (Koblin et al., 1998). Participants in several studies have reported fear that HIV vaccine clinical trial participation would negatively impact intimate relationships (Jenkins et al., 2000; Lesch et al., 2006; Mills et al., 2004; Newman, Duan, Rudy, Roberts, et al., 2004; Rudy et al., 2005). In a study of PWID in China, perceived social risks was significantly associated with refusal to participate in a future HIV vaccine clinical trial (Yin et al., 2008). The impact of HIV vaccination and trial

participation on intimate partnerships has generally been discussed in the context of women's participation and/or vaccine uptake (Mills et al., 2006); however, it is important to note that the fear has also been reported by men (Jenkins et al., 2000).

In a study of over 4800 MSM and PWID in the US, 27% reported a fear that others would perceive that they had HIV if they participated in an HIV vaccine trial, and 24% reported that others would perceive them as "high-risk". Nearly one in five believed that others would not want to have sex with them if they participated in an HIV vaccine clinical trial (Koblin et al., 1998). In a more recent study of MSM and high-risk heterosexual women participating in a phase 3 clinical trial in North America, 18% had at least one negative social impact from trial participation (Fuchs et al., 2007).

While studies on social influences surrounding HIV vaccine uptake and clinical trial participation have generally focused on negative impacts, some have highlighted the positive role that peer influence may play in vaccine promotion. Research conducted among gay and bisexual men in the US demonstrated that perception of peers' interest in HIV vaccine clinical trials was significantly associated with personal willingness to participate in a trial (Gross et al., 1996). In a more recent study of PWID in China, perceived familial support for HIV vaccine clinical trial participation was associated with willingness to participate in a trial (Yin et al., 2008). Several studies have emphasized the importance of involving local individuals in vaccine promotion (Frew et al., 2007; Kelley, Hannans, Kreps, & Johnson, 2012; Lesch et al., 2006; Lindegger, Quayle, &

Ndlovu, 2007; Newman et al., 2011), and participants have suggested that peers, family members, and community members may be perceived by many as the most reliable source of information on HIV vaccination (Sayles et al., 2010). Some authors have specifically mentioned the importance of vaccine communication between partners, especially men's encouragement of female partner(s)' HIV vaccination (Kakinami et al., 2008; Rudy et al., 2005).

This evidence clearly points to the potential impact of social influence on HIV vaccine uptake, however, relatively few quantitative studies have explored social influences related to HIV vaccination (Mills et al., 2004; Newman & Logie, 2010). Research specifically addressing individuals' willingness to encourage others to receive an HIV vaccine is especially scarce, though some studies have examined individuals' willingness to discuss clinical trial participation with peers (Allen et al., 2005; Frew et al., 2011; Jenkins et al., 2005; Kelley et al., 2012; Valente et al., 2009). A telephone-survey of over 3500 adults in the US, found that 29% of respondents sampled from the general population and 68% of a targeted sample of MSM would support others' participation in HIV vaccine research (Allen et al., 2005). In a social network study conducted by Valente and colleagues (2009) involving HIV positive adolescents and adults, 59 participants and their immediate peers expressed willingness to invite 421 social network members to participate in an HIV vaccine study. In a study conducted by Frew and colleagues (2011) in a racially-diverse sample urban adults, 48% reported that they were likely or definitely willing to "get others involved in HIV vaccine research" (P. M. Frew, personal communication, July 18, 2013). The study also

revealed that, controlling for various individual-, social- and community-level characteristics, subjective norms were significantly associated with willingness to involve others (Frew et al., 2011).

Limitations of extant research on social influences surrounding HIV vaccination

While studies on social influences surrounding HIV vaccine clinical trials have been foundational in examining the positive aspects of peer influence, findings may not be generalizable to the promotion of an approved HIV vaccine. Previous research has shown that HIV vaccine clinical trial participation and HIV vaccine acceptability may involve different motives and barriers (Newman, Duan, et al., 2008).The underrepresentation of PWID in studies examining peer influence on HIV vaccine acceptability also presents a limit to the scope of previous studies' applicability. Moreover, with the exception of the study by Valente and colleagues (2009), these studies have not fully investigated with *whom* participants would discuss HIV vaccination and clinical trial participation. These limitations present an important gap in understanding, as vaccine promotion may not be an all-or-none phenomenon, but one that individuals engage in selectively depending on personal characteristics, the attributes of the peer, and/or the nature of the relationship. Understanding the characteristics of relationships in which HIV vaccine promotion is most likely to occur is important to determining not only the feasibility of a peer-based strategy, but also its ability to reach those most at risk.

Risk Compensation

While social support for and acceptability of HIV vaccination are of concern, so too is the potential for negative behavioral change. In addition to revealing that HIV vaccine uptake may be sub-optimal, HIV vaccination studies have raised concerns about *risk compensation*. Risk compensation occurs when diminished perceived susceptibility resulting from participation in some preventive intervention causes a subsequent increase in risk behavior (Hogben & Liddon, 2008). Given that the first HIV vaccines on the market are likely to be only partially effective, risk compensation could substantially dampen and, in some circumstances, negate the public health impact of the vaccine (Andersson et al., 2007; Blower, Schwartz, & Mills, 2003; Fonseca et al., 2010; Gray et al., 2003).

A recent systematic review of mathematical models of HIV/AIDS interventions found that only 28% examined risk compensation (Johnson & White, 2011). Two simulation studies based on the epidemiology of HIV in South Africa and Brazil found that risk compensation in response to a 40% effective HIV vaccine could result in 30% fewer averted infections than would a scenario involving no risk compensation (Andersson et al., 2007; Fonseca et al., 2010). While the parameters, definitions, and contexts of these studies are not identical, they both highlight the impact of decreased condom use on the efficacy of HIV vaccine initiatives. In fact, both models predicted that with the right combination of risk compensation and vaccine efficacy, an HIV vaccine campaign could

actually *increase* HIV incidence (Andersson et al., 2007; Fonseca et al., 2010). Andersson and colleagues (2007) determined that an HIV vaccine efficacy level of 43% was the tipping point; vaccination programs involving an at least 43% effective vaccine would have a positive impact on HIV incidence regardless of risk compensation, while the impact of lower efficacy vaccines would be contingent on levels of behavior change (Andersson et al., 2007).

Interestingly, according to a simulation based on the epidemiology of HIV in the US, if vaccine recipients engaged in sexual risk compensation, defined in this study as having 25% more sexual partners than their unvaccinated counterparts, vaccination programs would actually prevent *more* HIV infections than if there was no risk compensation. However, this trend was only apparent for vaccines with at least 65% efficacy; with vaccines of less than 65% efficacy, risk compensation negatively affected the impact of vaccination. The paradoxical result for vaccines of greater than 65% efficacy could be a result of the authors' assumptions regarding sexual mixing in the population; that is, if vaccinated individuals who increased their number of sexual partners accounted for a larger fraction of the overall number of sexual partnerships in the population, then an HIV infected individual would have a greater chance of having sex with a vaccinated partner than with an unvaccinated person (thereby, preventing the spread of HIV) (Johnson & White, 2011). This study not only underscores the need for further research into the consequences of risk compensation, but suggests a need to critically re-examine assumptions underlying mathematical models of HIV vaccine impact.

Intent to engage in risk compensation

In studies asking participants about their personal likelihood of risk compensation, few anticipate that they would increase their risk behavior (Barrington, Moreno, & Kerrigan, 2008; Macphail, Sayles, Cunningham, & Newman, 2012; O'Connell et al., 2002). Some participants admitted that they would "lighten up" on condom use (Newman, Duan, Rudy, & Johnston-Roberts, 2004). In a study of MSM and transgender people in Thailand, 35% reported that they would increase sexual risk behavior if given a highly efficacious vaccine (Newman et al., 2010). In studies of high-risk adults in the US, the percentage intending to risk compensate was reported to be near 20% in one study conducted in Atlanta (Crosby & Holtgrave, 2006) and approximately 10% in a more recent study conducted in Los Angeles (Newman, Lee, et al., 2009).

While few participants (in most studies) report a personal intent to engage in risk compensation, many anticipate that *other people* will increase risk behavior. In an array of HIV vaccine acceptability studies across various settings, participants have expressed concern that sexual risk compensation will occur if an HIV vaccine is disseminated (Koniak-Griffin, Nyamathi, Tallen, González-Figueroa, & Dominick, 2007; Newman, Lee, et al., 2009; Newman, Roungprakhon, et al., 2012; Olin et al., 2006; Webb et al., 1999). Female participants in particular have expressed concern that vaccinated men will decrease their condom use (Newman, Roungprakhon, et al., 2012; Sayles et al., 2010).

Risk Compensation during HIV Vaccine Clinical Trials

Findings from research embedded within HIV vaccine trials are equally inconsistent, with some studies finding no substantial increase in sexual risk behavior in response to participating in HIV vaccine trials (Bartholow et al., 2005; Jenkins et al., 2005; Lampinen et al., 2005; Martin et al., 2010; van Griensvan et al., 2004) and others finding that risk behavior can increase substantially (Chesney, Chambers, & Kahn, 1997). The variability across studies can be attributable in part to differences in populations and characteristics of the vaccine trials. For example, studies have shown that the degree of participants' post-vaccination behavior change may be influenced by a number of demographic, attitudinal, behavioral, and vaccine-related factors, including gender (Jackson et al., 1995; Sayles et al., 2010), age (Crosby & Holtgrave, 2006), efficacy of the vaccine (Bishai et al., 2004; Chesney et al., 1997; Newman, Duan, Rudy, & Johnston-Roberts, 2004; Newman, Lee, et al., 2009) and pre-vaccination levels of risk behavior (Chesney et al., 1997; Crosby & Holtgrave, 2006).

The data on behavior change during HIV vaccine clinical trials should be interpreted with caution, as the quality and methodological rigor of behavioral data collection has varied. Recent research involving interviews with HIV Vaccine Trials Network (HVTN) staff members has demonstrated that, until the STEP study, behavioral data collection was very limited. Behavioral data collection instruments were often developed near the trial commencement, which left no time for piloting or back translation. Staff members reported that they did not

understand the relevance of the behavioral data collection, and thought that the items were added out of investigators' personal research interests. Staff also reported that they desired more contextual information about the high-risk populations they were sampling in order to better administer the questions. Authors noted several logistical barriers that make thorough behavioral data collection in the context of a clinical trial difficult, including attempts to minimize respondent burden and lack of behavioral expertise among protocol development teams. HVTN protocols since the STEP study have attempted to address these limitations and the behavioral data has greatly improved in quality over the past several years (Andrasik et al., 2013).

Limitations of extant research on risk compensation

A review of HIV vaccine acceptability literature conducted by Newman and Logie (2010) identified only four quantitative studies that had assessed risk compensation. To date, these studies have been almost exclusively individual-level in focus. Social networks can play an important role in HIV and STI transmission (De, Singh, Wong, Yacoub, & Jolly, 2004; Friedman et al., 1997; Klovdahl et al., 1994; Potterat, Rothenberg, & Muth, 1999; Rothenberg, Potterat, & Woodhouse, 1996; Rothenberg, Potterat, et al., 1998; Rothenberg, Sterk, et al., 1998), HIV risk behavior (De, Cox, Boivin, Platt, & Jolly, 2007; Friedman et al., 1997), and involvement in preventative interventions (Coyle, Needle, & Normand, 1998; Latkin et al., 2013; Wang, Brown, Shen, & Tucker, 2011; Weeks, Clair, Borgatti, Radda, & Schensul, 2002; Weeks, Convey, et al., 2009;

Weeks, Li, et al., 2009), yet the HIV vaccine acceptability literature provides limited insight into the role that networks play in shaping likelihood of engaging in risk compensation.

Previous studies have asked participants if they would engage in more frequent risk behavior and/or if they would increase their number of risk partners, ignoring the possibility that risk compensation could occur unevenly across different types of risk relationships. In the same vein, by asking participants only about the *number* of risk relationships they may form in response to vaccination, these studies fail to capture how the formation of new risk relationships in response to HIV vaccination could transform the structure of a community's entire risk network. Furthermore, most research on risk compensation to date has queried participants about the likelihood of risk compensation given personal receipt of the vaccine; the possibility that risk behavior may increase among non-recipients of the vaccine in response to partner(s)' vaccination has been largely unexplored.

Individual-level measures have been used to inform risk compensation parameters in mathematical models aimed at determining the percent efficacy required for an HIV vaccine to impact HIV incidence (Andersson et al., 2007). However, if risk compensation increases the connectivity of risk networks, the impacts of risk compensation on HIV incidence may be underestimated. HIV vaccination inherently will disrupt flows of HIV through risk networks; the degree of disruption, however, will depend on behavioral changes and the network position of those who risk compensate. Thus, the distribution of risk

compensation within risk networks could be an important factor in determining the effectiveness of community HIV vaccine initiatives.

To address these gaps, studies with a *sociometric* design (Friedman, Curtis, Neaigus, Jose, & Des Jarlais, 1999) are needed. Sociometric studies entail eliciting network data from participants and their named partners to construct an overall network structure. In the context of risk compensation, this would enable the actual (or current) network structure to be compared to a network constructed on the basis of participants' anticipated behavior change. Comparisons could then be made to determine if there are increases in network size, density, centrality, and cohesiveness, all of which have been demonstrated to play a role in network-level HIV and STI transmission (Bearman, Moody, & Stovel, 2004; De et al., 2004; Friedman et al., 1997; Helleringer, Kohler, Chimbiri, Chatonda, & Mkandawire, 2009; Klovdahl et al., 1994; Potterat et al., 1999; Rothenberg, Potterat, et al., 1998; Rothenberg, Sterk, et al., 1998). If these indexes increase due to risk compensation, future simulation studies on HIV vaccine impact should include these as parameters in the models.

Underrepresentation of People who Use Drugs in HIV Vaccine Acceptability Research

Studies have called for increased representation of PWID in vaccine research, specifically that related to hepatitis C (HCV) and HIV (Baral, Sherman, Millson, & Beyrer, 2007). In 2012, nearly 100,000 participants were involved in HIV prevention research trials, approximately 3% of which were PWID (HIV

Vaccines and Microbicides Resource Tracking Working Group, 2013). Of the 15 quantitative studies from the US included in a recent meta-analysis of HIV vaccine acceptability research (Newman & Logie, 2010), only three explored HIV vaccine acceptability among drug users (Crosby et al., 2004; Newman, Duan, Lee, et al., 2006; Newman, Lee, et al., 2009), and none reported results stratified by drug use. There have been several qualitative studies examining HIV vaccine acceptability among people who use drugs. However, the geographic scope of these studies is limited, given that nearly all were based in Los Angeles (Newman, Duan, et al., 2008; Newman, Duan, Rudy, Roberts, et al., 2004; Newman, Lee, et al., 2009; Newman, Seiden, et al., 2009; Roberts et al., 2005; Rudy et al., 2005). In each of these studies, drug users made up only a minority of the sample and were predominantly recruited from SEPs. Two other qualitative studies that have involved drug users were only peripherally focused on HIV vaccination and took place in San Francisco (Seal et al., 2003) and among female inmates in Rhode Island (Lally et al., 2006). The results from the qualitative research on HIV vaccine acceptability have generally been reported in the collective, which may suggest that the perspectives of PWID are not dissimilar to that of other high-risk participants. However, further research is needed to explore if this is the case.

More research is also needed to explore risk compensation related to drug use. With rare exception (Bogard & Kuntz, 2002; Fonseca et al., 2010), simulation modeling examining the impact of HIV vaccination has focused exclusively on risk compensation in terms of condom use (Andersson et al.,

2007; Andersson, Paltiel, & Owens, 2011; Blower & McLean, 1994; Gray et al., 2003). Studies have primarily asked individuals about their personal likelihood of decreasing condom use and/or increasing their number of sexual partners in response to receiving the vaccine. Few quantitative studies have examined risk compensation within the context of drug-related risk behavior (e.g., increased syringe sharing), though participants in qualitative research have discussed the possibility of increased syringe sharing and increased sexual risk behavior among PWID (Newman, Duan, Rudy, & Johnston-Roberts, 2004). Research on PWID enrolled in the AIDSVAX clinical trial in Thailand found that, over the course of the trial, syringe sharing and frequency of injection drug use decreased (Martin et al., 2010; van Griensvan et al., 2004). Of note, however, the timing of the trial (1999 – 2003) coincided with Thailand's "War on Drugs" (Martin et al., 2010). Given the HIV risk conferred by injection drug use and transmission potential presented by behaviors such as syringe-sharing, the exclusive focus on HIV vaccination in the context of sexual transmission could present a significant impediment to developing effective vaccine roll-out strategies among high-risk, drug-using populations.

HIV Vaccine Acceptability among High-risk Populations in Rural Areas

Everything that is known about HIV vaccine acceptability among drug users comes from samples recruited in urban settings. The content presented in this chapter is based on a review of over 140 original studies, systematic reviews, and meta-analyses on HIV vaccine acceptability, clinical trial

participation, and risk compensation; of these, none were conducted in a rural setting in the US. This gap is concerning in light of national surveillance data that indicate the number of AIDS cases continues to rise in many rural communities, particularly in the South (Centers for Disease Control and Prevention, 2008, 2011). Given the historically low prevalence of HIV in rural areas and the common misconception that HIV is an "urban problem", many rural communities are unequipped to deal with the social, economic, and healthcare burden posed by an increase in the local prevalence of HIV and AIDS.

In perhaps nowhere is this more applicable than in rural Central Appalachia, which encompasses some of the most economically distressed counties in the US (Appalachian Regional Commission, 2011). Marked health disparities (Halverson, 2004), insufficient health infrastructure (Halverson, 2004), and prevalent misuse of prescription drugs (Cicero, Inciardi, & Munoz, 2005; Havens et al., 2007; Zhang et al., 2008) present significant challenges to public health in Appalachia. Currently, HIV prevalence is low in this population (Kentucky Cabinet for Health and Human Services, 2012), but evidence from Eastern Kentucky suggests that many drug users exhibit the requisite biological and behavioral risk factors for HIV (Havens et al., 2013; Young & Havens, 2012). A cohort study of drug users in Eastern Kentucky revealed that over 75% had engaged in injection drug use (Young & Havens, 2012), 80% reported recent unprotected sex (Crosby, Oser, Leukefeld, Havens, & Young, 2012), and 54% tested positive for HCV (Havens et al., 2013). Furthermore, drug users in the cohort were embedded in a highly cohesive and centralized sexual and

equipment-sharing network that could facilitate HIV transmission (Young, Jonas, Mullins, Halgin, & Havens, 2013).

No study to date has explored Appalachian residents' attitudes toward HIV vaccination. The most related research has been that conducted on human papillomavirus (HPV) vaccine acceptability. Research on HPV vaccination has indicated that there are unique social and cultural factors that influence vaccine uptake among Appalachians (Katz et al., 2009). The qualitative research revealed that concerns about stigma and confidentiality, mistrust of the medical community and of "outsiders" in general, as well as suspicion of pharmaceutical companies and government intrusion played a role in shaping HPV vaccine attitudes in Appalachia (Katz et al., 2009). Considering the heightened level of stigma associated with HIV in Appalachia (Basta, 2010), it is highly likely that many of the same issues could impact HIV vaccine uptake. Given these risk factors and myriad cultural, social, and economic complexities, Appalachia is a setting in which thorough preliminary knowledge of potential barriers and facilitators to program implementation is essential in achieving effective intervention.

Significance of Dissertation Research

Key to the ultimate success of the HIV vaccine development effort is the establishment of effective dissemination strategies. Without feasibility research to identify potential barriers and facilitators to HIV vaccination, community implementation strategies cannot be planned, nor can vaccine delivery channels

be prepared. Health providers, researchers, and practitioners in Appalachia are in a uniquely advantageous position to prepare for the roll-out of the HIV vaccine among its high-risk populations. In many communities characterized by high-risk behavior, practitioners and program planners must contend with an already substantial burden of HIV and AIDS. In Appalachia, however, interventionists have the opportunity to focus efforts on a truly preemptive approach to HIV prevention.

The current gap in knowledge about HIV vaccine attitudes, uptake patterns, and risk compensation within social networks of high-risk individuals could present a critical impediment to the development of vaccine dissemination strategies, particularly in those settings with existing sociocultural and economic challenges to program implementation, such as in Appalachia. Using extensive data on drug users' risk behaviors, risk networks, and network-level attitudes and norms around vaccine acceptability, this dissertation examines new dimensions of HIV vaccine acceptability and risk compensation in an under-studied, high-risk population from Appalachian Kentucky. The dissertation reveals important factors that could influence the translation of HIV vaccine development efforts into a successful community-based HIV vaccine campaign.

Summary

The studies presented in this dissertation address critical gaps in existing knowledge about HIV vaccine acceptability. The following three chapters address three distinct analyses and will be summarized in a final concluding chapter.

Study 1 examines demographic, behavioral, and psychosocial correlates to HIV vaccine acceptability among a sample of high-risk drug users in Appalachia. Study 2 investigates drug users' willingness to encourage their risk partners (injection and/or sexual) and other peers to receive an approved, preventive HIV vaccine. Specifically, Study 2 uses formal network analysis to examine the association between dyadic characteristics of relationships and respondents' willingness to encourage vaccination among specific peers. Study 3 determines network-level correlates to and consequences of drug- and sex-related HIV risk compensation (i.e. increased levels of drug- and sex-related HIV risk behaviors in response to receiving an HIV vaccine).

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Chapter 2 : HIV vaccine acceptability among high-risk drug users living in a rural, low-prevalence community

Abstract

A vaccine could substantially impact the HIV epidemic, but adequate uptake is a concern, particularly in populations with low perceived HIV risk. This study examined HIV vaccine acceptability among high-risk drug users in a rural community in the United States. Interviewer-administered questionnaires collected data on risk behavior and attitudes toward HIV vaccination from 433 HIV-negative drug users (76% with history of injection) enrolled in a cohort study in Central Appalachia. HIV vaccine acceptability was measured on a 4-point Likert scale. Generalized linear mixed models were used to determine correlates to individuals' report that they were "very likely" to receive a HIV vaccine (i.e. "maximum vaccine acceptability", or MVA). Adjusted odds ratios (AORs) and corresponding 95% confidence limits are reported. Only 23% believed that they were at risk for HIV, yet 91% reported that they would accept a preventive HIV vaccine that was 90% effective. The most commonly cited barrier to vaccine acceptability was cost (76%). Men were significantly less likely to report MVA (AOR: 0.33, 95% CI: 0.21 – 0.53). MVA was more common among participants who believed that they were susceptible to HIV (AOR: 2.27, 95% CI: 1.26 – 4.08), that an HIV vaccine would benefit them (AOR: 2.80, 95% CI: 1.69 – 4.67), and who had positive experiential attitudes toward HIV vaccination (AOR: 1.84, 95% CI: 1.07 – 3.16). MVA was also more common among participants who believed that others would encourage them to get vaccinated and anticipated that their behavior would be influenced by others' encouragement (AOR: 1.79, 95% CI: 1.07 – 3.01). Despite low perceived risk, vaccine acceptability was nearly unanimous among individuals with a history of injection drug use. Cognitive factors such as perceived risks and benefits, as well as social norms could play an important role in influencing HIV vaccine coverage in this population of rural drug users.

Introduction

Since 1987, the scientific community has been in pursuit of an effective HIV vaccine (Girard, Osmanov, Assossou, & Kieny, 2011). In 2012, investments in global HIV vaccine research and development totaled US$847 million (HIV Vaccines and Microbicides Resource Tracking Working Group, 2013). In response to the possibility that an HIV vaccine is on the horizon, researchers have mobilized to examine the feasibility of disseminating the vaccine. The estimated uptake for a high-efficacy HIV vaccine is only 38% of the projected need (Esparza et al., 2003). In high-risk populations around the world, numerous studies on HIV vaccine acceptability have been conducted. A meta-analysis published in 2010 revealed that the average level of HIV vaccine acceptability was only moderate (66 on a 100-point scale) and that acceptability varied widely across studies (range: 37 - 94) (Newman & Logie, 2010). The variability across studies may indicate that factors influencing acceptability are context- and population-specific.

People who use drugs have been significantly underrepresented in research on HIV vaccine acceptability. Of the 15 quantitative studies from the US included in a review by Newman and Logie (2010), only three included drug users in their sample (Crosby, Holtgrave, Bryant, & Frew, 2004; Newman et al., 2006; Newman, Lee, et al., 2009), none of which reported results stratified by drug use. While there have been qualitative studies on HIV vaccine acceptability involving people who use drugs, the scope of these studies is limited, given that nearly all were based in Los Angeles (Newman, Duan, Kakinami, & Roberts,

2008; Newman, Duan, Rudy, Roberts, & Swendeman, 2004; Newman, Lee, et al., 2009; Newman, Seiden, Roberts, Kakinami, & Duan, 2009; Roberts, Newman, Duan, & Rudy, 2005; Rudy et al., 2005). Furthermore, drug users made up only a portion of the sample for each of these studies and findings were generally reported in the collective. Thus, the unique perspectives of drug users in regard to HIV vaccine acceptability remain largely unknown.

There are no studies to date evaluating HIV vaccine acceptability in a high-risk, rural population in the US. National surveillance data indicate that while the prevalence of AIDS has gradually declined in most urban areas since the mid 1980's, the number of AIDS cases continues to slowly increase in many rural communities, particularly in the South (Centers for Disease Control and Prevention, 2008, 2011). Given the historically low prevalence of HIV in rural areas and the common misconception that HIV is an "urban problem", many rural communities are unequipped to deal with the social, economic, and healthcare burden posed by an increase in the local prevalence of HIV and AIDS.

In perhaps nowhere is this more applicable than in rural Central Appalachia, which encompasses some of the most economically distressed counties in the US (Appalachian Regional Commission, 2011). The Appalachian region is characterized by marked health disparities (Halverson, 2004), an under-resourced health infrastructure (Halverson, 2004), and prevalent misuse of prescription drugs (Cicero, Inciardi, & Munoz, 2005; Havens et al., 2007; Zhang et al., 2008). While HIV is currently uncommon in this population (Kentucky Cabinet for Health and Human Services, 2012), recent evidence from Eastern

Kentucky suggested that many nonmedical prescription drug users were infected with hepatitis C (HCV) (Havens et al., 2013), had engaged in injection drug use (IDU) (Young & Havens, 2012) and frequent unprotected sex (Crosby, Oser, Leukefeld, Havens, & Young, 2012), and were embedded in a highly cohesive and centralized sexual and equipment-sharing network that could facilitate HIV transmission (Young, Jonas, Mullins, Halgin, & Havens, 2013). Given these risk factors and myriad cultural, social, and economic complexities, Appalachia is a setting in which greater knowledge of potential barriers and facilitators to HIV vaccine acceptability will be essential in achieving adequate coverage.

Given the lack of HIV vaccine acceptability research in this population, research on human papillomavirus (HPV) vaccination in Appalachia may provide the most relevant insight into factors that could influence uptake. HPV vaccine acceptance research has indicated that there are a number of social and cultural factors influence vaccine uptake among Appalachians, including concerns about stigma and confidentiality, mistrust of the medical community and of "outsiders" in general, as well as suspicion of pharmaceutical companies and government intrusion (Katz et al., 2009). Considering the heightened level of stigma associated with HIV in Appalachia (Basta, 2010), it is likely that many of the same issues could impact HIV vaccine uptake.

Considering the lack of formative research on HIV vaccine acceptability in Appalachia, a theoretically-grounded approach is essential. Previous studies on HIV vaccine acceptability use the Theory of Reasoned Action (TRA) (Frew et al., 2010; Frew, Archibald, Hixson, & del Rio, 2011; Frew, Archibald, Martinez, del

Rio, & Mulligan, 2007), Theory of Planned Behavior (TPB) (Gagnon & Godin, 2000), or the Health Belief Model (HBM) (Liau, Zimet, & Fortenberry, 1998; Zimet, Fortenberry, & Blythe, 1999; Zimet, Liau, & Fortenberry, 1997). The present study is based on the Integrative Model of Behavioral Prediction (IM) (Fishbein, 2008), which is built upon the frameworks of the TRA (Fishbein & Ajzen, 1975), TPB (Ajzen, 1991), HBM (Rosenstock, 1960), and Social Cognitive Theory (Bandura, 1998). According to the IM, behavior is directly affected by behavioral intention, which is in turn influenced by attitudes, perceived norms, and personal agency. Demographic, behavioral, and other contextual factors serve as background variables that influence attitudes, perceived norms, and personal agency. The model has successfully been applied to the study of other types of vaccine uptake (Dillard, 2011; Painter et al., 2010; Painter et al., 2011), as well as risk reduction intention and behavior in high-risk populations (e.g. (Bleakley, Hennessy, Fishbein, & Jordan, 2011; Hennessy et al., 2010; Kasprzyk, Montaño, & Fishbein, 1998). The purpose of this paper was to examine demographic, behavioral, and IM-based psychosocial correlates to HIV vaccine acceptability among a sample of HIV negative, high-risk drug users in Appalachia.

Methods

Sample

The data used for this analysis were collected during the 24-month assessment of the longitudinal Social Networks among Appalachian People

(SNAP) study. Recruitment and assessment are described in detail elsewhere (Havens et al., 2013; Young et al., 2013). Briefly, the SNAP study began in 2008 with the recruitment of 503 adult drug users from a rural, Appalachian region in Kentucky. To be eligible, participants were required to have used prescription opioids, heroin, crack/cocaine, or methamphetamine to get high in the prior 30 day period. Participants were recruited using respondent driven sampling (RDS) and data were collected using questionnaires administered by community-based staff. Participants completed follow-up interviews and HIV testing at 6-month intervals. The 24-month follow-up interview was completed by 435 participants between March 2012 and May 2013.

Following their 24-month SNAP interview, participants were invited to complete an interviewer-administered questionnaire on their attitudes toward HIV vaccination. Two participants in jail were not interviewed due to time constraints, but all other participants (n=433) were invited and consented to complete the questionnaire. Participants were compensated $35 for participation. Before completion of the survey, participants were read a short script reminding them that HIV can be transmitted through sharing drug equipment and having unprotected sex, that HIV is the cause of AIDS, and that there is currently no cure for HIV and AIDS. The script informed participants that scientists were working on a vaccine, and that the vaccine referred to throughout the questionnaire would not cure HIV, but would protect against acquisition (efficacy levels were specified in individual questions). The University of Kentucky

Institutional Review Board approved the protocol and a Certificate of Confidentiality was obtained.

Network data collection

The SNAP interview elicited information about participants' social networks (methods described in detail elsewhere (Young et al., 2013). Participants gave the first name and last initial of up to 24 network members, including eight from/with whom they had received social support, used drugs (excluding alcohol and marijuana), and engaged in sex during the past 6 months. In the present study, network-based psychosocial measures (described below) were assessed for risk network relationships, or those in which partners engaged in sex or IDU together. Network analyses and visualizations were conducted using UCINET (version 6) (Borgatti, Everett, & Freeman, 2002) and NetDraw (version 2) (Borgatti, 2002), respectively.

HIV Vaccine Acceptability. HIV vaccine acceptability was assessed with the following: “Imagine that an affordable HIV vaccine was approved and made available to you in the next 12 months. This vaccine would prevent you from getting HIV almost all of the time (90% effective). How likely would you be to get this vaccine?”, followed by a 4-point Likert scale ranging from 'very unlikely' to 'very likely'. Due to skewness in the response distribution, small stratum-specific sample sizes (only 5% responded 'very unlikely' and 4% 'unlikely'), and violation of the proportional odds assumption in ordinal regression, the outcome variable was dichotomized for analysis. The distribution of responses necessitated that the variable be recoded so that 0 = Very unlikely, Unlikely, Likely and 1 = Very

likely. Given the questionable association between intent and behavior in HIV vaccine research (Poole, 2012), this conservative dichotomization scheme may provide a better indication of future uptake. Hereafter, those who were 'very likely' to accept the vaccine are referred to as reporting “maximum vaccine acceptability” (MVA).

Demographic characteristics. Data were also collected on participants’ age, gender, race, marital status, educational attainment, employment, income, and health insurance status. With the exception of age and income, which were assessed as continuous variables, all other demographic variables were analyzed as dichotomous.

Risk Behavior. Five IDU-related behaviors and three sexual behaviors were entered in the analysis. To be consistent with the recall period specified for the network data, the analysis focused on behavior in the past 6 months. Participants reported if they had recently engaged in IDU, used an unclean needle, gave/loaned/sold a used needle to someone, and/or bleached their needles before use in the past 6 months. Participants also reported their total number of sexual partners in the past 6 months; due to a positively skewed distribution, the variable was dichotomized (1 = multiple partners, 0 = one or fewer partners). Data on the frequency with which participants engaged in unprotected sex in the past 6 months, including unprotected sex with people who inject drugs (PWID), were also collected.

Psychosocial Measures. The questionnaire was based on a modified version of the IM (Montaño & Kaspryzyk, 2008). Table 2.1 describes the items

and coding scheme used for analysis. Three constructs were examined: attitudes (instrumental and experiential), subjective norms (descriptive and injunctive), and personal agency (perceived behavioral control and self-efficacy). Similar constructs have been used in previous research (Frew et al., 2010; Frew et al., 2011; Frew et al., 2007). *Experiential attitude* refers to an emotional response to the idea of performing a behavior, while *instrumental attitude* involves cognitive appraisal of performing the behavior (Fishbein, 2007). Experiential attitudes were examined with three items (coefficient alpha = 0.68) that had been used in a similar study (Gagnon & Godin, 2000). Elements of the *instrumental attitude* measure were adapted from the HBM (Rosenstock, 1960); these include perceived severity of HIV, perceived susceptibility to HIV, perceived benefits of HIV vaccination, and perceived barriers to getting the vaccine. Perceived susceptibility was assessed using a general measure and a network-based measure, the latter of which was computed as a product of the responses given on the two network-based items described in Table 2.1.

Injunctive norms are a person's beliefs about and motivation to comply with what others think he/she should do. *Descriptive norms* refer to a person's perceptions about others' behavior and his/her motivation to comply with (i.e. imitate) their actions (Cialdini, Reno, & Kallgren, 1990; Fishbein, 2009). The distinction between injunctive and descriptive norms is important given that several studies have found that descriptive norms can independently contribute to the prediction of intent (Rivis & Sheeran, 2003) and that the relative influence of each on intent varies across behaviors (Smith-McLallen & Fishbein, 2008).

Descriptive and injunctive norms are each comprised of two sub-constructs: normative beliefs and motivation to comply. In this study, each sub-construct was measured with general and network-based measures (Table 2.1). The general measure assesses participants' perception of what *most* people would do and encourage them to do. The network-based measure ask participants about the anticipated vaccination behavior of each named network member and about each network member's likelihood of encouraging the respondent to get the vaccine. The overall *injunctive norms* and *descriptive norms* constructs for general and network-based measures were computed as a product of the responses given on the questions referring to their sub-constructs.

According to the IM, two constructs related to personal agency also influence individuals' intentions: self-efficacy and perceived behavioral control (Montaño & Kaspryzyk, 2008). *Self-efficacy* is the belief in one's general capabilities to exercise control over his/her behavior (Bandura, 1991), while *perceived behavioral control* focuses on one's abilities to perform a behavior in light of various barriers (Ajzen, 2011). While the distinctiveness and methods of operationalizing these constructs have been debated (McCaul, Sandgren, O'Neill, & Hinsz, 1993; Terry & O'Leary, 1995) there is some evidence that the two constructs are discrete and collectively contribute to understanding protective health behaviors (McCaul et al., 1993; Povey, Conner, Sparks, James, & Shepherd, 2000). In this study, *self-efficacy* was assessed with three items (coefficient alpha = 0.73) and *perceived behavioral control* was assessed with one (Table 2.1).

Statistical Analyses

Given that participants were nested within social networks, autocorrelation was inherent; therefore, standard regression techniques were not appropriate (Agresti, 2002). Generalized linear mixed models for bivariate and multivariate analyses were estimated using the PROC GLIMMIX procedure (SAS software, version 9.3) with a random effect for subject and a logit link function (SAS Institute, 2011). All p-values were adjusted for multiple comparisons using the Sidak method (Šidák, 1967), and odds ratios (ORs), adjusted odds ratios (AORs), and 95% confidence intervals (CIs) were reported. Collinearity in multivariate analysis was assessed using the %COLLIN_2011 macro (Zack, Singleton, Satterwhite, Delaney, & Wall, 2011). Condition indexes of greater than 30 and corresponding variance decomposition proportions of greater than 0.5 were considered indicative of collinearity (Kleinbaum & Klein, 2010). All results were compared to the output of node-level regression performed within UCINET (Borgatti et al., 2002). Node-level regression generates significance values based on permutation-testing. The algorithm first determines the observed slope coefficients then recalculates the coefficients over 10000 repetitions involving the random redistribution of values among network members. The p-value for the association of each covariate with the dependent vector is equal to the proportion of permutations that yielded a statistic as extreme as the initial slope coefficients that were produced (Hanneman & Riddle, 2005).

Due to the number of demographic, behavioral, and theoretical variables relative to the sample size, a screening strategy was necessary to reliably

establish the model. Therefore, each demographic and behavioral variable was assessed independently for its association with the outcome, and only those reaching significance ($p < 0.05$) in bivariate analyses were entered into the multivariate analyses. Due to the a priori nature of the IM, all psychosocial variables were entered into the multivariate model regardless of bivariate significance, as suggested by Hennessy and colleagues (2010).

To examine the contribution of each theoretical construct to the performance of the overall model, a series of F tests were performed based on a linearized approximation to the GLIMMIX models being considered. A statistically significant F statistic ($p < 0.05$) on indicates that the group of variables under consideration, if dropped from the model, would result in a significant decrease in its predictive ability, as indicated by change in the residual log (pseudo) likelihood of the overall model.

Results

Descriptive data are presented in Table 2.2. Most respondents were White (94%), 55% were male, and 74% were unmarried. The median age was 34 years (range: 21 – 68). Most (76%) reported a lifetime history of IDU and 34% reported recent IDU (past 6 months). Receptive and distributive needle sharing were relatively uncommon (reported by 8% and 4%, respectively), but 13% had shared cookers, cottons, and/or rinse water and few had bleached a syringe before use (8%). Approximately 24% reported multiple sex partners in the past 6 months and 71% had engaged in unprotected sex. Nearly 20% had unprotected sex with

PWID. Of note, most participants (95%) were nonmedical users of prescription drugs, fewer than 12% reported crack/cocaine use and only 5% reported heroin use.

Attitudes toward HIV and HIV vaccination

Nearly everyone (99%) perceived HIV as severe or very severe, but only 23% believed they were likely to get HIV in their lifetime. Nevertheless, 72% reported that an HIV vaccine would benefit them. On a checklist of possible barriers to HIV vaccine uptake, cost was most commonly endorsed (76%), followed by number of doses (30%) and transportation and time to visit a clinic (22% and 11%, respectively). Of note, 13% indicated that concern about the provider's disclosure of their vaccination status to others would be a barrier to their vaccine uptake. Most participants reported that they would be very likely (59%) or likely (32%) to receive an HIV vaccine.

Nearly 83% of participants reported that most people they knew would get vaccinated against HIV if a vaccine was available. However, only 51% reported that they would be influenced by others' behaviors (i.e. that they would be more likely to accept the vaccine if most people they knew got vaccinated). Nearly all participants (94%) believed that most people would be supportive of their HIV vaccination and 60% reported that they would be more likely to be vaccinated if most people encouraged them.

The majority (64%) believed that they would have personal control over their ability to get vaccinated. However, 76% were not sure or only somewhat sure that they would be able to get vaccinated if they had to pay for it out of

pocket, had to travel out of town to get it (58%), or if their friends/partner were not supportive (39%).

Most participants (n=355, 82%) named at least one risk partner in the social network portion of the questionnaire. Of these, 27% reported that at least one of their risk partners would be likely acquire HIV and 14% believed that at least one partner posed a risk for HIV transmission to them. Most participants (84%) indicated that at least one network member would be likely or very likely to get an HIV vaccine, and 47% reported that they personally would be more likely to get vaccinated if a partner accepted the vaccine. Nearly 87% of participants reported that at least one network partner would encourage them to get vaccinated against HIV and 56% reported that they were would be more likely to get vaccinated if a network member encouraged them. Of note, there was a significant association between network-based and general measures of descriptive norms ($\chi^2 = 104.8$, $p < 0.001$) and of injunctive norms ($\chi^2 = 102.3$, $p < 0.001$).

Bivariate results involving individual-level variables

Bivariate results are presented in Table 2.3. Men were significantly less likely to report MVA (OR: 0.37, 95% CI: 0.25 - 0.55). PWID were significantly more likely to report MVA (OR: 1.80, 95% CI: 1.18 - 2.74), as were those who engaged in unprotected sex with PWID (OR: 1.97, 95% CI: 1.17 - 3.31). Other demographic and behavioral characteristics were not significantly associated with the outcome.

As hypothesized, several attitudinal constructs were associated with MVA. Individuals who believed they were likely or very likely to get HIV (OR: 2.85, 95% CI: 1.70 - 4.76) and those who believed that an HIV vaccine would be beneficial to them (OR: 3.17, 95% CI: 2.05 - 4.90) were more likely to report MVA. Participants who gave positive ratings on all three experiential attitude items (described in Table 2.1) were more likely report MVA (OR: 2.03, 95% CI: 1.27 - 3.25). Participants who indicated there would be at least one barrier (from the checklist described in Table 2.1) to their ability to receive the vaccine were less likely to report MVA (OR: 0.57, 95% CI: 0.35 - 0.94).

Descriptive and injunctive norms were both associated with MVA. Respondents who reported that most people they know would accept an HIV vaccine *and* that they personally would be more likely to accept the vaccine if others did so were significantly more likely to report MVA (OR: 1.73, 95% CI: 1.17 - 2.57). Of note, both of the component constructs of descriptive norms (e.g., normative beliefs and motivation to comply) were also significantly associated with the outcome. Participants who believed that most people would encourage them to receive the vaccine and who reported being more likely to accept the vaccine if others encouraged them were nearly twice as likely to report MVA (OR: 1.93, 95% CI: 1.31 - 2.86). Only one component construct of injunctive norms (motivation to comply with others' recommendations) was significantly associated with the outcome. The normative belief that most others would encourage vaccination approached significance ($p = 0.074$).

Of the two measures of personal agency, perceived behavioral control and self-efficacy, only the former was significantly associated with the outcome. Participants who believed they would have personal control over their own vaccination were significantly more likely to indicate MVA (OR: 1.58, 95% CI: 1.06 - 2.36). Self-efficacy approached significance in its association with the outcome (OR: 1.64, 95% CI: 0.99 - 2.74, p = 0.056).

Bivariate results involving network-based variables

There was a reduced sample size (n = 355) for analysis of network-based variables, as these items were not completed by the 78 respondents who did not name a risk partner. Only one of the bivariate models involving network-based characteristics would converge using GLIMMIX. Descriptive normative belief (i.e. perception that at least one risk network partner would accept the HIV vaccine) was significantly associated with MVA (OR: 2.10; 95% CI: 1.18 – 3.72). Other network-based variables were examined using node-level regression, which revealed that only injunctive normative beliefs and descriptive norms neared statistical significance (p = 0.074 and p = 0.089, respectively).

Multivariate results

Multivariate results are described in Table 2.4. Gender, recent IDU, and unprotected sex with PWID were entered into multivariate analysis with all psychosocial constructs. The highest condition index observed was 27.9, indicating no apparent collinearity in the model. The direction and statistical significance of all associations in the multivariate model were consistent with results produced by node-level regression conducted in UCINET.

Controlling for all other variables in the model, men were significantly less likely to report MVA (AOR: 0.33, 95% CI: 0.21 - 0.53). Participants who believed they were susceptible to HIV (AOR: 2.29, 95% CI: 1.27 - 4.12), perceived that the vaccine would benefit them (AOR: 2.78, 95% CI: 1.67 - 4.63), and reported positive experiential attitudes (AOR: 1.87, 95% CI: 1.09 - 3.20) were significantly more likely to report MVA. Perceived barriers to vaccination and perceived severity of HIV were not associated with the outcome. Despite the significant association between three attitudinal measures and the outcome, the F test for the group of attitudinal variables was not significant ($p = 0.113$), indicating that the removal of the variables from this model would not substantially affect its predictive ability.

Controlling for other variables in the model, injunctive norms remained significantly associated with vaccine acceptability (OR: 1.78, 95% CI: 1.06 - 2.99). Although descriptive norms was not independently associated with the outcome, the F test indicated that the two constructs (i.e. injunctive and descriptive norms) significantly contributed to the predictive ability of the model ($p = 0.004$). Conversely, perceived behavioral control and self-efficacy were not independently associated with the outcome after adjustment for other variables, and did not substantially contribute to the overall model ($p = 0.213$).

Discussion

In this sample of rural drug users, 91% were likely or very likely to accept a 90% effective, preventive HIV vaccine. This percentage is comparable to that

found in other urban and suburban populations in the US (Lally et al., 2006; Seal et al., 2003; Webb, Zimet, Mays, & Fortenberry, 1999). Vaccine acceptability was significantly higher among PWID; only 3% of those who had injected in the past 6 months indicated that they would be unlikely or very unlikely to accept an HIV vaccine. People who had sex with PWID were also significantly more likely to report MVA. However, neither of these associations remained significant when adjusting for psychosocial constructs and gender. Men were significantly less likely to indicate that they were very likely to receive an HIV vaccine, after adjustment for behavioral characteristics and psychosocial constructs. Previous research on the association between gender and HIV vaccine acceptability is mixed, with one finding that acceptability was higher among women (Suraratdecha, Ainsworth, Tangcharoensathien, & Whittington, 2005) and another finding that it was higher among men (Bishai, Pariyo, Ainsworth, & Hill, 2004). In general, gender difference in HIV vaccine acceptability have not been reported. However, in this setting, the findings suggest that a one-size-fits-all approach to HIV vaccine promotion may not be appropriate or productive and that targeted strategies should be developed to address possible gender-differences in vaccine uptake.

Given their low income and high rate of unemployment, it is unsurprising that most participants reported that cost would be a barrier to vaccine acceptability. Pragmatic barriers such as dosing and transportation were reported by a sizable minority. Consistent with other studies (Newman & Logie, 2010), these data underscore the importance of minimizing out-of-pocket costs to

achieve adequate coverage. It is also notable that nearly one in eight reported concern that providers would disclose their vaccination status to others. Appropriate training of providers about breaches of confidentiality and public assurance of privacy in HIV vaccine uptake will be important.

In the present study, perceived susceptibility to HIV was significantly associated with vaccine acceptability. This finding is consistent with previous research (e.g., (Bishai et al., 2004; Liau & Zimet, 2000; Suraratdecha et al., 2005; Zimet et al., 1999; Zimet et al., 1997). In the present study, only 23% believed they were likely or very likely to be infected with HIV in the future. However, despite low perceived vulnerability to HIV, 72% believed that an HIV vaccine would benefit them. Consistent with previous research (Liau & Zimet, 2000; Zimet et al., 1999), perceived benefits of HIV vaccination were associated with vaccine acceptability. Thus, HIV vaccine promotion campaigns involving positive messaging about the benefits of vaccination may be as or more successful than those focused on marketing the threat of HIV. This approach would be consistent with Prospect Theory (Kahneman & Tversky, 1982), which suggests that in situations involving low risk and high certainty regarding the outcomes of the behavior, gain-framed messages may be more appropriate than loss-framed messages (Rothman & Salovey, 1997). Recent research has evaluated the applicability of this concept to promoting participation in HIV vaccine clinical trials (Evangeli, Kafaar, Kagee, Swartz, & Bullemor-Day, 2012).

Findings regarding the importance of perceived social norms may also inform appropriate and effective strategies for HIV vaccine promotion. Descriptive

data revealed that nearly 40% were not sure or only somewhat sure that they would be able to get the HIV vaccine if a friend and/or partner was unsupportive. Adjusting for gender, risk behavior, and other psychosocial characteristics, participants who believed that most people would encourage them to receive an HIV vaccine and who reported they would be motivated to comply with those recommendations were significantly more likely to report MVA. This finding may serve as preliminary evidence that peer-promotion of HIV vaccination could be a successful strategy in this population. In this context, the lack of an association between descriptive norms (i.e. perceptions of others' vaccination behavior) and vaccine acceptability in multivariate analysis deserves comment. These data suggest that passive diffusion of vaccine uptake through the social network (i.e. via imitation of others' behavior) is unlikely, and underscore the importance of an active, intentional approach to peer-based promotion.

The findings from this study have several theoretical and methodological implications. The findings highlight the importance of assessing both the injunctive and descriptive dimensions of social norms and of coupling measures of normative beliefs with assessments of individuals' motivation to comply. In the present study, most participants reported that people would accept an HIV vaccine, but far fewer reported that they would be influenced by others' behavior. Without the measure of motivation to comply, the influence of descriptive norms could have been over-estimated. Although individuals may underestimate their susceptibility to peer influence, data on compliance with norms may provide

preliminary insight into who may be most responsive to strategies such as social marketing.

The present study evaluated global measures of social norms (i.e. beliefs about what "most people" would do/say) and network-based measures, in which participants were asked about descriptive and injunctive norms specific to each of their named risk network members. Contrary to expectation, the global measures out-performed the network-based measure of social norms. The finding may be a result of the fact that normative data about network members were only assessed for network members with whom the participant was having sex or engaging in injection drug use. The influence of non-risk network members, such as those providing social support, were not captured and may have been influential. In future research, it will be important to examine the relative influence of different social referents on individuals' beliefs about HIV vaccination.

The present study is not without limitations. The research focused on *intent* to receive an HIV vaccine and, until an HIV vaccine is approved, the correspondence between intentions and *actual* vaccine uptake remains unknown. The use of one-item measures to assess theoretical constructs in the present study could also be problematic to establishing psychometric validity and reliability. However, due to the elevated respondent burden presented by the inclusion of network-based measures and the time constraints of conducting some interviews in jail, the use of scales was not feasible. Finally, generalization of findings from this study to other regions of Appalachia and other rural areas in

the US should be made with caution, as cultural and social influences across settings are likely to vary.

In this rural community, despite low perceived vulnerability to HIV, most drug users were readily willing to accept a preventive HIV vaccine. Minimization of out-of-pocket costs will be essential. Social norms could also play a major role in influencing HIV vaccine uptake in this community, and if leveraged appropriately, could present an effective mechanism for promoting the HIV vaccine. To plan for effective promotion and dissemination strategies among populations at high risk for HIV, continued research is needed to explore influences on HIV vaccine acceptability among people who use drugs.

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Table 2.1 Individual-level psychosocial measures based on a modification of the Integrative Model of Behavioral Prediction

Construct	Measure
Experiential attitude	• [3-items] For me, getting an HIV vaccine would be… ["stressful - relaxing", "frightening – comforting", "irresponsible – responsible"][a]
Instrumental attitude	
Susceptibility	• If you did not get a vaccine, how likely do you think you would be to get HIV in your lifetime? [b]
Severity	• In your opinion, how serious would it be if you were infected with HIV?[c]
Benefits	• In your opinion, how much would an HIV vaccine benefit you? [d]
Barriers	• What factors would make it difficult for you to receive the HIV vaccine? [cost, number of doses, transportation/time to visit clinic, concern that provider would disclose vaccination status to others, other (open-ended)]
Subjective Norms	
Descriptive	• If an HIV vaccine became available, most of the people important to me would get it. [e]
Motivation to comply	• If most people got the HIV vaccine, would you be [More likely to get it/Less likely to get it/Would not affect my decision] [f]
Injunctive	• Most people important to me would be supportive of me getting the HIV vaccine. [e]
Motivation to comply	• If most people encouraged you to get the HIV vaccine, would you be [More likely to get it/Less likely to get it/Would not affect my decision][f]
Personal Agency	
Behavioral control	• How much personal control do you feel that you would have over getting the HIV vaccine?[g]
Self-efficacy	• [3-items], How sure are you that you could get the HIV vaccine if [you had to pay for it out of pocket/you had to travel out of town to get it/your friend or partners did not want you to get it]?[h]
Network-based measures	
Susceptibility	• How likely do you think it is that [network member] would ever get infected with HIV? [b]
	• How likely do you think it is that [network member] would ever infect you with HIV? [b]
Descriptive norms	• How likely do you think [network member] would be to get an HIV vaccine? [b]
Motivation to comply	• If [network member] got the HIV vaccine, would you be...[f]
Injunctive norms	• If [network member] got the HIV vaccine, how likely would they be to encourage you to get it? [b]
Motivation to comply	• If [network member] encouraged you to get the HIV vaccine, would you be... [f]

[a] Measured on 4-point semantic differential scales; dichotomized where 1=rating of three or four on all items, 0=rating of one or two on at least one item.

[b] Measured on 4-point scale dichotomized where: 0=Very unlikely/Unlikely, 1=Likely/Very likely
[c] Measured on 4-point scale dichotomized where: 0=Not serious at all/Somewhat serious, 1=Very serious/Extremely serious
[d] Measured on 4-point scale dichotomized where: 0=Not at all/Little, 1=Some/a lot
[e] Measured on 4-point scale dichotomized where 0=Strongly disagree/Disagree, 1=Agree/Strongly agree
[f] Dichotomized where 0=Less likely to get it/Would not affect my decision, 1=More likely to get it
[g] Measured on 4-point scale dichotomized where 0=No control/Some control, 1=A lot of control/Complete control
[h] Each measured on 4-point scales dichotomized where 0=Not sure at all/Somewhat sure, 1=Very sure/Extremely sure. Total measure was dichotomized where 1=rating of one on all items, 0=rating of zero on at least one item.

Table 2.2 Demographic and behavioral characteristics of the sample (n=433)

Characteristic	N (%)
Demographic	
Male	239 (55.2)
Age – median (IQR)	34 (29 – 41)
White	407 (94.0)
High school graduate	251 (58.0)
Married	111 (25.6)
Unemployed	169 (39.0)
Income in past 30 days[a] – median (IQR)	$698 (200 – 1100)
Uninsured	285 (65.8)
Drug use in past 6 months	
Nonmedical use of prescription drugs[b]	368 (95.0)
Cocaine	51 (11.8)
Methamphetamine	35 (8.1)
Heroin	23 (5.3)
Crack	14 (3.2)
IDU-related behaviors (past 6 months)	
Injected drugs at least once	146 (33.7)
Injected with unclean needle	33 (7.6)
Gave/loaned/sold an unclean needle	16 (3.7)
Shared injection equipment[c]	55 (12.7)
Bleached injection equipment[c]	35 (8.1)
Sexual behavior (past 6 months)	
Number of sex partners	
Zero	76 (17.6)
One partner	254 (58.7)
Two partners	56 (12.9)
Three or more partners	47 (10.9)
Unprotected sex with at least one partner	308 (71.1)
Unprotected sex with PWID	85 (19.6)

IQR: interquartile range; PWID: person who injects drugs; IDU: injection drug use

[a] Includes income from employment, unemployment compensation, welfare, pension/social security, child support, friends/family, and illegal activities

[b] Includes nonmedical use of methadone, OxyContin, oxycodone, buprenorphine, Roxicodone, hydrocodone, other opiates (e.g., Neurontin, Ultram, morphine, Demerol, Opana, Embeda, Avinza), and benzodiazepines

[c] Cookers, cottons, and/or rinse water

Table 2.3 Bivariate correlates to vaccine acceptability (n=433)

Characteristic	Vaccine Acceptability: Not very likely[a] (n=176)	Vaccine Acceptability: Very likely (n=257)	Bivariate: OR (95% CI)	Bivariate: p-value
Demographic				
Male	122 (69.3)	117 (45.5)	0.37 (0.25- 0.55)	<0.001**
White	163 (92.6)	244 (94.9)	1.50 (0.68 - 3.32)	0.321
Age - mean (SD)	36.3 (9.3)	34.9 (8.1)	0.98 (0.96 - 1.00)	0.108
Income (n=432) - mean (SD)	$908 (1473)	$913 (1125)	1.00 (1.00 - 1.00)	0.968
High school graduate	93 (52.8)	158 (61.5)	1.42 (0.97 - 2.10)	0.075
Uninsured	114 (64.8)	171 (66.5)	1.08 (0.72 - 1.62)	0.705
Married	41 (23.3)	70 (27.2)	1.23 (0.79 - 1.92)	0.358
Behavioral (past 6 months)				
Injected drugs	46 (26.1)	100 (38.9)	1.80 (1.18 - 2.74)	0.006**
Injected with unclean needle	9 (5.1)	24 (9.3)	1.91 (0.87 - 4.22)	0.109
Distributed unclean needle[b]	5 (2.8)	11 (4.3)	1.53 (0.52 - 4.49)	0.440
Shared injection equipment[c]	18 (10.2)	37 (14.4)	1.48 (0.81 - 2.69)	0.204
Bleached injection equipment[c]	9 (5.1)	26 (10.1)	2.09 (0.95 - 4.58)	0.066
Had multiple sex partners	35 (19.9)	68 (26.5)	1.45 (0.91 - 2.30)	0.116
Had unprotected sex	120 (68.2)	188 (73.2)	1.27 (0.83 - 1.94)	0.264
Unprotected sex with PWID	24 (13.6)	61 (23.7)	1.97 (1.17 - 3.31)	0.010*
Attitudes about HIV				
Severity of HIV	173 (98.3)	254 (98.8)	1.47 (0.29 - 7.39)	0.641
Susceptibility to HIV	23 (13.1)	77 (30.0)	2.85 (1.70 - 4.76)	<0.001**
Network HIV susceptibility[d]	15 (10.8)	35 (16.2)	β = 0.078[e]	0.125
Has a partner at risk for HIV[d]	33 (23.7)	62 (28.7)	β = 0.064[e]	0.188
Has a partner that poses risk for HIV transmission[d]	15 (10.8)	35 (16.2)	β = 0.078[e]	0.127
Benefits of HIV vaccine	103 (58.5)	210 (81.7)	3.17 (2.05 - 4.90)	<0.001**
Barriers to HIV vaccination	149 (84.7)	195 (75.9)	0.57 (0.35 - 0.94)	0.028*
Experiential attitude	127 (72.2)	216 (84.0)	2.03 (1.27 - 3.25)	0.003**
Subjective norms				
Descriptive norms	65 (37.1)	130 (50.6)	1.73 (1.17 - 2.57)	0.006**
Normative beliefs	132 (75.4)	226 (87.9)	2.38 (1.43 - 3.96)	0.001**
Motivation to comply	75 (42.9)	143 (55.6)	1.67 (1.13 - 2.47)	0.010*
Network descriptive norms[d]	55 (39.6)	101 (46.8)	β = 0.082[e]	0.089
Normative beliefs[d]	108 (77.7)	190 (88.0)	2.10 (1.18 - 3.72)	0.011*
Motivation to comply[d]	61 (43.9)	105 (48.6)	β = 0.062[e]	0.235
Injunctive norms	85 (48.6)	166 (64.6)	1.93 (1.31 - 2.86)	0.001**
Normative beliefs	161 (92.0)	247 (96.1)	2.15 (0.93 - 4.96)	0.074
Motivation to comply	86 (49.1)	170 (66.1)	2.02 (1.36 - 3.00)	0.001**
Network injunctive norms[d]	71 (51.1)	117 (54.2)	β = 0.051[e]	0.294
Normative beliefs[d]	117 (84.2)	191 (88.4)	β = 0.085[e]	0.074
Motivation to comply[d]	75 (54.0)	122 (56.5)	β = 0.048[e]	0.324
Agency				
Behavioral control	101 (57.4)	175 (68.1)	1.58 (1.06 - 2.36)	0.024*
Self-efficacy	26 (14.8)	57 (22.2)	1.64 (0.99 - 2.74)	0.056

PWID: person who injects drugs; OR: odds ratio; CI: confidence interval; SD: standard deviation

* p<0.05; ** p<0.01

[a] Includes responses "very unlikely", "unlikely", and "likely"

[b] Sold, loaned, or gave needle to someone after using it

[c] Cookers, cottons, and/or rinse water

[d] Data were missing for the 78 participants who did not report at least one risk network member. Therefore, percentages were computed based on 139 who were not very likely to get the vaccine and 216 who were very likely to get the vaccine.
[e] The model would not converge using PROC GLIMMIX; estimates were derived using permutation-based, node-level regression. Standardized beta estimates are reported.

Table 2.4 Multivariate correlates to being "very likely" to receive an HIV vaccine (n=432)[a]

Characteristic		AOR (95% CI)	p-value
Demographic			
Male		0.33 (0.21 - 0.53)	<0.001**
	Score test	--	--
Behavioral (past 6 months)			
Injected drugs		1.23 (0.70 – 2.15)	0.476
Unprotected sex with PWID		1.36 (0.70 – 2.64)	0.369
	Score test	F=2.44	0.118
Attitudes			
Perceived severity of HIV		0.66 (0.11 – 4.17)	0.660
Perceived susceptibility to HIV[2]		2.27 (1.26 - 4.08)	0.007**
Perceived benefits		2.80 (1.69 - 4.67)	<0.001**
Perceived barriers		0.62 (0.31 - 1.24)	0.180
Experiential attitude		1.84 (1.07 - 3.16)	0.027*
	Score test	F=2.41	0.121
Subjective norms			
Descriptive norms[b]		1.17 (0.70 - 1.97)	0.547
Injunctive norms[b]		1.79 (1.07 – 3.01)	0.027*
	Score test	F=8.24	0.004**
Agency			
Perceived behavioral control		1.25 (0.77 - 2.03)	0.363
Self-efficacy		1.28 (0.64 - 2.54)	0.487
	Score test	F=1.52	0.218

PWID: person who injects drugs; AOR: adjusted odds ratio; CI: confidence interval
* p<0.05; ** p<0.01
[a] Data on norms were missing for one participant resulting in the inclusion of 432 in the analysis
[b] Refers to the general measure, not the network-based measure.

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Chapter 3 : Drug users' willingness to encourage social, sexual, and drug network members to receive an HIV vaccine: A social network analysis

Abstract

The ability of a vaccine to reduce HIV incidence depends on successful dissemination. Peer-based promotion may help to facilitate HIV vaccine uptake within risk networks, but its feasibility is unknown. The purpose of this study was to examine network-level correlates to drug users' willingness to encourage HIV vaccination among their risk partners and other peers. Data were collected from 433 rural drug users in the US. Risk network partnerships were defined as those involving sex and/or injecting drugs together. Non-risk relationships involved the use of non-injected drugs together or receipt of social support. Data were collected on recent (past 6 months) relationships, attitudes toward HIV vaccination, intent to increase risk behavior after vaccination (risk compensation), and likelihood of encouraging HIV vaccination of each partners. Quadratic assignment procedures regression was used for the dyadic analyses. Willingness to encourage HIV vaccination was reported in 521 and 555 risk- and non-risk relationships, respectively. Respondents were more likely to encourage risk partners with whom risk compensation was intended ($p=0.029$)and believed to be high risk for HIV ($p=0.019$) and. Encouragement was positively associated with belief that the partner would accept the vaccine and would reciprocate the encouragement (both $p<0.001$). Participants who expected the vaccine to be personally beneficial were more likely to encourage vaccination of risk ($p=0.012$) and non-risk partners ($p<0.001$). Network-based HIV vaccine promotion may be a successful strategy in drug users’ social networks, but risk compensation among those willing to promote the vaccine should be explored.

Introduction

A preventive vaccine could make a substantial impact on the HIV epidemic (Andersson et al., 2007; Fonseca et al., 2010; Stover, Bollinger, Hecht, Williams, & Roca, 2007). However, given that the first vaccines are likely to be only partially effective, successful dissemination among men who have sex with men (MSM), people who inject drugs (PWID), and high-risk heterosexual populations will be critical (Fonseca et al., 2010). Unfortunately, research on potential strategies for achieving adequate vaccine coverage among high-risk populations is currently lacking.

A number of vaccine-related characteristics (e.g., efficacy, duration of protection, side effects, cost) and psychosocial factors (e.g., risk perception, perceived benefits of vaccination) may play a role in HIV vaccine acceptability (Newman & Logie, 2010). Several qualitative studies identified social influences, particularly those regarding concerns about stigmatization and negative peer reactions, as potentially impeding vaccine uptake (Barrington, Moreno, & Kerrigan, 2007; Kakinami, Newman, Lee, & Duan, 2008; Newman, Duan, Rudy, Roberts, & Swendeman, 2004; Newman, Roungprakhon, Tepjan, Yim, & Walisser, 2012; Newman, Woodford, & Logie, 2012; Sayles, Macphail, Newman, & Cunningham, 2010). As a result, recent conceptual models of HIV vaccine uptake and clinical trial participation include social networks, norms, and peer influence among the key determinants (Lau et al., 2011; Sayles et al., 2010).

Social concerns reported by participants in HIV vaccine acceptability studies include fear that others will perceive vaccination as a sign of promiscuity

(Newman, Roungprakhon, et al., 2012; Rudy et al., 2005; Sayles et al., 2010) and that there will be generally negative reactions from family members (Kakinami et al., 2008; Newman et al., 2004) and intimate partners (Kakinami et al., 2008; Mills et al., 2004; Newman et al., 2004; Rudy et al., 2005). Studies examining individuals' willingness to participate in HIV vaccine clinical trials have revealed similar concerns (Fincham, Kagee, & Swartz, 2010; Fuchs et al., 2007; Jenkins et al., 2000; Koblin et al., 1998; Lesch, Kafaar, Kagee, & Swartz, 2006; Yin et al., 2008), including those regarding stigmatization of trial participants (Brooks, Newman, Duan, & Ortiz, 2007; Fincham et al., 2010; Jenkins, Temoshok, & Virochsiri, 1995; Jenkins et al., 2000; Koblin et al., 1998; Moutsiakis & Chin, 2007; Newman et al., 2006; Rudy et al., 2005; Smit et al., 2006; Starace et al., 2006) and the negative effects of trial participation on intimate relationships (Mills et al., 2004; Newman et al., 2004; Rudy et al., 2005; Yin et al., 2008).

This evidence underscores the prominent role of social influence on HIV vaccine acceptability. While most studies have focused on negative normative influences, others have highlighted the role that peer influence may play in vaccine promotion. Research has demonstrated that perception of peer and familial support for HIV vaccine clinical trial participation is significantly associated with personal willingness to participate in a trial (Gross et al., 1996; Yin et al., 2008). In fact, several studies have emphasized the importance of involving local individuals in HIV vaccine promotion (Frew, Archibald, Martinez, del Rio, & Mulligan, 2007; Kelley, Hannans, Kreps, & Johnson, 2012; Lesch et

al., 2006; Lindegger, Quayle, & Ndlovu, 2007; Newman et al., 2011), and some have specifically mentioned the importance of vaccine communication between intimate partners (Kakinami et al., 2008; Rudy et al., 2005).

Despite these findings and suggestions, relatively few quantitative studies have explored social influences related to HIV vaccination (Newman & Logie, 2010). Research specifically addressing individuals' willingness to encourage others to receive an HIV vaccine is especially scarce, though some studies have examined individuals' willingness to discuss clinical trial participation (Allen et al., 2005; Frew, Archibald, Hixson, & del Rio, 2011; Jenkins et al., 2005; Kelley et al., 2012; Valente et al., 2009). The largest of these studies, a telephone-survey of over 3500 adults in the US, found that 29% of respondents sampled from the general population and 68% of a targeted sample of MSM would support others' participation in HIV vaccine research (Allen et al., 2005).

While these studies have been foundational in exploring peer-based clinical trial recruitment, the findings may not be generalizable the promotion of an approved HIV vaccine. The underrepresentation of PWID in these studies also limits their applicability. Moreover, with the exception of the study by Valente and colleagues (2009), studies have not fully investigated with *whom* participants would discuss clinical trial participation. These limitations present an important gap in understanding, as vaccine promotion may not be an all-or-none phenomenon, but one that individuals engage in selectively depending on personal characteristics, the attributes of the peer, and/or the nature of the relationship. Understanding the characteristics of relationships in which HIV

vaccine promotion is most likely to occur is important to determining not only the feasibility of a peer-based strategy, but also its ability to reach those most at risk for HIV. The purpose of the present study was to investigate drug users' willingness to encourage their risk partners (injection and/or sexual) and other peers to receive a preventive HIV vaccine. Specifically, the study uses network analysis to examine the association between dyadic characteristics of relationships and respondents' willingness to encourage vaccination among specific peers.

Methods

Sample

The data used for this analysis were collected during the 24-month follow-up assessment of the Social Networks among Appalachian People (SNAP) study. SNAP is a longitudinal study with the aim of determining the prevalence of and risk factors for HIV, hepatitis C, and herpes-simplex 2 among illicit drug users in a rural community in Central Appalachia. The SNAP study eligibility criteria included the following: 1) being 18 years of age or older, 2) a resident of an Appalachian county in Kentucky, and 3) using of prescription opioids, heroin, crack/cocaine or methamphetamine to get high in the prior 30 day period. Additional details about the SNAP study are published elsewhere (Havens et al., 2013; Young, Jonas, Mullins, Halgin, & Havens, 2013).

From November 2008 to August 2010, participants (n=503) were recruited using respondent driven sampling. Data were collected via interviewer-

administered questionnaires at baseline and at 6-month intervals thereafter. HIV testing was performed at baseline and each follow-up using the OraQuick® *ADVANCE*™ Rapid HIV-1/2 Antibody Test (OraSure, Bethlehem, PA).

From March 2012 to May 2013, participants (n=435) completed their 24-month SNAP study interview. All participants tested HIV negative. After the interview, participants (n=433) were invited to complete an interviewer-administered questionnaire on their attitudes toward HIV vaccination and willingness to encourage others to receive the vaccine. Two participants who were interviewed in jail were not invited due to time limits. All invited participants consented to participate and were compensated $35 for participation. The protocol was approved by the University of Kentucky Institutional Review Board and a Certificate of Confidentiality was obtained.

Network data collection

The SNAP interview also entailed the collection of network data (methods described in detail elsewhere (Young et al., 2013)). Briefly, a name-generator questionnaire was used to establish drug use, sex, and social support networks. Participants gave the first name and last initial of up to eight individuals from/with whom they had received social support, used drugs (excluding alcohol and marijuana), and engaged in sex during the past 6 months. For each network member, or 'alter', named, additional demographic information was gathered (e.g., gender and approximate age). To determine if an alter was a participant in the SNAP study, their name and demographic information was cross-referenced against that of participants enrolled in the study and through consultation with the

community-based study staff. These techniques are consistent with those used in other studies (Friedman et al., 1997; Klovdahl et al., 1994; Rothenberg et al., 1995; Woodhouse et al., 1994).

For the purposes of these analyses, a *risk network* and *non-risk network* were constructed. The *risk network* consisted of sexual relationships and/or relationships in which partners injected drugs together. The *non-risk* network consisted of all other relationships (i.e. social support and co-usage of non-injected drugs). Of note, both networks included *all* named alters (study participants and non-participants). For analysis, each network was represented in the form of a person-by-person adjacency matrix, $\boldsymbol{A}$. NetDraw (version 2) (Borgatti, 2002) was used for network visualization.

Measures

Demographic similarity matrixes. Three adjacency matrixes were constructed to represent demographic similarity among participants. An adjacency matrix in which $\boldsymbol{A}_{ij}$ represented the absolute difference in age (years) between ego (i.e. the respondent) and each alter was constructed. Of note, the age difference was based on ego's report of the alter(s)' ages, as the actual ages of alters not in the study was unknown. A binary (1/0) adjacency matrix for gender similarity was also constructed, in which $\boldsymbol{A}_{ij}=1$ when ego and alter were the same gender. Other measures of demographic similarity could not be assessed, as respondents were not asked about alter(s)' race, education, income, and other characteristics.

Ego and alter characteristics. Six matrices representing ego and alter characteristics were also examined. Three matrices represented alter characteristics, as reported by the respondent, including alter gender, age (years), and recent injection drug use (IDU; binary). Networks were also constructed to represent the respondent's gender, age, and IDU. For example, if a respondent had engaged in IDU in the past 6 months, each of his/her ties to alter(s) would receive a value of 1 in the adjacency matrix. Perceived benefit of HIV vaccination was assessed with the following item: "In your opinion, how much would an HIV vaccine benefit you?" [1=not at all, 2=a little, 3=some, 4=a lot]. The response value was entered into an adjacency matrix. Perceived benefit of HIV vaccination has been examined in similar research (Liau & Zimet, 2000).

Relationship characteristics. In the SNAP interview, respondents were asked how long they had known each of their alters (months), how frequently they communicated (6-point Likert scale, with increasing values representing more frequent communication), the geographic distance between their residences (9-point Likert scale with increasing values indicating farther distances), how much they trusted each alter (10-point scale), whether or not the alter was a family member (binary), and whether or not the respondent received social support and financial support from each alter (both binary). Matrices were constructed from each of these variables.

Risk Behavior. For the analysis of the risk network, seven behavioral matrices were constructed. Six were binary and represented whether or not the respondent had (1) used drugs with the alter, (2) injected drugs with the alter, (3)

injected drugs *and* had sex with the alter, (4) given used injection equipment to alter, (5) received used injection equipment from the alter, and (6) discussed risk reduction (i.e. condom use and/or bleaching injection equipment). The seventh matrix contained data representing a scale of the frequency of HIV risk behavior, in which the values of the ties represented the sum of three Likert scales on which participants rated the frequency of unprotected sex (4-point scale) and frequency of needle and cooker sharing (5-point scales) with the alter.

Psychosocial measures. Three psychosocial measures used were also analyzed. These items, which were asked only about risk network members, examined descriptive and injunctive norms, risk perception, and perceived benefits of HIV vaccination. Descriptive norms are perceptions about the behaviors of others, while injunctive norms relate to a person's beliefs about what others think he/she should do (Cialdini, Reno, & Kallgren, 1990; Fishbein, 2009). In the present study, descriptive and injunctive norms were assessed on an alter-by-alter basis with the following questions repeated for each named alter: "How likely do you think [network member] would be to get an HIV vaccine?" and "If [network member] got an HIV vaccine, how likely would they be to encourage you to get it?" An adjacency matrix was constructed to represent responses given on a 4-point Likert scale ranging from 'very unlikely' to 'very likely'.

Matrices were also constructed based on participants dyad-specific risk perceptions: "How likely do you think it is that [network member] would ever get infected with HIV?" and "How likely do you think it is that [network member]

would ever infect you with HIV?" Responses were given on a 4-point Likert scale ranging from 'very unlikely' to 'very likely'.

Respondents also answered three items to assess intent to engage in sexual risk compensation: "If [you/alter/you and alter] got an HIV vaccine that was 90% effective, would you use a condom with them... ['Much less often', 'Less often', 'More often', 'Much more often', 'We wouldn't change how often we used a condom']". Three injection-related items with the same response options were also given: "If [you/alter/you and alter] got an HIV vaccine that was 90% effective, would you use share injection equipment...". Using these data, a binary network was constructed in which $\boldsymbol{A}_{ij}=1$ if respondents answered that they would increase their risk behavior on any one of the six risk compensation items.

Encouragement and discouragement of HIV vaccination. Data were collected on participants' likelihood of recommending an HIV vaccine to their network members. Participants were asked, “If an HIV vaccine that was 90% effective was available, who would you encourage to get it?”, and “If an HIV vaccine that was 90% effective was available, who would you discourage from getting it?” Each question was followed by three response options, "everyone", "no one", and "some select people". Participants who selected "everyone" were assumed to be willing to encourage/discourage all of their network members, and those who responded "some select people" were given a checklist of their named network members to indicate which ones they would encourage/discourage. Data on willingness to encourage risk and non-risk network members to receive the vaccine were used to construct two adjacency matrices in which the cell values

represented whether a respondent would encourage (1) or not encourage (0) their alter to receive the vaccine. Participants were also allowed to free-list other individuals whom they would encourage to get the vaccine, but because relational characteristics were unknown, these data were not included in the dyadic analyses.

Statistical Analyses

Network-level analyses were conducted to determine the dyadic correlates to encouragement of HIV vaccination in both the risk and non-risk networks. To account for potential autocorrelation, each analysis was conducted within UCINET (version 6) (Borgatti, Everett, & Freeman, 2002) and statistical significance was determined using permutation-based testing (Hanneman & Riddle, 2005). Specifically, double semi-partialling quadratic assignment procedures multiple regression (MR-QAP) (Dekker, Krackhardt, & Snijders, 2007; Krackhardt, 1987) was used. MR-QAP preserves the underlying dyadic structure of network data while providing a robust test of association between networks (Dekker et al., 2007). MR-QAP proceeds in two steps: 1) standard multiple regression is conducted across corresponding cells of the dependent and independent matrices, and 2) random permutations (10,000) are conducted across rows and columns of the matrices and the regression is recomputed. Values of r-square and the coefficient(s) are stored for each permutation and a p-value is computed based on the proportion of permutations that yield a coefficient

as extreme as the one computed from the observed data (Dekker et al., 2007; Krackhardt, 1987).

The vaccine encouragement networks were regressed on each of the demographic, psychosocial, and behavioral matrices described above. Of note, the psychosocial and behavioral measures only applied to the risk network and were not entered in the analysis of the non-risk network. Covariates reaching significance ($p < 0.05$) were entered into a multivariate model to examine their independent association with the encouragement network. Only the direction and significance of the parameter estimates from MR-QAP are interpretable in the present study, as the procedure is intended for use with continuous outcome data. There is currently no logistic regression procedure available in UCINET that accounts for circumstances in which covariates are not assessed for every pair of participants.

Results

Table 3.1 displays the demographic and behavioral profile of participants. Briefly, 94% were White, 45% were female, and the median age was 34 years (range: 21 – 68). The majority were not currently married (74%). Most (76%) reported a lifetime history of IDU and 34% reported IDU in the past 6 months. In the past six months, approximately 24% had multiple sex partners and 71% had unprotected sex. Nearly all (95%) reported nonmedical use of prescription drugs in the past 6 months and few reported use of cocaine (12%), methamphetamine (8%), heroin (5%), or crack (3%) (data not shown).

Relationships in the risk and non-risk networks are described in Table 3.2. Of the 433 participants, 356 reported a sexual relationship and/or one in which they inject drugs together. These 356 participants reported 582 risk ties; 78% were sexual only, 12% involved injecting together, and 10% involved injection and sex. The average number of alters named in the risk network was 0.74 (SD: 1.14, range: 0 - 8) compared to 0.82 (SD: 1.39, range: 0 - 8) in the non-risk network. A total of 1316 alters were named, including 243 who were participants in the vaccine study, nine who were SNAP participants but lost to follow-up at the time of the vaccine study, and 1064 who were not participants in the SNAP study.

Most participants (n=273, 63.0%) would encourage everyone to receive the vaccine and relatively few (n=30, 6.9%) would encourage *no one* to receive the vaccine. Almost one-third (n=129, 29.8%) reported that they would encourage HIV vaccination to only some select people. In the risk and non-risk networks, there were 521 and 555 relationships in which in which a person was willing to encourage an alter's vaccination, respectively.

Overall, 92.8% (n=402) would encourage at least one person to receive the vaccine. On the open-ended question, 13 respondents listed specific people they would recommend to get the vaccine. Ten respondents gave first names and last initials of individuals who were not in the SNAP study, including one who gave the names of his/her children. Other responses included, “anyone who could be at risk or would be IV drug users”, “people who are injecting drugs or

people who have unprotected sex", and "underage children who are approaching adulthood".

Only 13 (3.0%) participants reported that they would *discourage* someone from getting the vaccine, including eight (1.8%) who would discourage everyone and five (1.2%) who would discourage only some select people. In total, participants would discourage nine alters in the risk network and 21 in the non-risk network from receiving the vaccine. Of note, however, in eight of the 30 relationships involving discouragement of HIV vaccination, the respondent also reported that they would encourage their vaccination. These relationships were analyzed as ties involving encouragement and are visualized as so in Figures 3.1 and 3.2. Data on encouragement and discouragement of vaccination within the risk and non-risk networks are displayed in Figures 3.1 and 3.2, respectively.

Correlates to HIV vaccine encouragement in the risk network

Bivariate and multivariate results are described in Table 3.3. Frequency of communication ($p = 0.049$), trust ($p = 0.039$), perceptions that an alter would be likely to get the vaccine (descriptive norms, $p < 0.001$), and perceptions that an alter would be likely to encourage the respondent to receive the vaccine (injunctive norms, $p < 0.001$) were positively associated with likelihood of encouraging an alter to receive an HIV vaccine. Likelihood of encouragement was also associated with the respondents' belief that the alter was at risk for HIV ($p = 0.039$) and was likely to transmit HIV to them ($p = 0.037$). Respondents were also more likely to encourage vaccination among those with whom they would intend to engage in risk compensation ($p = 0.016$). Men were less likely to

encourage their alters to receive the vaccine ($p = 0.007$), but were more likely to receive a recommendation to get the vaccine ($p = 0.002$). Finally, respondents' rating of the personal benefit of HIV vaccination was positively associated with likelihood of encouraging alters to receive a vaccine ($p < 0.001$). Demographic similarities, duration of relationship, kinship, geographic proximity, risk reduction communication, and risk behavior were not associated with encouragement.

In multivariate analyses, injunctive and descriptive norms remained significantly associated with encouragement ($p < 0.001$ and $p < 0.001$, respectively), as did rating of alter(s)' risk for HIV ($p = 0.019$) and perceived benefits of HIV vaccination ($p = 0.012$). The positive association between risk compensation intent and encouragement also remained significant ($p = 0.029$). Controlling for these variables, trust, frequency of contact, HIV risk posed by partner, and ego and alters' gender were no longer significant.

Correlates to HIV vaccine encouragement in the non-risk network

In non-risk relationships, encouragement of HIV vaccination was less likely in relationships of longer duration ($p = 0.008$), those between family members ($p = 0.015$), and those involving receipt of financial support ($p = 0.001$). Respondents were more likely to encourage alters with whom they reported using drugs ($p = 0.001$), and were more likely to encourage alters who injected drugs ($p=0.003$) and who were of a younger age ($p = 0.037$). Younger respondents were more likely to encourage their alters ($p = 0.014$), as were those who reported recent IDU ($p = 0.001$) and who perceived greater personal benefits of HIV vaccination ($p < 0.001$). In multivariate analyses, drug co-usage

remained significantly associated with encouragement ($p = 0.028$), as did perceived benefits of HIV vaccination ($p < 0.001$).

Discussion

In this sample of drug users, the majority (63%) was willing to encourage all of their risk and non-risk alters to receive a preventive HIV vaccine. However, 30% reported they would be selective in whom they would encourage. In multivariate analysis, respondents were more likely to encourage risk partners who they believed to be at high risk for HIV and, notably, those with whom they intended to engage in risk compensation. Participants who expected the HIV vaccine to be personally beneficial were also more likely to encourage vaccination among their risk network members. The strongest correlates to encouragement were those related to perceived social norms; participants were more likely to encourage risk network members who they believed would be accepting of the HIV vaccine and who would reciprocate the encouragement.

The correlates to vaccine encouragement among non-risk network members were somewhat different. In bivariate analyses, respondents were more likely to encourage vaccination in relationships of shorter duration and in those not involving a family member or a person from whom they receive financial support. Respondents were also more likely to encourage alters with whom they used drugs. Younger individuals and PWID were more commonly the target of encouragement than those who were older and did not inject. Similarly, younger participants and PWID were more likely to promote vaccination among

their peers than were their counterparts, as were those who expected HIV vaccination to be personally beneficial. This latter association and the association between drug co-usage and encouragement remained significant in multivariate analysis.

Contrasts between the present study and those investigating HIV vaccine clinical trial participation should be interpreted with caution given differences in design and outcome. However, it is notable that the proportion of participants (93%) who were willing to encourage at least one of their peers to receive an HIV vaccine exceeds the proportion willing to promote clinical trial participation in previous research (Allen et al., 2005; Frew et al., 2011). Previous studies have demonstrated the ability of a few index individuals to encourage trial participation among a vast number of peers (Kelley et al., 2012; Valente et al., 2009). In a social network study conducted by Valente and colleagues (2009) involving HIV positive adolescents and adults, 59 participants and their first-degree alters expressed willingness to invite 421 social network members to participate in an HIV vaccine preparedness study. In the current study, 433 participants reported willingness to encourage vaccination in 1076 relationships. The number of individuals who would receive a recommendation to be vaccinated could not be determined due to an inability to rule out overlap among alters not participating in the study. However, the findings clearly indicate that peer-based promotion could be a promising and feasible strategy to enhance HIV vaccination.

In this study, perceived norms were strongly associated with individuals' willingness to encourage HIV vaccination among risk network members. This

finding is corroborated by previous research conducted by Frew and colleagues (2011) in a racially-diverse sample of urban adults. The study found that, controlling for various individual-, social-, and community-level characteristics, normative beliefs were significantly associated with willingness “get others involved in HIV vaccine research”. Consistent with the present study, Frew and colleagues (2011) found that beliefs about the benefits of HIV vaccination and HIV vaccine research were associated with willingness to encourage participation among others.

In addition to demonstrating feasibility and the importance of social norms, this study provides insight into the ability of peer-based HIV vaccine promotion to reach those at high-risk for infection. Within the risk network, respondents were more likely to encourage risk partners who they believed to be at high risk for HIV, and in the non-risk network, those with whom they use drugs. These findings are consistent with previous research which identified encouragement of HIV vaccine trial participation as more common in relationships involving drug co-usage (Valente et al., 2009).

In light of these results, however, it is important to note that vaccine encouragement was significantly more likely to occur in relationships in which the respondent intended to increase risk behavior if they or their partner received an HIV vaccine. If individuals intend to encourage vaccination among those most at risk for HIV *and* to risk compensate with those they encourage, this dynamic could present a negative unintended consequence of peer-promotion of a partially effective HIV vaccine. Supplementary analyses revealed that risk

compensation intent was predominantly related to reduced condom use and that those intending to risk compensate did not require that they *and* their partner both be vaccinated in order to risk compensate. This finding clearly highlights a need for future research on peer-promotion of HIV vaccination and trial participation to include a measure of risk compensation intent, and for simulation studies examining the impact of various promotion strategies to take into account potential for risk compensation.

Interpretation of the findings from this study should be done in consideration of its limitations. At this stage of vaccine development, research is limited to examining individuals' intentions to perform behaviors related to HIV vaccination, but as some have noted (Poole, 2012), the correspondence between intentions and behavior may be limited in some cases. Also, the use of one-item measures in the study to examine psychosocial constructs was not ideal. However, minimization of respondent-burden was essential given the number of alter-specific questions. Finally, though this study used a sociometric network approach, the study was limited in its ability to determine overlap between some network ties due to the naming of alters who were non-participants.

The present study is the first social network study to focus on drug users' willingness to encourage HIV vaccination among their risk and non-risk peers. While the findings should be generalized with caution, the study demonstrates the potential promise of a peer-based strategy to HIV vaccine promotion among people using drugs and underscores the need for additional behavioral research. Future simulation studies are also needed to examine the efficiency of a peer-

based approach compared to and/or in conjunction with other marketing strategies. This study raises important topical and methodological areas for further research. Consistent with previous studies (Jenkins et al., 2005; Valente et al., 2009), the data demonstrate that future research should include measures of respondents' selectivity in communicating about HIV vaccination, specifically assessing *to whom* they would promote vaccination and/or trial participation. This study also highlights the need to explore risk compensation intentions among those willing to promote the vaccine. Most importantly, additional studies are needed to explore strategies for promotion of HIV vaccination among PWID. When an HIV vaccine is made available, expediency in roll-out will be important, as delays in dissemination could "result in millions of new infections that might otherwise have been averted (Newman & Logie, 2010), p 1755)."

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Table 3.1 Individual- and network-level characteristics of the sample (n=433)

Characteristic	N (%)
Individual-level	
Demographic	
Male	239 (55.2)
Age – median (IQR)	34 (29 – 41)
White	407 (94.0)
High school graduate	251 (58.0)
Married	111 (25.6)
Unemployed	169 (39.0)
Income in past 30 days[a] – median (IQR)	$698 (200 – 1100)
Uninsured	285 (65.8)
Injection drug use	
Lifetime history of injection drug use	331 (76.4)
Injection drug use in past 6 months	146 (33.7)
Injected with unclean needle in past 6 months	33 (7.6)
Gave/loaned/sold unclean needle in past 6 months	16 (3.7)
Shared injection equipment in past 6 months	55 (12.7)
Sexual behavior (past 6 months)	
Number of sex partners	
Zero	76 (17.6)
One partner	254 (58.7)
Two partners	56 (12.9)
Three or more partners	47 (10.9)
Unprotected sex with at least one partner	308 (71.1)
Unprotected sex with PWID	85 (19.6)
Network-level	
Risk Network	
Number of relationships involving sex and IDU[b]	60
Number of relationships involving sex only	451
Number of relationships involving IDU[b] only	71
Non-risk network	
Number of relationships involving drug co-usage[c] and social support	219
Number of relationships involving social support only	429
Number of relationships involving drug co-usage[c] only	202

IQR: interquartile range; PWID: person who injects drugs; IDU: injection drug use

[a] Includes income from employment, unemployment compensation, welfare, pension/social security, child support, friends/family, and illegal activities

[b] Reported engaging in injection drug use together

[c] Reported using non-injected drugs together.

Table 3.2 Bivariate and multivariate dyadic correlates to encouragement of HIV vaccination among network members (n=432[a])

	Risk Network (582 relationships)				Non-risk Network (851 relationships)			
	Bivariate		Multivariate		Bivariate		Multivariate	
	β[b]	p-value	β[b]	p-value	β[b]	p-value	β[b]	p-value
Demographic similarities								
Same gender[c]	0.001	0.436			0.007	0.436		
Age difference[c,d] (years)	0.006	0.459			-0.045	0.105		
Relationship characteristics								
Duration (months)[c]	0.063	0.068			-0.092	0.008**	-0.015	0.392
Frequency of contact[c]	0.075	0.049*	0.033	0.227	-0.008	0.433		
Distance[e]	-0.010	0.294			0.004	0.473		
Kinship	-0.015	0.320			-0.084	0.015*	0.000	0.497
Trust[c]	0.077	0.039*	-0.008	0.441	-0.031	0.200		
Social support	0.035	0.233			-0.038	0.183		
Receives financial support	0.046	0.124			-0.115	0.001**	-0.059	0.079
Psychosocial								
Descriptive norms[f]	0.387	<0.001**	0.244	<0.001**	---	---		
Injunctive norms[f]	0.353	<0.001**	0.203	<0.001**	---	---		
Partner's risk for HIV[f]	0.076	0.039*	0.116	0.019*	---	---		
HIV risk posed by partner[f]	0.075	0.037*	-0.016	0.380	---	---		
Intent to risk compensate	0.080	0.016*	0.069	0.029*	---	---		
Behavior								
Use drugs together	0.061	0.104			0.135	0.001**	0.081	0.028*
Inject drugs together	0.064	0.110			---	---		
Distributive needle sharing	0.030	0.356			---	---		
Receptive needle sharing	0.047	0.213			---	---		
Inject together *and* sexual partners	0.024	0.393			---	---		
Frequency of risk behavior	-0.028	0.280			---	---		
Risk reduction communication	0.066	0.056			---	---		
Ego's characteristics								

Male	-0.110	0.007**	-0.014	0.407	0.071	0.062		
Age	-0.039	0.200			-0.103	0.014*	-0.051	0.137
Recent injection drug use	-0.004	0.406			0.141	0.001**	0.027	0.283
Perceived benefit of HIV vaccine	0.207	<0.001**	0.100	0.012*	0.367	<0.001**	0.344	<0.001**
Alter's characteristics								
Male	0.125	0.002**	0.068	0.120	0.054	0.074		
Age[c,d]	0.020	0.317			-0.066	0.037*	0.010	0.410
Recent injection drug use	0.064	0.064			0.110	0.003**	0.007	0.425

*p<0.05, **p<0.01

[a] One person did not complete the question on willingness to encourage others to receive an HIV vaccine.

[b] β values reported are standardized and, in multivariate analyses, adjusted for all other variables in the model.

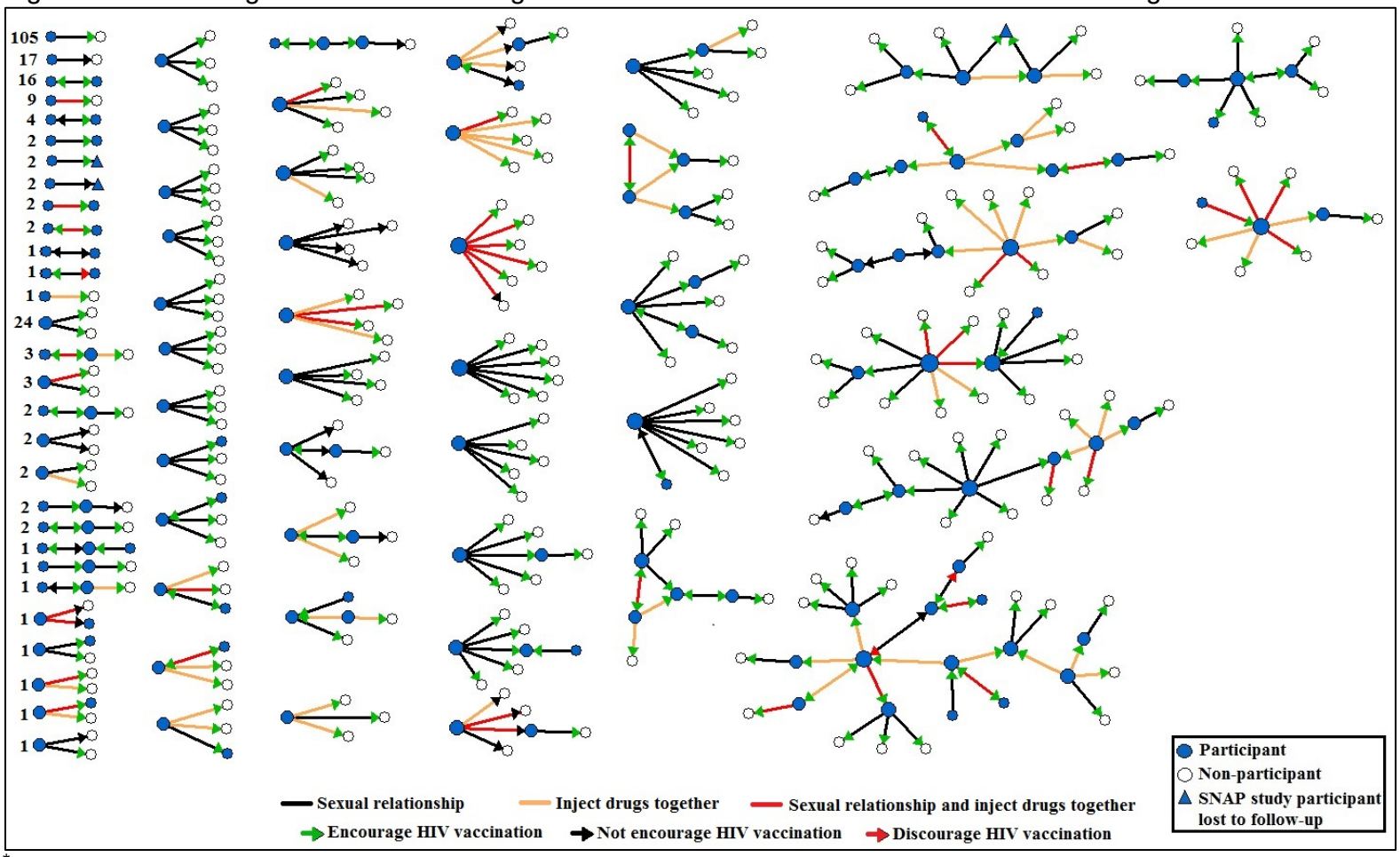
[c] In the non-risk network, 850 relationships were analyzed due to one missing value.

[d] In the risk network, 580 relationships were analyzed, as the ages for two alters were missing.

[e] In the risk network and non-risk network, 581 and 848 ties were analyzed, respectively, due to missing distance values for alters.

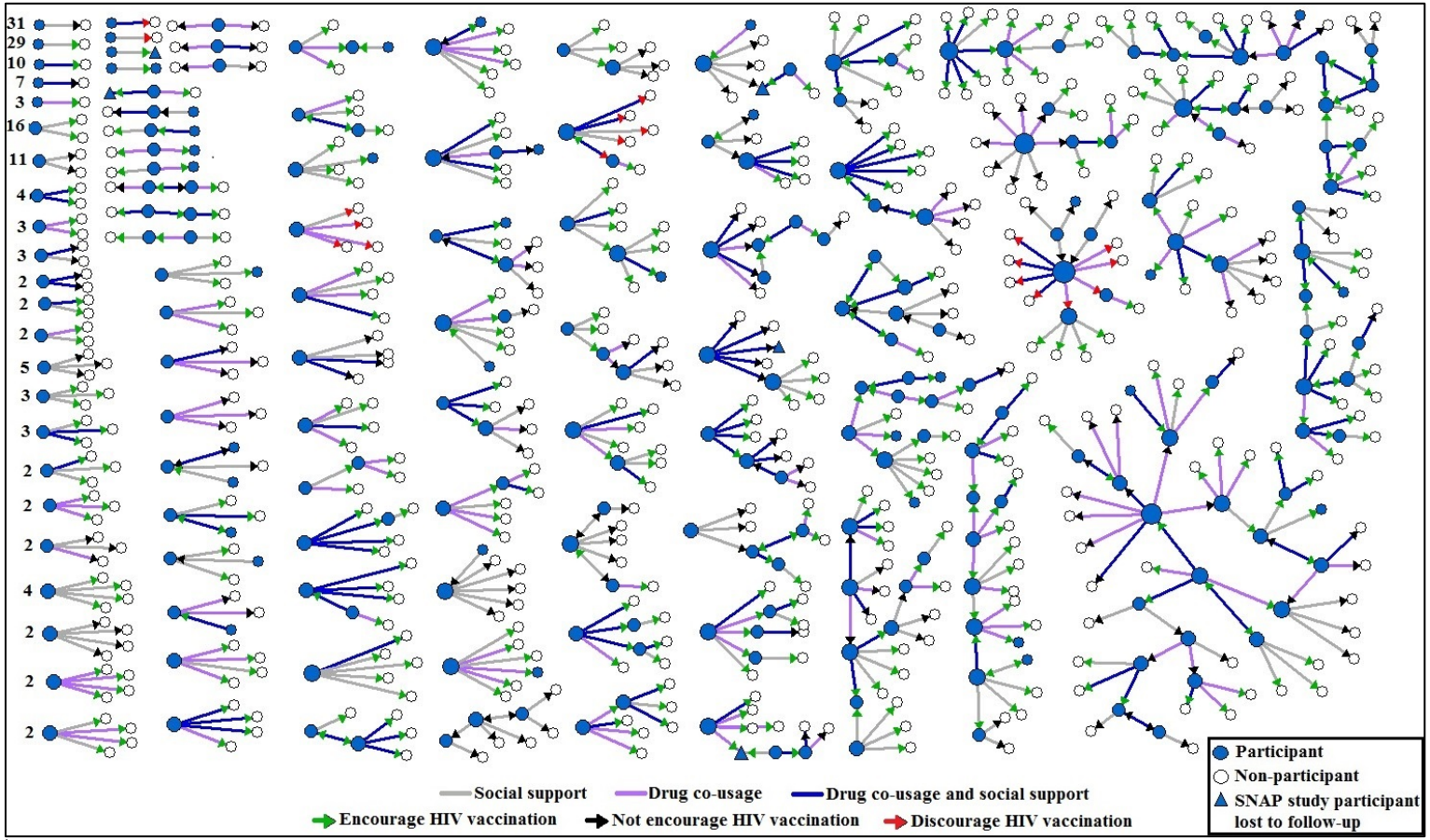
[f] In the risk network, 581 relationships were analyzed due to one missing value.

Figure 3.1 Encouragement and discouragement of HIV vaccination in a risk* network of drug users



* Risk relationships include those in which partners engage in sex and/or injection drug use.

Figure 3.2 Encouragement and discouragement of HIV vaccination in a non-risk* network of drug users



* Non-risk relationships include those in which the alter provides social support and/or the partners use drugs together (not including injection drug use).

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Chapter 4 : Will HIV Vaccination Reshape HIV Risk Behavior Networks? A Social Network Analysis of Drug Users' Anticipated Risk Compensation

Abstract

A successful vaccine could substantially impact the HIV epidemic; however, risk compensation (increased risk behavior after vaccination) is a significant concern. While the impact of risk compensation on individual-level HIV risk has been explored, the impact on community-level risk network structure is largely unknown. This study examined the impact of drug users' anticipated HIV vaccine-related risk compensation on the overall structure of their risk network. Social network analysis was conducted on data collected from 433 drug users (76% with history of injection) enrolled in a longitudinal study in a rural community in the southern US. HIV risk network ties were those in which partners had unprotected sex and/or shared injection equipment in the past 6 months. Dyad-specific data were collected on self-reported likelihood of increasing/initiating risk behavior in response to HIV vaccination. Intention to increase in risk behavior was reported for 30 current relationships and five new risk relationships would be initiated. These changes resulted in a 5% increase in the number of ties in the overall risk network (n=142 to n=149). The initiation of new relationships resulted in the connection of otherwise disconnected components of the risk network; the largest component doubled in size from five to ten. These preliminary data suggest that HIV vaccine-related risk compensation may impact risk network structure. The potential for network-level changes to mitigate the positive impact of HIV vaccination (particularly a low-efficacy vaccine) should be carefully examined.

Introduction

HIV vaccines have the potential to make a substantial impact on the HIV epidemic. However, many have voiced concerns about the possibility that HIV vaccination could elicit increases in risk behavior. This phenomenon occurs when diminished perceived susceptibility resulting from participation in some preventive intervention causes a subsequent increase in risk behavior (Hogben & Liddon, 2008). Given that the first HIV vaccines on the market are likely to be only partially effective, risk compensation could substantially dampen and, in some circumstances, offset the vaccine's public health benefit (Andersson et al., 2007; Blower, Schwartz, & Mills, 2003; Fonseca et al., 2010; Gray et al., 2003). In fact, some models have predicted that with a combination of frequent risk compensation and low vaccine efficacy, an HIV vaccine campaign could actually *increase* HIV incidence (Andersson et al., 2007; Fonseca et al., 2010).

Findings on the hypothetical likelihood that HIV vaccinated individuals will engage in risk compensation have been mixed. In HIV vaccine acceptability studies implemented in diverse settings, participants have expressed concern that others would increase their sexual risk behavior if vaccinated (Koniak-Griffin, Nyamathi, Tallen, González-Figueroa, & Dominick, 2007; Newman et al., 2009; Newman, Roungprakhon, Tepjan, Yim, & Walisser, 2012; Olin et al., 2006; Webb, Zimet, Mays, & Fortenberry, 1999). Females, in particular, have expressed concern that men will decrease condom use if vaccinated (Newman et al., 2012; Sayles, Macphail, Newman, & Cunningham, 2010). However, in studies asking participants about their personal likelihood of risk compensation,

fewer anticipate behavioral changes (Barrington, Moreno, & Kerrigan, 2008; Macphail, Sayles, Cunningham, & Newman, 2012; O'Connell et al., 2002). Nevertheless, participants in some studies have admitted that they would "lighten up" on behaviors such as condom use (Newman, Duan, Rudy, & Johnston-Roberts, 2004). In studies of high-risk adults in the US, the percentage intending to risk compensate has been reported to be near 20% in one study conducted in Atlanta (Crosby & Holtgrave, 2006) and approximately 10% in a more recent study in Los Angeles (Newman et al., 2009).

Findings from research embedded within HIV vaccine trials have generally identified no substantial increase in risk behavior during trial participation (Bartholow et al., 2005; Francis et al., 2003; Guest et al., 2005; Jenkins et al., 2005; Lampinen et al., 2005; Martin et al., 2010; Robb et al., 2012; van Griensvan et al., 2004), though there is some evidence to the contrary (Chesney, Chambers, & Kahn, 1997). While cited frequently as evidence that risk compensation may not be as problematic as once anticipated, risk behavior within clinical trials may not reflect individual’s behavior should an HIV vaccine be approved for use. Furthermore, the methodological rigor of behavioral data collection during many early HIV vaccine clinical trials has been limited (Andrasik et al., 2013), and data for the most frequently cited studies on HIV vaccine related risk compensation were collected over ten years ago. Given the changes that have occurred in the epidemiology (Centers for Disease Control and Prevention, 2013), prevention and treatment (Padian et al., 2011), and public discourse (El-Sadr, Mayer, & Adimora, 2010) surrounding HIV in the past

decade, more research is needed to examine the current dynamics of risk compensation.

There are significant gaps in the extant literature on HIV vaccine-related risk compensation. A review of HIV vaccine acceptability literature conducted by Newman and Logie (2010) identified only four quantitative studies that assessed risk compensation. In qualitative and quantitative studies, drug-using populations have been underrepresented relative to men who have sex with men (MSM), commercial sex workers, and other high-risk populations. Despite evidence that changes in injection risk behavior could affect the long-term, population-wide impact of a low efficacy HIV vaccine (Bogard & Kuntz, 2002), simulation models predicting the impact of risk compensation have primarily focused on changes in condom use (Andersson et al., 2007; Andersson, Paltiel, & Owens, 2011; Blower & McLean, 1994; Fonseca et al., 2010; Gray et al., 2003).

Few studies have examined drug users' anticipated changes in syringe sharing (Meyers, Metzger, Navaline, Woody, & McLellan, 1994; Newman et al., 2004; Newman et al., 2009), including in the context of HIV vaccine clinical trials (Martin et al., 2010; Robb et al., 2012; van Griensvan et al., 2004). Findings from these studies are mixed. In an early study of people who inject drugs (PWID) from Philadelphia, 22% reported that they would increase needle sharing if vaccinated (Meyers et al., 1994). Yet, in more recent studies of PWID recruited from syringe exchange programs in Los Angeles, few have reported intent to increase syringe sharing (Newman et al., 2004; Newman et al., 2009), some citing the continued risk for hepatitis C (HCV) transmission (Newman et al.,

2004). Given the limited geographic scope of these studies and the overall paucity of risk compensation research among PWID, more research is needed to fully examine the possibility of increased syringe sharing in response to HIV vaccination.

The methodology employed in most HIV vaccine risk compensation studies to date has focused exclusively on individuals. Despite an abundance of evidence suggesting that social networks can play an important role in HIV and STI transmission (De, Singh, Wong, Yacoub, & Jolly, 2004; Friedman et al., 1997; Klovdahl et al., 1994; Potterat, Rothenberg, & Muth, 1999; Rothenberg, Potterat, & Woodhouse, 1996; Rothenberg, Potterat, et al., 1998), HIV risk behavior (De, Cox, Boivin, Platt, & Jolly, 2007; Friedman et al., 1997), and involvement in preventive interventions (Coyle, Needle, & Normand, 1998; Latkin et al., 2013; Wang, Brown, Shen, & Tucker, 2011), the HIV vaccine acceptability literature is devoid of insights into the role that networks play in shaping likelihood of risk compensation.

Previous individual-level studies have captured *if* and *to what degree* individuals will engage in risk compensation, but they have not captured *with whom* or to what extent the behavior change could *differ across relationships*. Consequently, there is currently a gap in understanding about how HIV vaccination could alter the dynamics and structure of HIV risk networks. Individual-level measures have been used to inform risk compensation parameters in mathematical models aimed at determining the percent efficacy required for an HIV vaccine to achieve impact on population-wide HIV incidence.

However, if risk compensation increases the connectivity of risk networks, the impact of risk compensation on HIV incidence may be underestimated. HIV vaccination inherently will disrupt the transmission of HIV through risk networks, but the degree of disruption will depend on behavioral changes and the network position of those who engage in risk compensation. Thus, the distribution of risk compensation within risk networks could be an important factor in determining the effectiveness of community HIV vaccine initiatives.

The current study used network analysis to examine drug users' risk relationships and anticipated risk compensation. Participants' current risk network was compared to a simulated "post-vaccination" risk network, constructed according to participants' intended risk compensation (under variable hypothetical vaccination scenarios) with each of their current partners and new partners. The overarching aim of the study was to introduce a new methodological and conceptual approach for examining risk compensation in the context of HIV vaccination.

Methods

Sample

This study was implemented in the context of the ongoing longitudinal Social Networks among Appalachian People (SNAP) study, the methods of which have been described in detail elsewhere (Havens et al., 2013; Young, Jonas, Mullins, Halgin, & Havens, 2013). The purpose of SNAP is to examine the epidemiology of HIV, HCV, and herpes-simplex 2 among illicit drug users in a

rural Appalachia. Eligibility criteria for the study included being at least 18 years of age, residing in an Appalachian county in Kentucky, and use of prescription opioids, heroin, crack/cocaine or methamphetamine to get high in the prior 30 day period. Participants (n=503) were recruited from November 2008 to August 2010 using respondent driven sampling. Participants completed interviewer-administered questionnaires and HIV testing at baseline and every six months afterward. From March 2012 to May 2013, 435 participants completed their 24-month follow-up assessment. All participants tested HIV negative using the OraQuick® *ADVANCE*™ Rapid HIV-1/2 Antibody Test (OraSure, Bethlehem, PA).

Following their 24-month interview, 433 participants were invited and consented to complete an interviewer-administered questionnaire on their attitudes toward HIV vaccination and intent to change behavior if vaccinated against HIV. Two 24-month SNAP participants were not invited, as they were interviewed in jail and time-constraints prohibited the interviewers' ability to administer the questionnaire. Participants were compensated $35 for their time. The protocol was approved by the University of Kentucky Institutional Review Board and a Certificate of Confidentiality was obtained.

Network data collection

The SNAP interview included a name-generator questionnaire that was used to establish drug, sex, and social support networks. To construct the three networks, participants gave the first name and last initial of up to eight individuals from/with whom they had received social support, used drugs (excluding alcohol and marijuana), and engaged in sex during the past 6 months. Respondents also

reported the gender and approximate age of each network member, or 'alter'. The reported names and demographic information were then cross-referenced against those of others enrolled in the study to construct the network of relationships among participants (i.e. the 'sociometric network'). If the relationship could not be confirmed through the cross-referencing procedure, the community-based interviewers were consulted for their knowledge of reported relationships. If cross-referencing nor consultation of interviewers revealed a confirmed linkage, the named network member was determined to not be enrolled in the study (i.e. outside of the sociometric network). These techniques are consistent with those used in similar studies (Friedman et al., 1997; Klovdahl et al., 1994; Rothenberg et al., 1995; Woodhouse et al., 1994).

These data were used to produce a 'risk network' consisting of sexual relationships and/or relationships in which partners engaged in injection drug use (IDU) together. Two versions of this network were constructed: a *Complete Network*, which included all named alters (study participants and non-participants), and a *Sociometric Network*, which only included relationships between SNAP participants. For analysis, each network was represented in the form of an actor-by-actor adjacency matrix, $\boldsymbol{A}_{ij}$ (example shown in Figure 4.1). Network analysis and visualization were conducted using UCINET (version 6) (Borgatti, Everett, & Freeman, 2002) and NetDraw (version 2) (Borgatti, 2002).

Measures

Risk Behavior. For the present analyses, four behavioral networks were constructed. One network contained valued data representing the current

frequency of HIV risk behavior; the values represented the sum of three Likert scales on which participants rated the frequency of unprotected sex (0=always use condoms, 1=use condoms half the time, 2=use condoms less than half the time, 3=never use condoms) and frequency of needle and cooker sharing (0=never, 1=less than once per month, 2=weekly, 3=weekly, 4=daily) with the alter. Thus, the value for the summed risk behavior scale could range from 0 to 11. This network was considered to be the "**pre-vaccination network**", as it represented risk behavior in the absence of an HIV vaccine.

Four additional binary networks were constructed to represent whether or not the respondent (1) had sex with the alter, (2) injected drugs *and* had sex with the alter, (3) had given unclean injection equipment to alter, and (4) received unclean injection equipment from the alter. In each of these directed networks, $\boldsymbol{A}_{ij}=1$ if the respondent answered affirmatively.

Risk Compensation. For each sex partner and/or partner with whom drug injection equipment was shared, respondents were asked about their likelihood of increasing risk behavior if they, their partner, or both they and their partner received an HIV vaccine. Specifically, respondents were asked three items to assess sex-related risk compensation, "If [you/alter/you and alter] got an HIV vaccine that was 90% effective, would you use a condom with them... ['Much less often' (+2), 'Less often' (+1), 'More often' (-1), 'Much more often' (-2), 'We wouldn't change how often we used a condom' (0)]". Respondents were also asked three injection-related items, "If [you/alter/you and alter] got an HIV vaccine that was 90% effective, would you use share injection equipment..."

['Much less often' (-2), 'Less often' (-1), 'More often' (+1), 'Much more often' (+2), 'We wouldn't change how often we shared equipment' (0)]. These data were used to construct a risk compensation adjacency matrix (see panel 2 of Figure 4.1).

Respondents were also given the option to name new individuals with whom they would initiate risk behavior if they received the HIV vaccine. Specifically, respondents were asked, “Imagine that you got an HIV vaccine that was 90% effective. Is there anyone else you can think of who you may start [having sex/sharing works] with? For example, [list of all social support, drug, and sex network members named in the SNAP interview].” Respondents then gave the name (first and last initial), age, and gender of each individual. These data were cross-referenced using the same procedures described above to determine if the new relationship was with someone participating in the SNAP study. Each new relationship was conservatively assigned a value of "1" in the post-vaccination network (described below).

Using these data, binary **risk compensation networks** corresponding to the *Complete Network* and *Sociometric Network* were constructed. In these networks, $\boldsymbol{A}_{ij}=1$ if respondents answered that they would increase their risk behavior on any one of the six items and $\boldsymbol{A}_{ij}=0$ if they would not increase their risk behavior. These networks served as the outcomes for the dyadic analyses presented in Table 4.2.

The **post-vaccination network** was also constructed using the risk compensation data. The maximum values from the three sexual and injection-

related risk compensation questions were added to the Likert scale ratings given for the dyad's current unprotected sex and equipment sharing behavior, respectively. The resulting condom use and equipment sharing ratings were then summed to produce a valued "post-vaccination network" representing each dyad's frequency of risk behavior in the presence of HIV vaccination. An example of this process is shown in Figure 4.1.

Demographic similarity matrices*.* Matrices representing demographic similarity were also constructed, including one that represented the absolute difference in age (years) between the respondent (i.e. **ego**) and each of their alters and one that represented gender similarity (1=same gender, 0=different gender). Of note, the age difference was based on the respondent's report of alter ages; the actual age of alters not participating in SNAP was unknown.

Ego and alter characteristics. To determine if characteristics of the egos and/or alters affected likelihood of risk compensation, matrices were constructed to represent ego and alter characteristics, the latter as reported by the respondent. These characteristics include gender (1=male, 0=female), age (years), and IDU in the past 6 months (binary). A matrix was also constructed to represent respondents' perceptions of the benefits of HIV vaccination, based on their responses to the following, "In your opinion, how much would an HIV vaccine benefit you?" Responses were given on a 4-point Likert scale ranging from "not at all" to "a lot".

Relationship characteristics*.* Matrices were also constructed to represent the following relationship characteristics: duration of the relationship

(months), frequency of communication (6-point scale, ranging from 1=less than once a year to 6=everyday), geographic distance between their residences (9-point scale, with increasing values indicating further distances), how much they trusted each alter (10-point scale), and whether or not the respondent received social and financial support from each alter (both binary). Participants were also asked, "How likely do you think it is that [network member] would ever get infected with HIV?" and "How likely do you think it is that [network member] would ever infect you with HIV?" Responses were given on a 4-point Likert scale ranging from 'very unlikely' to 'very likely'. These data were used to construct two matrices.

Statistical Analyses

Network-level analyses were conducted to determine the dyadic correlates of intention to engage in risk compensation. To account for potential autocorrelation among participants, double semi-partialling quadratic assignment procedures multiple regression (MR-QAP) (Dekker, Krackhardt, & Snijders, 2007; Krackhardt, 1987b) was conducted in UCINET (Borgatti et al., 2002). MR-QAP is robust to multi-collinearity (Dekker et al., 2007) and involves a permutation-based test of association between matrices while preserving the underlying structure of network data. The regression proceeds in two steps: 1) standard multiple regression is conducted across corresponding cells of the dependent and independent matrices, and 2) random permutations (10000 for the present analyses) are conducted across rows and columns of the matrices and the regression is recomputed storing values of r-square and the coefficient. For each

coefficient, the program counts the proportion of random permutations that yield a coefficient as extreme as the one computed in step 1 (Dekker et al., 2007; Krackhardt, 1987a).

In this analysis, MR-QAP was used to regress the risk compensation matrix on each of the demographic, psychosocial, and behavioral matrices described above. Matrices reaching significance ($p < 0.05$) were entered into a multivariate model to examine their independent association with the risk compensation network. MR-QAP is designed for use on outcome matrixes containing continuous rather than binary data. However, there is currently no available method in UCINET to conduct a binary logistic QAP regression that accounts for missing data. The matrices used in this analysis have missing values due not to missing data on measures, but to the fact that risk compensation was not assessed for every possible combination of participants. The imputation of zeros for missing values could have inflated the observed association and increased likelihood of Type 1 error. Due to the use of a linear technique to model a binary outcome, only the direction and significance of the parameter estimates are interpretable.

To examine changes that may occur to the overall risk network structure in the presence of HIV vaccination, symmetrized versions of the pre-vaccination and post-vaccination risk networks were compared. Unlike the directed networks analyzed in the QAP analyses described above, symmetrized networks do not take into account *who* reported the information; for example, if one person reports having sex with an alter, the relationship is presumed to be reciprocal.

For ordinal and continuous data, data were symmetrized by taking the maximum value reported for each relationship. For example, in Figure 4.1, a value of four would have been assigned or the relationship between participants C and D.

For each network, structural measures of network size, cohesiveness (diameter, component structure, density, and k-cores) and centrality were computed. Each of these measures were chosen a priori based on evidence that they can play a role in network-level HIV and STI transmission and related behaviors in risk networks (Bearman, Moody, & Stovel, 2004; De et al., 2007; De et al., 2004; Friedman et al., 1997; Helleringer, Kohler, Chimbiri, Chatonda, & Mkandawire, 2009; Klovdahl et al., 1994; Potterat et al., 1999; Rothenberg, Potterat, et al., 1998; Rothenberg, Sterk, et al., 1998). Network size*,* or *diameter,* is the length of the longest path in the network (Wasserman & Faust, 1994). *Components* are network structures within which all individuals are connected directly or indirectly through at least one path (Hanneman & Riddle, 2005). *Isolates* are participants who are disconnected from everyone in the network. *Density,* for binary matrices, is the number of connections in the network reported as a fraction of the total connections possible. For valued data, density represents the average value of relationships within the network (Hanneman & Riddle, 2005). The density of the two networks was compared by using a bootstrap paired sample t-test conducted in UCINET. The paired sample t-test of density on the valued networks determined if there was a difference in the mean overall tie strengths of the pre- and post-vaccination networks (Hanneman & Riddle, 2005).

Network Centralization (Freeman, 1979), based on computation of degree centrality (Freeman, 1979), represents the degree to which the networks are centralized around one or a few actors (Valente, 2010). The centralization value, which ranges from 0 to 1, reflects the extent to which all network members are connected through one central actor (i.e. visualized in the shape of a star) (Freeman, 1979; Wasserman & Faust, 1994). Higher values of centralization are indicative of more hierarchy (Valente, 2010). Finally, *k-cores* capture information on participants' location within cohesive risk network subgroups. A *k*-core is a maximal subgroup of individuals within a network that are all connected to at least *k* other members in the group. For example, a 2-core refers to a group of two or more people who are connected to at least two other members of the group (Friedman et al., 1997). Two-cores are hypothesized to be conducive to HIV and STI transmission (De et al., 2004; Friedman et al., 1997); thus, for the present analysis, networks were compared in terms of the number of 2-cores present in the network.

Of note, most indices required dichotomization of valued data; however, degree centrality, centralization, and density could also be computed on valued data. For these three indices, the valued and binary comparisons are presented.

Results

Participants were predominantly White (94%), 45% were female, and only 25% were married. The median age of participants was 34 years (range: 21 – 68). Just over half (58%) had graduated from high school, 39% were

unemployed, and the median monthly income (from all sources) was $698. Most (82%) reported at least one sexual partner in the past 6 months, 24% reported having multiple partners, 71% reported unprotected sex with at least one partner, and 20% reported unprotected sex with a PWID.

The risk network is shown in Figure 4.2. Of the 433 participants, 353 reported at least one sexual relationship and 45 reported a relationship that involved sharing drug injection equipment. Overall, the network contained 511 sexual relationships, 417 of which involved unprotected sex. The network included 68 relationships that involved equipment sharing, including 37 that involved equipment sharing *and* sex.

Risk compensation in current relationships

Figure 4.3 shows relationships involving intended risk compensation (shown as red lines). There were 30 relationships in which the respondent reported a likelihood of risk compensation, including three that would involve increased equipment sharing and 27 that would involve increased unprotected sex (there were no relationships involving intent to increase equipment sharing *and* unprotected sex). There were some individuals who would increase their sexual risk behavior with many partners, including one person that reported risk compensation for six sexual relationships and another who reported it for four relationships. Overall, sexual risk compensation resulted in the addition of fourteen relationships to the risk network (i.e. individuals who previously always used condoms would begin having unprotected sex); the other sixteen relationships involving intended risk compensation occurred within relationships

already involving either unprotected sex or equipment sharing. Of note, reported intention to *increase* condom use after HIV vaccination resulted in the removal of four relationships in the risk network.

As shown in Table 4.1, which describes responses to the risk compensation questions, the likelihood of risk compensation did not vary substantially by vaccination scenario (i.e. vaccination of self, partner, or of self and partner). Sexual risk compensation was intended in only 5.3% of sexual relationships in the network and risk compensation related to equipment sharing was only intended in 4.4% of equipment sharing relationships. Interestingly, condom use was intended to *increase* after HIV vaccination in 4.7% of sexual relationships. Overall, the vast majority of participants reported they would not change their sexual or injection-related risk behavior under any vaccination scenario (91.2% and 93.3%, respectively).

Risk compensation involving initiation of new risk relationships

On the open-ended questions, four respondents listed specific people with whom they would begin having unprotected sex (n=3) and/or sharing equipment (n=1). Three respondents gave first names and last initials of a total of four individuals who were confirmed to be in the study, and one person named someone not in the study.

Dyadic correlates to likelihood of risk compensation

Table 4.2 describes bivariate analysis of dyadic correlates of intended risk compensation. Risk compensation was more likely to occur between partners who had known each other for a shorter time ($p = 0.005$), communicated less

frequently (p = 0.023), and resided further from each other (p = 0.033). Respondents also reported a greater likelihood of risk compensation with partners they perceived to be at a greater risk for acquiring HIV (p = 0.043). Demographic characteristics and similarities, trust, receipt of social and financial support, receptive/distributive equipment sharing, and perception of the HIV risk posed by partners were not associated with likelihood of risk compensation. In multivariate analysis, only duration of the relationship (p = 0.011) retained its significant associations with risk compensation intent.

Structural changes to the risk network due to risk compensation

Descriptive comparisons of the pre-vaccination and post-vaccination networks are shown in Table 4.3. The complete post-vaccination network contained fifteen more relationships and fifteen fewer isolates than the pre-vaccination network. In both the complete and sociometric networks, diameter of the post-vaccination network was twice that of the pre-vaccination network. The size of the main component increased from 14 to 16 due to risk compensation; however, the overall average component size remained similar (2.63 and 2.70, respectively). The average degree centrality and the centralization of the post- and pre-vaccination network were also similar.

Risk compensation resulted in a *decrease* in transitivity, a measure of network cohesion (0.69% to 0.63%). The decrease in transitivity was likely due to the fact that individuals drawn into the network through risk compensation were not connected to other members of the network, creating more triads that did not exhibit closure. The number of 2-cores remained constant across the two

networks, but density (based on binary data) was significantly higher in the post-vaccination network compared to the pre-vaccination network (0.00035 vs. 0.00036, $p < 0.001$). As shown in Table 4.3, similar patterns were present when the analyses were restricted to the sociometric network.

Discussion

Risk compensation in this sample was relatively uncommon; only 4% reported an intention to decrease condom use with a partner and 1% to increase sharing injection equipment if they, their partner, or they *and* their partner received an HIV vaccine. Risk compensation in the form of initiating sexual and/or equipment sharing with new partners was similarly rare (1%). The percentage of participants reporting an intention to risk compensate if given a highly efficacious vaccine is nearly half that reported in a study conducted among high-risk individuals recruited from clinics, syringe exchange programs, and Latino community-based organizations in Los Angeles (Newman et al., 2009) and one-fourth that reported among MSM, African American women, and drug users in Atlanta (Crosby & Holtgrave, 2006) and PWIDs from Philadelphia (Meyers et al., 1994).

The current study is the first to explore risk compensation under three vaccination scenarios: vaccination of self, partner, and self *and* partner. Interestingly, levels of risk compensation under the partner-vaccination scenario were nearly identical to that under personal vaccination. Previous research has generally assumed that risk compensation would be initiated by the vaccine

recipient, but this study provides evidence that partners of recipients may also initiate increased risk behavior. This dynamic is important to explore in future HIV vaccine acceptability research and in the context of HIV vaccine clinical trials.

While the individual-level data are valuable, only under examination at the dyadic level do the complex dynamics of risk compensation become apparent. More than 500 sexual partnerships and nearly 70 equipment-sharing relationships were reported by the drug users enrolled in this study. Intent to engage in sexual risk compensation was reported for 27 relationships, and intent to increase equipment sharing was reported for three. Thus, the 24 individuals who intended to increase their risk behavior would actually put 35 individuals at increased risk for HIV transmission, a number that increases to 48 when you consider second-order connections (i.e. partners of partners).

It is also important to note that in 5% of sexual relationships, condom use was anticipated to *increase* following HIV vaccination. This finding is corroborated by previous research reporting decreases in sexual risk behavior among participants enrolled in HIV vaccine clinical trials (Bartholow et al., 2005; Guest et al., 2005; van Griensvan et al., 2004). The potential for decreased risk behavior is important given evidence from simulation studies suggesting that to achieve maximal impact with a partially effective vaccine, vaccine uptake must be coupled with behavioral risk reduction (Andersson et al., 2011; Blower & McLean, 1994). From the dyadic level, it is important to note that most of the relationships for which there was intended risk reduction currently involved *no* condom use. Thus, unless the couple decided to begin abstaining from

unprotected sex completely, the impact of behavioral risk reduction would result in minimal change in HIV risk for first- and second-order partners.

While some studies have examined individual-level correlates to risk compensation (Chesney et al., 1997; Crosby & Holtgrave, 2006), few have characterized the types of relationships in which risk compensation is most likely to occur. Evidence from bivariate analyses suggests that risk compensation was more likely to occur in what could be considered as less well-established relationships. Specifically, participants were significantly more likely to report intent to engage in risk compensation in relationships of shorter duration involving less frequent communication. Participants were also more likely to engage in risk compensation with partners who lived further from them and with those they perceived to be at a higher risk for HIV. Although only duration was significantly associated with risk compensation in the multivariate model, the bivariate findings are concerning and deserving of further research.

While seemingly counterintuitive, the increased likelihood of risk compensation in relationships involving partners perceived to be at higher risk for HIV is actually consistent with the cognitive mechanism underlying risk compensation (Hogben & Liddon, 2008). Inhibition is a necessary prerequisite for disinhibition; that is, increased risk behavior would only be expected to occur in those relationships which were originally perceived as posing a risk. However, from a public health standpoint and from the perspective of those examining changes in HIV incidence in vaccine clinical trials, these findings have important implications. Future research should expand their measures of risk compensation

to assess not only *if* people risk compensate, but also *with whom* they risk compensate.

Individual- and dyad-level changes in risk behavior can only be fully understood in the context of the larger social network in which high-risk individuals are embedded. The present study is the first to provide preliminary evidence that risk compensation could affect the connectivity of risk networks. The structural changes observed in the risk network, which was comprised of relationships involving injection equipment sharing and/or unprotected sex, were only slight, but conceptually important. The density of the risk network constructed on the basis of participants' risk compensation intentions was significantly greater than that of the current risk network. The increase in density resulted from the addition of fifteen risk relationships to the "post-vaccination" network due to risk compensation.

Generalization of the study's findings should be made with caution and in light of its limitations. First, the measure of risk compensation was based on intention; intended behavior change may or may not correspond with patterns of future risk behavior (Armitage & Conner, 2001; Webb & Sheeran, 2006). This study took place among a unique population of rural drug users who live in a region with low HIV incidence (Kentucky Cabinet for Health and Human Services, 2010), the generalizability to urban settings with higher HIV burden may be limited. Though they would have provided valuable insight, contextual data on the circumstances and motivations surrounding risk compensation were not

collected. In the future, qualitative approaches are needed to fully explore the complexity of anticipated behavior change in response to HIV vaccination.

This study provides a methodological framework in which to examine anticipated risk compensation in future HIV vaccine preparedness cohorts and to examine the network-level impact of behavioral change in future HIV vaccine clinical trials. This study also suggests that network-level change be considered in the paramaterization of mathematical models projecting the impact of risk compensation on the success of future HIV vaccines. Overall, the findings from this study on the infrequency of intended risk compensation, particularly that related to syringe sharing, are encouraging and underscore the positive potential impact of a future HIV vaccine.

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Table 4.1 Intent to engage in sexual and injection-related risk compensation in three HIV vaccination scenarios

	Vaccination of self		Vaccination of partner		Vaccination of self and partner		Total	
	Egos n (%)[a]	Dyads n (%)[b]	Egos n (%)[a]	Dyads n (%)[b]	Egos n (%)[a]	Dyads n (%)[b]	Egos n (%)[a]	Dyads n (%)[b]
Change in condom use								
Much less often	6 (1.7)	8 (1.6)	6 (1.7)	8 (1.6)	6 (1.7)	8 (1.6)	7 (2.0)	9 (1.8)
Less often	10 (2.8)	17 (3.3)	10 (2.8)	17 (3.3)	10 (2.8)	18 (3.5)	10 (2.8)	18 (3.5)
More often	13 (3.7)	18 (3.5)	11 (3.1)	16 (3.1)	12 (3.4)	17 (3.3)	13 (3.7)	18 (3.5)
Much more often	6 (1.7)	6 (1.2)	6 (1.7)	6 (1.2)	6 (1.7)	6 (1.2)	6 (1.7)	6 (1.2)
Would not change	324 (91.8)	460 (90.2)	326 (92.4)	462 (90.6)	324 (91.8)	460 (90.2)	322 (91.2)[c]	458 (89.8)[c]
Change in equipment sharing								
Much less often	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Less often	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
More often	2 (4.4)	2 (2.9)	2 (4.4)	2 (2.9)	2 (4.4)	2 (2.9)	2 (4.4)	2 (2.9)
Much more often	1 (2.2)	1 (1.5)	1 (2.2)	1 (1.5)	1 (2.2)	1 (1.5)	1 (2.2)	1 (1.5)
Would not change	42 (93.3)	65 (95.6)	42 (93.3)	65 (95.6)	42 (93.3)	65 (95.6)	42 (93.3)[c]	65 (95.6)[c]

Bold indicates responses consistent with intent to engage in risk compensation

[a] Percentages are based on the total number of participants reporting at least one sexual (n=353) or equipment-sharing relationship (n=45). Of note, 31 people reported a relationship with someone with whom they had sex *and* shared injection equipment. The total number of respondents is greater than 367 because each respondent could give a different response for each named alter.

[b] Percentages for rows corresponding to changes in condom use and equipment sharing are based on the total number of sexual (n=510) and equipment-sharing relationships (n=68), respectively.

[c] Number of respondents and dyads in which no change was reported under *all* three vaccination scenarios.

Table 4.2 Bivariate and multivariate correlates to risk compensation intent in 582 risk network relationships

	Bivariate		Multivariate	
	β	p-value	Adjusted β	p-value
Demographic similarities				
Same gender	-0.068	0.087		
Age difference[a] (years)	-0.052	0.101		
Relationship characteristics				
Duration (months)	-0.106	0.005**	-0.095	0.011*
Frequency of contact	-0.092	0.023*	-0.043	0.168
Distance[b]	0.099	0.033*	0.063	0.139
Trust	-0.032	0.211		
Social support	-0.021	0.272		
Receives financial support	-0.013	0.449		
Partner's risk for HIV[b]	0.081	0.043*	0.064	0.078
HIV risk posed by partner[b]	0.071	0.052		
Behavior				
Used drugs together	-0.029	0.211		
Sexual relationship (Ref: inject together)	0.063	0.121		
Inject together *and* sexual partners	0.074	0.090		
Distributive needle sharing	-0.005	0.367		
Receptive needle sharing	0.000	0.674		
Frequency of risk behavior	-0.055	0.103		
Ego's characteristics				
Male	0.057	0.133		
Age	0.005	0.449		
Recent injection drug use	0.030	0.311		
Perceived benefit of HIV vaccination	0.060	0.096		
Alter's characteristics				
Male	-0.052	0.150		
Age[b]	-0.061	0.072		
Recent injection drug use	0.007	0.358		

*p < 0.05, **p < 0.01; IDU: injection drug use; β: standardized beta estimates

[a] Due to two missing values, 580 relationships were included in analysis.

[b] Due to one missing value, 581 relationships were included in analysis.

Table 4.3 Comparison of pre- and post-vaccination risk networks

	Complete Network		Sociometric Network	
Characteristic	Pre-vaccination	Post-vaccination	Pre-vaccination	Post-vaccination
Number of relationships	448	463	142	149
Number of isolates	867	852	276	269
Components				
Number of components[a]	243	243	74	74
Size of main component	14	16	5	10
Size of components				
N=14	1	1	0	0
N=10	1	1	0	1
N=9	2	2	0	0
N=8	2	2	0	0
N=7	2	3	0	0
N=6	3	3	0	0
N=5	11	9	1	1
N=4	7	8	4	4
N=3	39	39	6	5
N=2	175	174	63	63
Mean component size[a]	2.63	2.70	2.23	2.32
Centrality and centralization				
Degree centrality (valued) – mean (SD)	1.53 (2.43)	1.56 (2.46)	1.77 (3.06)	1.78 (3.06)
Degree centrality (binary) – mean (SD)	0.53 (0.80)	0.55 (0.82)	0.42 (0.59)	0.45 (0.63)
Centralization (valued)	0.43	0.43	0.20	0.20
Centralization (binary)	0.24	0.24	0.59	0.58
Cohesion				
Transitivity	0.69%	0.63%	10.0%	7.1%
Number of 2-cores	2	2	2	2
Density (valued)	0.9904[b]	0.9970[b]	0.0067[c]	0.0069[c]
Density (binary)	0.00035[d]	0.00037[d]	0.0019[e]	0.0020[e]
Diameter	4	8	3	6
Intent to change behavior given HIV vaccination				
Relationships with intent to increase risk behavior	30		7	
Relationships with intent to decrease risk behavior	24		8	

SD: standard deviation

[a] Excluding isolates

[b] Difference was no statistically significant ($p = 0.356$).

[c] Difference was not statistically significant ($p = 0.139$).

[d] Difference was statistically significant ($p < 0.001$).

[e] Difference was statistically significant ($p = 0.019$).

Figure 4.1. Illustration of procedure for constructing pre- and post-vaccination risk networks for comparison

Pre-vaccination

	A	B	C	D
A	0	4	0	3
B	4	0	5	0
C	0	5	0	2
D	3	0	4	0

+

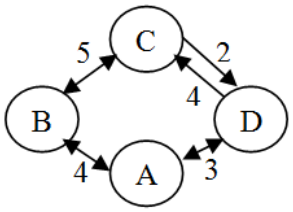
Risk Compensation

	A	B	C	D
A	0	2	0	-2
B	0	0	1	0
C	0	0	0	0
D	-2	0	0	0

=

Post-vaccination

	A	B	C	D
A	0	6	0	1
B	4	0	6	0
C	0	5	0	2
D	1	1	4	0



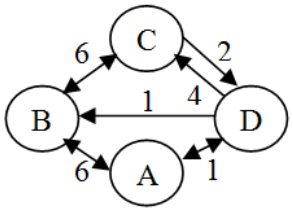
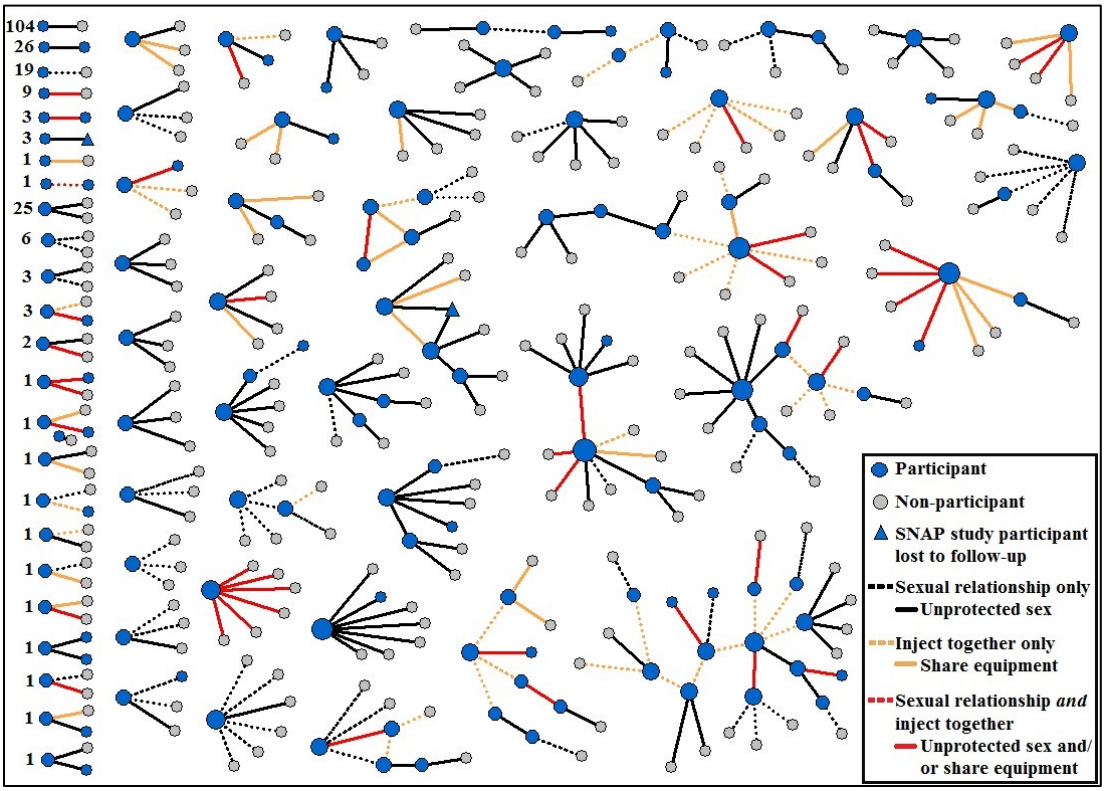


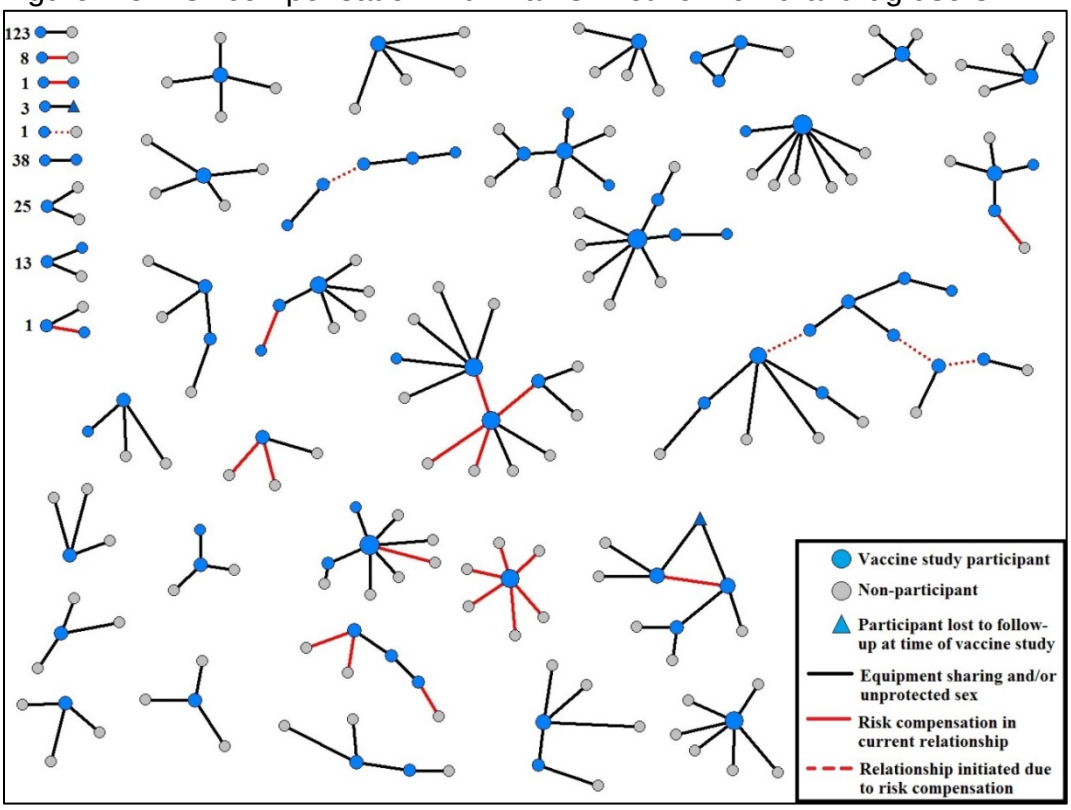
Figure 1 displays a network of risk relationships among participants A, B, C and D. The corresponding adjacency matrixes are also presented. The values of the pre- and post-vaccination network ties represent frequency of HIV risk behavior, or the sum of three Likert scales on which participants rated the frequency of unprotected sex and frequency of needle and cooker sharing with the alter. Values in the risk compensation matrix represent the degree of behavior change anticipated to occur after HIV vaccination, with negative numbers representing a decrease in risk behavior, zeros representing no change, and positive numbers representing risk compensation. To construct the post-vaccination matrix, the risk compensation matrix was added to the pre-vaccination matrix. Participant D reported that they would initiate a risk relationship with Participant B, so a tie was added and a one was entered in the corresponding cell of the post-vaccination matrix.

Figure 4.2 Sexual and injection-related risk networks of respondents and named alters



Nodes are sized by degree centrality (i.e. number of partners).

Figure 4.3 Risk compensation within a risk network of rural drug users



Nodes are sized by degree centrality (i.e. number of partners). The figure does not include the 95 participants who did not someone with whom they shared equipment or had unprotected sex

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Chapter 5 : Conclusion

The analyses outlined in this dissertation were developed in response to gaps identified in the existing literature on individuals' willingness to receive an HIV vaccine. Previous research has revealed that low vaccine uptake is a concern (Newman & Logie, 2010), as is the potential for risk compensation (e.g. engagement in increased levels of risk behavior in response to vaccination). In fact, simulation models have predicted that with the right combination of risk compensation and vaccine efficacy, an HIV vaccine campaign could *increase* HIV incidence (Andersson et al., 2007; Fonseca et al., 2010). Thus, being able to understand and predict behavior in the first years of a new HIV vaccination program will be crucial for being able to preemptively address obstacles to program success.

Unfortunately, there are glaring limitations in the extant research on HIV vaccine acceptability and risk compensation. Drug-using populations have been significantly underrepresented in existing research on HIV vaccine acceptability, and risk compensation within the context of drug-related risk behavior (e.g. syringe sharing) has been largely unexplored. Furthermore, the methodology employed in HIV vaccine acceptability studies to date has been almost exclusively individual-level in focus, despite an abundance of evidence suggesting that social networks can play an important role in HIV transmission and risk behavior (De, Cox, Boivin, Platt, & Jolly, 2007; Friedman et al., 1997; Klovdahl et al., 1994; Potterat, Rothenberg, & Muth, 1999; Rothenberg et al., 1998), as well as involvement in preventive interventions (Coyle, Needle, &

Normand, 1998; Latkin et al., 2013; Wang, Brown, Shen, & Tucker, 2011). The influence of network-level social norms on HIV vaccine acceptability has been largely unexplored, and few studies have examined if networks can be leveraged to promote HIV vaccination among hard-to-reach populations.

Perhaps most notably, no research to date has been conducted on the effect that risk compensation may have on the connectivity of risk networks. Previous individual-level studies have captured *if* and *to what degree* individuals will engage in risk compensation, but they have not captured *with whom* or to what extent behavior change could differ *across relationships*. Consequently, there is currently little understanding of how social network structure could influence vaccine uptake, or perhaps more importantly, how HIV vaccination could alter the dynamics and structure of HIV risk networks. If risk compensation increases the connectivity of risk networks, HIV vaccination may increase community HIV risk exponentially more than that which has been estimated based on individual-level studies of risk compensation.

Studies described in Chapters 2 through 4 are the first of their kind to explore HIV vaccine acceptability, vaccine promotion, and risk compensation using social network analysis. The analyses presented in this dissertation are also the first to be conducted among a *rural* sample of illicit drug users in the US. The data collection for the presented analyses was implemented in the context of the ongoing longitudinal study of HIV, hepatitis C, and herpes simplex-2 among drug users in Appalachia (methods described in detail elsewhere (Havens et al., 2013; Young, Jonas, Mullins, Halgin, & Havens, 2013). Data for the longitudinal

study are collected using interviewer-administered questionnaires administered every 6 months. Findings from the study to date indicate that drug users in the region are engaging in HIV risk behavior at alarmingly high rates (Crosby, Oser, Leukefeld, Havens, & Young, 2012; Havens et al., 2013; Young & Havens, 2012). From March 2012 to May 2013, 433 participants completed their 24-month follow-up assessment and, immediately afterward, were invited to complete an interviewer-administered questionnaire on their attitudes toward HIV vaccination. The analyses presented in Chapters 2 through 4 are based on data generated from these questionnaires.

Study 1 examines demographic, behavioral, and psychosocial correlates to HIV vaccine acceptability. Findings indicated that, despite low perceived susceptibility to HIV, nearly all were willing to accept a preventive HIV vaccine with 90% efficacy. Generalized linear mixed models were used to determine correlates, chosen a priori based on the Integrative Model of Behavioral Prediction (Fishbein, 2008), to individuals' report that they were "very likely" to receive an HIV vaccine (i.e. "maximum vaccine acceptability"). Significantly fewer men than women reported being "very likely" to accept an HIV vaccine. Participants who believed that they were susceptible to HIV, would personally benefit from HIV vaccination, and would have positive affective responses to receipt of an HIV vaccine were more likely to report maximum vaccine acceptability. The odds of reporting MVA were also significantly higher among participants who believed that most people would encourage them to get an HIV vaccine and that they (the respondents) would be more motivated to get the

vaccine in response. In the multivariate model, variables related to normative influence were the only ones that, collectively, had a significant contribution to the predictive ability of the model. These data indicate that social norms could play a major role in influencing HIV vaccine uptake in this community, and that peer-promotion should be explored as a potential strategy for promoting the HIV vaccine among drug users in this rural community.

Study 2 builds upon the findings of Study 1 by examining specific network-level correlates to participants' willingness to encourage their HIV risk network members to receive the HIV vaccine. The results demonstrate that the majority were willing to encourage HIV vaccination among their non-risk social network members (i.e. people with whom they use non-injected drugs or from whom they receive social support) and risk partners (i.e. people with whom they have sex or inject drugs). However, nearly one in three reported that they would be *selective* in deciding whom they would encourage to receive the vaccine. Dyad-level analyses were conducted to determine the characteristics of relationships in which HIV vaccine promotion was likely to occur. In non-risk relationships, participants were more likely to encourage partners with whom they used drugs. In risk partnerships, respondents were more likely to encourage those perceived to be (1) at high risk for HIV, (2) willing to accept the HIV vaccine, and (3) likely to reciprocate the encouragement of HIV vaccination. Most notably, participants were more likely to encourage partners with whom they intended to engage in risk compensation.

Thus, Study 2 extends the findings of Study 1 by providing additional evidence that peer-based vaccine promotion could be a feasible and successful strategy for reaching high-risk individuals in this rural community. However, the study calls attention to a potential unintended consequence of peer-based vaccine promotion; that is, individuals may be more likely to promote HIV vaccination among those with whom they intend to increase risk behavior. Thus, these findings not only underscore the need for careful planning and oversight for peer-based vaccine promotion in this population, but also point to a need to better understand the dynamics of risk compensation.

The purpose of Study 3 was three-fold. First, the extent of anticipated risk compensation related to condom use and injection equipment sharing was determined. Second, analyses were conducted to determine the characteristics of relationships in which risk compensation was most likely. Third, by combining data on current risk behavior and anticipated risk compensation, a risk network was constructed to simulate how connectivity may change in response to HIV vaccine dissemination. The simulated network was compared to the current risk network on structural properties known to be associated with HIV and STI risk.

The study revealed that few participants anticipated increases in their risk behavior if they, their partner, or they and their partner received a HIV vaccine. Risk compensation related to syringe sharing and the initiation of risk relationships with new partners was especially rare. Risk compensation was intended for 30 relationships in the risk network. Dyadic analyses revealed that risk compensation was most likely to occur in relationships of shorter duration.

Risk compensation resulted in a 5% increase in the number of ties in the risk network. The change did not substantially affect the risk network's structural properties (e.g., centralization, transitivity, *k*-coreness), but did result in significantly greater network density and a two-fold increase in the size of the largest connected component. These data provide the first preliminary evidence that risk compensation may result in change in risk network structure. This finding is important for informing the design of future studies on risk compensation, particularly in the context of HIV vaccine clinical trials, and in suggesting new parameters for inclusion in mathematical modeling of HIV vaccine impact.

Limitations

The primary limitation of this dissertation research is that all outcomes are based on *intent*. Some have suggested that intent is a poor predictor of behavior (Gollwitzer, 1999). Meta-analyses have found that the average correlation between intention and behavior is moderate (0.47 - 0.62) (Armitage & Conner, 2001; Randall & Wolff, 1994; Sheppard, Hartwick, & Warshaw, 1988). A more recent meta-analysis of 47 experimental studies found only a small to medium effect size (d=0.36) for the association between intent and behavior, and that the association between beliefs and behavior was not fully mediated by intent (Webb & Sheeran, 2006). Similar concerns regarding the association between intent and behavioral in HIV vaccine research have also been voiced (Poole, 2012). Unfortunately, the association between intent and behavior in HIV vaccine research will be unknown until a vaccine is approved. Some evidence from

research on uptake of other vaccines, including that of the HPV and flu vaccines, have demonstrated that intent is an important predictor of vaccine uptake (Liao, Cowling, Wendy Wing Tak, & Richard, 2011; Painter et al., 2011; Patel et al., 2012).

Several measurement factors have been found to modify the association between intent and behavior, including *correspondence* (i.e. degree of match between elements of the behavior defined in the intent items and that of the actual behavioral outcome), time elapsed between measurement of intention and observation of behavior (McEachan, Conner, Taylor, & Lawton, 2011), discrepancies between participants' affect at measurement and time of behavior (Ajzen, 2011), and differences in the physical context in which measurement is completed and behavior is performed (Cooke & French, 2011). The latter two factors are difficult to address in cross-sectional studies. Issues of correspondence and time-elapsed between measurement and performance of the behavior are especially difficult to address in HIV vaccine acceptability research given that the exact characteristics of the forthcoming vaccine are yet to be known, as is the timeline for approval. However, the questionnaire used in this dissertation research attempted to address correspondence by being specific about vaccine characteristics throughout the questionnaire. In each item used in the analyses presented in Chapters 2 through 4, respondents were prompted to assume that the vaccine was 90% effective. For the item on HIV vaccine acceptability, respondents were also asked to rate their likelihood of accepting the vaccine if it was made available to them *within the next 12 months*.

The data used in this dissertation were based on self-report. Though extant research has demonstrated that self-reported data on drug use and HIV risk behavior are good indicators of actual drug use and behaviors (Darke, 1998; Latkin, Vlahov, & Anthony, 1993), self-reported data remains subject to recall and social desirability bias. In the current study, the possibility for information bias was minimized by embedding the vaccine questionnaire within an established, longitudinal study. The community-based interviewers who administered the questionnaire have been involved with the study for five years and have an established rapport with the participants.

Conclusion

Despite limitations, this dissertation makes a substantial contribution to the existing literature on HIV vaccine acceptability. The study is the first of its kind to investigate HIV vaccine acceptability among rural drug users in the US. The study is also the first to use social network analysis to determine dyad-level correlates of peer-to-peer encouragement of HIV vaccination among drug users. Finally, Study 3 provides the first evidence to date from social network analysis that risk compensation could reshape the structure of risk networks. These findings could be of value in planning future HIV vaccine dissemination strategies among drug users in rural Central Appalachia, and more immediately, could have methodological and conceptual implications for future behavioral research on HIV vaccination. This dissertation demonstrates the value of social network analysis to exploring issues of vaccine uptake and promotion, but the need for similar research in other high-risk populations remains. Regardless of changes in risk

behavior, HIV vaccination will have a substantial impact on the HIV epidemic and will inherently disrupt flows of HIV through risk networks; the degree of disruption, however, will depend on the network position of those who receive the vaccine and those who engage in risk compensation.

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