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Connecting the Dots: Network Analysis for Examining Psychosocial Syndemic Conditions Among High-Risk HIV-Negative Men who Have Sex with Men

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UNIVERSITY OF MIAMI

CONNECTING THE DOTS: NETWORK ANALYSIS FOR EXAMINING
PSYCHOSOCIAL SYNDEMIC CONDITIONS AMONG HIGH-RISK HIV-
NEGATIVE MEN WHO HAVE SEX WITH MEN

By

Jasper S. Lee

A THESIS

Submitted to the Faculty
of the University of Miami
in partial fulfillment of the requirements for
the degree of Master of Science

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Connecting the Dots: Network Analysis for
Examining Psychosocial Syndemic Conditions
Among High-Risk HIV-Negative Men who
Have Sex with Men.

Abstract of a thesis at the University of Miami.

Thesis supervised by Professor Steven A. Safren.
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Introduction: In the U.S., HIV acquisition risk is highest among men who have sex with men (MSM). Syndemics, psychosocial problems that interact with each other and poor health behavior, are additively associated with increased condomless anal sex, HIV incidence, and HIV prevalence among MSM. However, information about how these syndemics interrelate with each other is under-explored.

Methods: To examine the associations between nine syndemics in 194 MSM at high risk of HIV acquisition, we examined bivariate polychoric correlations, and then compared exploratory factor analyses (EFA) to a network analysis. Syndemics were assessed by self-report measures. Network analyses (presented graphically) consist of variables, called nodes, and the partial associations between variables, called edges. This regularized network employed the graphical LASSO algorithm and Extended Bayesian Information Criteria with a hyperparameter of $\gamma=.5$ to produce a graphically parsimonious yet sensitive network.

Results: Correlation analyses revealed many associations between syndemics, but this was not always the case. EFA suggested that the 1-, 2-, and 3-factor solutions were possible based on various methods for determining potential factor solutions. However,

the 1-factor solution appeared to be the most appropriate for these data, in which suicidal ideation (SI), injection drug use (IDU), depression, social anxiety, intimate partner violence, substance use, and sexual compulsivity had substantial loadings ($\geq .30$). A pattern of interconnectedness emerged in this network analysis, which revealed that the relationships (absolute edge weights) between SI and IDU ($b=.52$, $SD=.22$, 95% CI[.17, .93]), IDU and substance use ($b=.41$, $SD=.18$, 95% CI[.18, .85]), social anxiety and SI ($b=.30$, $SD=.36$, 95% CI[.06, .77]), and depression and SI ($b=.27$, $SD=.14$, 95% CI[.05, .62]), were all significant. The most central nodes were SI, IDU, substance use, and depression.

Discussion: This is the first study to compare network analysis to EFA in syndemics. It is also one of the earliest studies to conduct a network analysis of syndemics to describe the interrelatedness of conditions, beyond additive associations. Network analysis may be methodologically preferable to EFA in examining the interrelatedness of syndemics because it provides measures of centrality, which can potentially indicate the conditions that drive increased HIV acquisition risk, and lends itself to a visual presentation of the interrelatedness among these intertwined problems. This study therefore has the potential to provide better understanding of the ways in which syndemics, among high-risk MSM, interrelate and, subsequently, affect health behavior.

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Chapter 1: Introduction

HIV Risk in Men Who Have Sex with Men

When the human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS) pandemic began, AIDS was considered a terminal illness and prognosis was extremely poor. Since its discovery, much progress has been made in understanding, defining, and treating HIV – the virus that causes AIDS. However, despite these advances, HIV remains a significant global concern. Overall, since the HIV/AIDS pandemic began, approximately 78 million individuals seroconverted to HIV-positive status, and approximately 35 million people died from AIDS-related causes (UNAIDS, 2016). Globally, it is estimated that by the end of 2015, approximately 36.7 million people were currently living with HIV worldwide (UNAIDS, 2016). In the United States alone, as of 2015, there were over 1.2 million people living with HIV (Centers for Disease Control and Prevention, 2015). HIV is a significant pandemic, and efforts to decrease HIV acquisition risk are needed, especially for those at highest HIV acquisition risk.

One group in which efforts to decrease HIV acquisition risk are especially important are men who have sex with men (MSM), as they are the group with the greatest HIV acquisition risk in the United States. MSM accounted for approximately 70% of all HIV incidence in 2014 (Centers for Disease Control and Prevention, 2018a), and recent estimates suggest that MSM are 83 times more likely than exclusively heterosexual men to have received a diagnosis of HIV at some point in their lifetime (Centers for Disease Control and Prevention, 2016). One factor that contributes to the high HIV acquisition risk for MSM is condomless anal sex. With respect to sexually transmitted HIV,

engaging in condomless anal sex confers the highest HIV acquisition risk, compared to all other types of condomless sex (Centers for Disease Control and Prevention, 2018b). The high HIV acquisition risk associated with condomless anal sex is due to a number of biological factors, such as the rectum being made of a thin mucous membrane that is susceptible to HIV and is prone to small tears due to friction, which allow HIV to more easily enter the blood stream (Wilton, 2011).

Psychosocial Risk Factors for Unprotected Sex in MSM

Decades of research to date have examined risk factors for condomless anal sex among MSM. A number of factors, such as psychosocial conditions, indirectly contribute to the increased HIV acquisition risk among MSM by increasing the likelihood of engaging in condomless anal sex (e.g., Safren, Reisner, Herrick, Mimiaga, & Stall, 2010). However, not all psychosocial conditions confer the same risk for engaging in condomless anal sex. Substance use, injection drug use, heavy alcohol use, and depression are each associated with increased risk of HIV acquisition (Koblin et al., 2006), as are childhood sexual abuse (CSA; Mimiaga et al., 2009), intimate partner violence (IPV; Mustanski, Garofalo, Herrick, & Donenberg, 2007), and posttraumatic stress (e.g., Safren, Blashill, & O’Cleirigh, 2011). Moreover, even within a given mental health condition, the relationship between severity of the condition and risk for engaging in condomless anal sex may not be linear. Depression, for example, appears to have a curvilinear relationship with sexual risk-taking behavior (e.g., condomless anal sex). MSM with moderate levels of depression are at higher risk for engaging in sexual risk-taking behavior than are those with low levels or those with high levels of depression, both among HIV-negative (Koblin et al., 2006) and HIV-positive (O’Cleirigh et al.,

2013) populations. Given the complexity of the relationship between certain psychosocial conditions and increased HIV acquisition risk via an increase in risk of sexual risk-taking behavior, it is important to consider the prevalence of psychosocial conditions among MSM.

Findings suggest that MSM are at significantly higher risk of having at least one mental health and/or psychosocial condition (e.g., depression, substance use, IPV, CSA etc.) than are exclusively heterosexual men over their lifetime (e.g., Gilman et al., 2001; Safren et al., 2010). Furthermore, as mentioned previously, these psychosocial conditions may be related to increased HIV acquisition risk behavior among MSM (e.g., Mustanski et al., 2007; Reisner et al., 2009; Rogers et al., 2003). In other words, not only are MSM at disproportionately greater risk for having a psychosocial condition at some point in their lives than are exclusively heterosexual men, but having a psychosocial condition is also related to increased engagement in HIV acquisition risk behavior. As detailed below, the increased HIV acquisition risk evidenced among MSM appears to exist within, and be exacerbated by, mental health and/or psychosocial conditions. Therefore, further research on the relationship between psychosocial conditions and HIV risk among MSM is needed.

Theory of Syndemic Production

The term “syndemic” was first used by Singer (1994) to describe the factors contributing to the HIV/AIDS crisis as a “set of synergistic or intertwined and mutual enhancing health and social problems” (p. 933). In other words, the comorbid psychosocial conditions (e.g., depression, substance use, IPV, CSA, etc.) that comprise a syndemic are thought to interact synergistically to confer greater risk for poor health

outcomes, above and beyond the risk conferred by only one psychosocial condition (Stall, Friedman, & Catania, 2008). In the specific case of HIV acquisition risk behavior, one theory poses an explanation for syndemic production among MSM.

The theory of syndemic production among MSM (Stall et al., 2008) employs a developmental perspective in explaining the etiology of syndemics among this population. The theory posits that, from childhood through adulthood, MSM experience a number of stressors (e.g., internalized homonegativity, microaggressions, overt discrimination, etc.), which place them at an increased vulnerability for experiencing psychosocial problems as they develop. Indeed, research has found that increased marginalization was associated with increased number of syndemic conditions in this population (Ferlatte, Hottes, Trussler, & Marchand, 2014). In turn, once an individual experiences one psychosocial condition, he or she has an increased likelihood of experiencing at least one other psychosocial condition (Kessler et al., 2005), thus comprising a syndemic. As MSM experience comorbid psychosocial syndemic conditions, the theory subsequently posits an increased likelihood of developing a physical health condition, such as HIV (Stall et al., 2008).

Studies of Syndemic Conditions and their Association to HIV Risk in Men Who Have Sex with Men

The theoretical link between the presence of psychosocial syndemic conditions and increased risk for HIV acquisition is indeed empirically supported. To date, much of the research on the relationship between psychosocial syndemic conditions and HIV risk in MSM has been cross-sectional (e.g., Bränström & Pachankis, 2018; Ferlatte et al., 2014; Hirshfield et al., 2015; Martinez et al., 2016; Mimiaga, Biello, et al., 2015; Mustanski et al., 2007; O’Cleirigh et al., 2018; Parsons et al., 2017; Parsons, Grov, &

Golub, 2012; Stall et al., 2003). This body of research, despite occurring among MSM with a variety of different age groups, demographic characteristics, and in various countries, generally suggests that increasing numbers of psychosocial syndemic conditions are related to increased HIV acquisition risk behavior. Specifically, an increase in the number of syndemic conditions endorsed is consistently associated with an increase in odds of (a) engaging in condomless anal sex (Ferlatte et al., 2014; Martinez et al., 2016; Mimiaga, Biello, et al., 2015; Mustanski et al., 2007; Parsons et al., 2012; Stall et al., 2003), (b) having multiple sexual partners (Martinez et al., 2016; Mustanski et al., 2007), (c) engaging in group sexual encounters (i.e., 4 or more partners in one sexual encounter; Hirshfield et al., 2015), and (d) of being HIV-positive (Mimiaga, Biello, et al., 2015; Mustanski et al., 2007; O’Cleirigh et al., 2018; Parsons et al., 2012; Stall et al., 2003). In addition, an increasing number of syndemic conditions is associated with an increase in the number of medical visits and overall medical care cost in one year among both HIV-positive and HIV-negative MSM (O’Cleirigh et al., 2018).

Overall, syndemic conditions are additively associated with increased HIV risk, though some cross-sectional studies have found more nuanced effects regarding the relationship between the number of syndemic conditions and HIV risk – providing evidence for the synergistic effects of syndemic conditions on HIV risk. One cross-sectional study among 1,470 MSM age 30 or under in Canada demonstrated the same risk of engaging in condomless anal sex among participants with zero or one condition. However, compared to these individuals, the risk of engaging in condomless anal sex was significantly higher among those with two or three or more syndemic conditions (Ferlatte et al., 2014). Similarly, in a cross-sectional study of 1,211 MSM in New England

(O’Cleirigh et al., 2018), one condition was associated with no increase in the odds of being HIV-positive, compared to zero conditions. Yet, among individuals with two syndemic conditions there was a 1.6-fold increase in the odds of being HIV-positive, and a 2.5-fold increase in odds for those with three to four syndemic conditions (O’Cleirigh et al., 2018). Lastly, in a large sample comparing gay- and bisexual-identified men to heterosexual-identified men in Sweden (Bränström & Pachankis, 2018), results suggest the relationship between the number of syndemic conditions and the likelihood of being HIV-positive is non-linear among gay-identified men. As the number of syndemic conditions increased, the likelihood of being HIV-positive also increased, though these increases were above and beyond what would be expected given the difference between zero and one condition, assuming a linear relationship. Overall, the increase in HIV acquisition risk appears to occur in the presence of two or more syndemic conditions, and increases in a non-linear function, providing evidence for the theory of synergistic interaction among syndemic conditions. However, given the cross-sectional nature of this research, temporality cannot be established.

There is an emerging set of longitudinal studies examining temporality of the association of syndemics to HIV risk and HIV acquisition in MSM, which therefore provide more robust evidence for potential causality. The first longitudinal study examined the associations between syndemic conditions and HIV prevalence and incidence among 1,292 MSM in Bangkok, Thailand (Guadamuz et al., 2014). Follow-up assessments were conducted every 4 months for up to 3.8 years from baseline. The syndemic conditions assessed for were a history of being raped, lack of social support, suicidal ideation and/or behavior, “club” drug use, frequent use of alcohol to intoxication,

and engaging in sex work. Cross-sectional results of this study are similar to other cross-sectional findings and support an association between an increasing number of syndemic conditions and increasing HIV prevalence and condomless anal sex. Additionally, a longitudinal association was found between syndemic conditions and HIV incidence, such that compared to those with zero syndemic conditions, those with four or five and those with one to three were significantly more likely to seroconvert (i.e., become HIV-seropositive) throughout the course of the study (Guadamuz et al., 2014). In other words, greater number of syndemic conditions at baseline was related to increased HIV incidence over the course of the study. This longitudinal association between increasing numbers of syndemic conditions and increasing odds of HIV incidence supports the directional and synergistic effects of syndemic conditions on increased HIV acquisition risk.

The second published longitudinal study of syndemics and HIV risk and HIV acquisition among MSM utilized data from a larger intervention trial (project EXPLORE; Koblin et al., 2006), and this study examined the relationships between syndemic conditions and risk of engaging in HIV acquisition risk behavior, between syndemic conditions and risk of HIV seroconversion, and interrelationships between the syndemic conditions themselves among 4,295 HIV-negative MSM in six U.S. cities (Mimiaga, O'Cleirigh, et al., 2015). Follow-up assessments were conducted every 6 months for 4 years from baseline. The syndemic conditions assessed in this study were depressive symptoms, CSA, heavy alcohol use, stimulant drug use, and polydrug use. Results of this study provide additional longitudinal support for an additive association between syndemic conditions and HIV seroconversion, such that increases in HIV seroconversion

risk were significantly positively related to increasing number of syndemic conditions. Those with four or five conditions evidenced the greatest relative risk of seroconversion, followed by those with three, then two, and then one condition(s). This positive association was also found between syndemic conditions and unprotected anal sex in the same pattern of increasing number of syndemic conditions and increasing risk. These findings provide further support for the temporality of the effects of syndemic conditions preceding increased risk of engaging in high risk HIV acquisition behavior and in seroconversion by treating the syndemic measure as time varying and examining the number of syndemic conditions just prior to seroconversion or unprotected anal sex. This study also examined the baseline value of syndemic conditions and the relationship to seroconversion and unprotected anal sex over follow-up, but found no significant differences between using baseline values or time varying values of syndemic conditions, nor found statistical or meaningful differences between the number of syndemic conditions one had at baseline or over follow-up. Additionally, this study also specifically investigated which combinations of syndemic conditions conferred the greatest risk of seroconversion and found 18 high-risk combinations. Of these 18 high-risk combinations, 15 contained stimulant use as a syndemic condition, suggesting that stimulant use may be a relatively key driving factor of increased risk in the context of syndemic conditions.

Another longitudinal study also examined the relative contribution of specific conditions to syndemic production of HIV risk to determine potential key syndemic conditions in relation to increased risk of engaging in condomless anal sex. In this study, 450 young MSM (YMSM) between 16 and 20 years old were recruited in Chicago and completed assessments at baseline and approximately 6 and 12 months later (Mustanski

et al., 2017). The syndemic conditions assessed in this study were analyzed as indicators of three latent constructs: substance use (indicators were binge drinking, alcohol use disorder, and polydrug use), violence (indicators were gay-related physical abuse, IPV, and CSA), and internalizing mental health (indicators were suicidal ideation, major depressive episode, and internalizing anxious/depressed). The substance use, violence, and internalizing mental health latent constructs were subsequently analyzed as indicators of a second-order primary syndemic component latent construct. The model demonstrated adequate fit (comparative fit index [CFI] = 0.93; root mean square error of approximation [RMSEA] = 0.03; weighted root mean square residual [WRMR] = 0.85). Results suggest that although each first-order latent construct provided information to the primary syndemic component, substance use provided more information than either the violence or internalizing mental health constructs. And, in the full model, the violence construct did not remain a significant indicator of the primary syndemic component. Associations between this primary syndemic component at baseline and number of male condomless anal sex partners at the 6-month follow-up as well as HIV incidence (i.e., seroconversion) at the 12-month follow-up were also analyzed. Results of these analyses indicate a positive association between the primary syndemic component at baseline and number of condomless anal sex partners at the 6-month follow-up, but no relationship was evidenced for HIV incidence at the 12-month follow-up (Mustanski et al., 2017). Overall, findings of this study also suggest a more nuanced relationship than a purely additive association between syndemic conditions and HIV acquisition risk, as some factors explained more variance in the primary syndemic component (i.e., substance use and internalizing mental health) than did others (i.e., violence).

Indeed, some have conceptualized the use of additive association between syndemic conditions and HIV acquisition risk as a limitation of this research. Tsai and Burns (2015) argue that, in an additive association, the increase in engaging in HIV acquisition risk behavior from two to three syndemic conditions would be equivalent to the increase from three to four syndemic conditions. However, these authors state such equivalence is theoretically in contrast to the concept of syndemics put forth by Singer (1994), in which the sum of the effect of syndemic conditions is thought to be greater than the total of each individual condition's effect. In other words, Tsai and Burns (2015) suggest that additive associations do not statistically account for the synergistic effects of syndemic conditions on HIV acquisition risk. Instead, these researchers propose the use of multiplicative models that, statistically speaking, better account for interaction effects between conditions. An additive approach may be more practical in evaluating risk, though the multiplicative approach may allow for testing synergistic effects. However, there is a major limitation to note of this methodology given the current literature available on syndemic conditions and HIV acquisition risk: Exactly which syndemic conditions should be specified to have an interaction? As an emerging field of study, there are discrepant findings across studies of syndemic conditions and HIV acquisition risk, and there is a lack of a standard set of syndemic conditions and assessments of such conditions examined across studies (Tsai & Burns, 2015; Tsai & Venkataramani, 2016). Therefore, it is difficult for researchers to select variables *a priori* for interaction terms because which syndemic conditions are interrelated or not related is largely unclear.

Indeed, few studies have examined potential clusters or classes of syndemic conditions that may be most relevant to increased HIV acquisition risk. Previous

examination of more specific groups of syndemic conditions has mostly employed theoretical relationships between constructs to group those of a similar nature (e.g., grouping alcohol use, injection drug use, and polydrug use together as a substance use group of syndemic conditions). For example, in Mustanski et al.'s (2017) longitudinal study, described previously, structural equation modeling was employed to determine relative contributions of first-order latent constructs of overarching types of syndemic conditions (with each latent construct consisting of three syndemic condition indicators that are theoretically similar to one another), to a second-order latent construct of a primary syndemic component. Yet, this methodology does not account for interaction between specific syndemic conditions of different theoretically derived groups.

In another approach, using latent class analyses, one study cross-sectionally examined relationships within syndemic conditions to assess for the presence of classes of syndemic conditions among a sample of 669 MSM in New York City (Starks, Millar, Eggleston, & Parsons, 2014). Results of these latent class analyses did not identify any patterns of interrelationships between specific syndemic conditions. Instead, the latent class analysis solution with the best model fit split the sample into two classes based on the number of syndemic factors endorsed, such that those with zero to two syndemic conditions were grouped into one class and those with three or more were grouped into the other class (Starks et al., 2014). In other words, by splitting the sample into two classes, as either low (0-2) or high (3 or more) on syndemic conditions, the authors conclude that these findings actually provide further evidence of the additive approach to examining the relationship between syndemic conditions and HIV acquisition risk.

However, as described below, latent class analysis is not the only statistical approach to investigating potential interrelationships between specific syndemic conditions.

Network Analysis

Network analysis is a statistical approach that may be helpful in examining interrelationships between syndemic conditions. Although network analysis has only recently been applied to health psychology research (Choi, Batchelder, Ehlinger, Safren, & O’Cleirigh, 2017; Santos, Fried, Asafu-Adjei, & Ruiz, 2017), it is a versatile statistical approach, capable of examining a wide variety of relationships between variables (Borsboom & Cramer, 2013). Previously, network analysis has often been used to examine social interactions among individuals (e.g., Scott, 2017) as well as to examine symptomatology of disorders (e.g., Cramer, Waldorp, van der Maas, & Borsboom, 2010). Network analysis is presented graphically, and consists of nodes (circles representing any type of variable) and edges (lines representing any type of relationship between nodes). Relationships between nodes are entered into an adjacency matrix in which all nodes are the rows and columns (Borsboom & Cramer, 2013). Using this matrix, a graphical depiction of the network is produced, and several graphical features of the network are used in its interpretation. The thickness and darkness of an edge represent the strength of the relationship, such that the thicker and darker an edge, the stronger the relationship between two nodes. And, the closer two nodes are depicted together, the stronger the relationship (Rhemtulla et al., 2016). In addition to the graphical representation, network analysis also provides empirical information on which nodes are most closely related to one another, and which nodes are most central to the overall construct of interest.

Network analysis provides indices of centrality that suggest how much direct connectivity a given node has in a network. Nodes with more connections are more central in a network, and more central nodes are potentially more important in a network than are less central nodes (Borsboom & Cramer, 2013; Rhemtulla et al., 2016). Three centrality indices are produced in network analysis: *betweenness*, *closeness*, and *node strength* (Boccaletti, Latora, Moreno, Chavez, & Hwang, 2006; Rhemtulla et al., 2016). *Betweenness centrality* is a measure of the path length of indirect connections between nodes, such that a node with high *betweenness* is on the shortest path indirectly connecting other nodes. *Closeness centrality* provides information on how close a node is, on average, to the other nodes in the network; a node with high *closeness* is, on average, nearest to the other nodes. Lastly, *node strength* is a measure of the overall strength of the relationships a node has with the other nodes. *Node strength* is calculated by adding the weights of each direct connection for a given node (Rhemtulla et al., 2016). Additionally, *node strength* is considered to be the main centrality index as it provides an empirical value indicating which nodes are the most influential in a given network (Opsahl, Agneessens, & Skvoretz, 2010). Given the assumption in network analysis that edges between nodes represent bidirectional relationships, nodes with high centrality may be the most clinically relevant targets of intervention as these central nodes are associated with much of the interrelationships in a network (Rhemtulla et al., 2016).

Much of the literature to date on network analysis of psychological conditions examines interrelationships between symptoms of one or more disorders, rather than between psychosocial conditions of a syndemic (Choi et al., 2017; Cramer et al., 2010; Epskamp & Fried, 2016; Rhemtulla et al., 2016). The use of network analysis to examine

symptomatology is appealing because, conceptually, it does not require the use of latent variables to explain the covariance between variables. Instead, network analysis assumes that nodes interact with and reinforce one another (Borsboom & Cramer, 2013; Cramer et al., 2010). In other words, network analysis of symptomatology treats symptoms not as a measurement of a disorder, but rather as part of the disorder itself (i.e., the network is the disorder). Thus, the use of network analysis to examine interrelationships between psychosocial conditions in the context of a syndemic is conceptually analogous to examining symptom—disorder interrelationships. Indeed, given syndemic theory, the concept in network analysis that nodes are mutually interacting and reinforcing is statistically appropriate for examining interrelationships between syndemic conditions.

Proposed Study

Taken together, research to date on the relationship between syndemic conditions and HIV acquisition risk among MSM has provided evidence for many questions, but has also raised and left many others largely unanswered. As previously mentioned, cross-sectional studies among MSM have generally shown a positive association between number of psychosocial syndemic conditions and HIV acquisition risk behavior or odds of being HIV-positive. Although causality and temporality cannot be determined, these cross-sectional studies have used additive models to examine the relationship between number of syndemic conditions and HIV acquisition risk. This relationship, though, appears to be more nuanced, and evidence of the synergistic effects of syndemic conditions has also been demonstrated by a non-linear relationship between increases in numbers of syndemic conditions and increases in HIV acquisition risk behavior or the likelihood of being HIV-positive. In addition, although limited in number, longitudinal

studies among MSM have also shown increasing odds of HIV incidence and of engaging in condomless anal sex for those with greater numbers of syndemic conditions. These longitudinal studies also begin to address the risk associated with specific syndemic conditions, identifying a substance use-related syndemic condition, specifically stimulant use, as an important factor contributing to increased risk. Moreover, research has also investigated clusters or classes of syndemic conditions. These clusters have been theoretically derived, not empirically, and classes have divided differences in risk not by specific conditions or patterns of conditions, but rather by the number of conditions, which further replicated the additive work of cross-sectional studies. To date, there is a paucity of research on which specific syndemic conditions are most related to increased HIV acquisition risk, which are most related to one another, and subsequently which often appear to cluster together in the context of syndemic conditions to increase risk.

As a first step, further research is needed to examine the interrelationships between psychosocial syndemic conditions. Therefore, the aims of the present study, presented below, will be examined. As these aims are all exploratory, *a priori* hypotheses will not be tested.

Aim 1: To examine correlations between psychosocial syndemic conditions.

Aim 2: To compare network analysis to exploratory factor analysis (EFA) for examining interrelationships of psychosocial syndemic conditions.

Aim 3: To explore the interrelationships between psychosocial syndemic conditions using network analysis. In order to investigate this aim, direct and indirect relationships between psychosocial conditions will be examined, as will the *node strength* centrality index.

The three types of analyses outlined above (i.e., correlations, EFA, and network analysis) provide similar, yet unique, information. Correlations will provide information on the strength and statistical significance of associations, allowing for preliminary examination of the interrelationships between syndemic conditions. EFA will examine for factor structure solutions, which determine the number of different latent factors among the interrelationships between syndemic conditions. In addition to a number of factors, EFA also provides information regarding which syndemic conditions better fit into a given factor and are more closely related. Lastly, network analysis, which utilizes the correlation matrix generated in the preliminary analyses, provides a graphical representation of the interrelationships between syndemic conditions. This graphical representation is interpretable, as it contains information on the strength of relationships via both edge weight and darkness as well as location. In other words, because the closer together two nodes are, the stronger the association is between the two, network analysis contains a sort of geography such that the location of one node in relation to another is important information. Additionally, network analysis also provides indices of centrality, which provide measures of the degree to which a node influences other relationships in the network. Overall correlation, EFA, and network analysis provide complementary information that each distinctly and uniquely add to the understanding of the interrelationships between syndemic conditions.

Chapter 2: Method

Participants and Procedures

Data for the present study were from the baseline visit of a longitudinal study that sought to identify acute HIV infections via frequent at-home HIV testing as described elsewhere (Blashill et al., 2016). Eligible participants were: 18 years or older, assigned male sex at birth, HIV-negative, and self-reported behaviors that would place them at high risk of acquiring HIV. Individuals were considered at high HIV acquisition risk if, in the past 6 months, they had condomless anal sex with an HIV-positive or unknown status male partner, had anal intercourse with 4 or more different male partners, had a sexually transmitted infection (STI) and intercourse with a male partner, or engaged in the exchange of money, shelter, drugs, or gifts for anal intercourse with a male partner.

Participants were ineligible if they were currently using or planning to use pre-exposure prophylaxis (PrEP) to reduce the likelihood of HIV acquisition, or were currently or had previously participated in an HIV vaccine trial and received the vaccination. In order to participate, eligible participants completed an informed consent process at the beginning of the baseline visit. All study procedures were approved and reviewed by the institutional review board at Fenway Health.

Interested individuals engaged in a pre-consent screening procedure to assess potential eligibility. Those who may be eligible were invited to complete a baseline visit, at which they completed computer assisted self-interview (CASI) self-report questionnaires as well as HIV voluntary counseling and testing.

Measures

Suicidal ideation. Suicidal ideation was measured via 1 item from the 9-item depression severity scale of the Patient Health Questionnaire (PHQ-9; Spitzer, Kroenke, Williams, & the Patient Health Questionnaire Primary Care Study Group, 1999). Responses were indicated on a 4-point Likert-type scale from 0 (*not at all*) to 3 (*nearly every day*). However, due to a low prevalence of any suicidal ideation, responses indicating any suicidal ideation, were combined and recoded as 1 (*at least several days*). Responses were then retained as a dichotomous measure of presence of any suicidal ideation in the past 2 weeks.

Depression. Depression was assessed using the other 8 items from the PHQ-9 (Spitzer et al., 1999). Participants indicated responses to items regarding frequency of experiencing different depressive symptoms in the past 2 weeks. Item responses were made using a 4-point Likert-type scale from 0 (*not at all*) to 3 (*nearly every day*). Responses were summed to create a continuous score of depressive symptoms, with higher numbers indicating increased depressive symptoms.

Social anxiety. Social anxiety was assessed using the 17-item Social Phobia Inventory (Connor et al., 2000), which measures severity of social anxiety symptoms. Participants indicated the severity using a 5-point Likert-type scale from 0 (*not at all*) to 4 (*extremely*). Responses were summed, resulting in a continuous score of the severity of social anxiety symptoms.

Sexual compulsivity. Sexual compulsivity, defined as an individual's ability to control sexual thoughts and behaviors, was measured via the 10-item Kalichman Sexual Compulsivity Scale (Kalichman et al., 1994). Responses were indicated on a 4-point

Likert-type scale in which responses range from 1 (*not at all like me*) to 4 (*very much like me*). Responses were summed to create a continuous score of the likelihood of sexual compulsivity, with higher scores corresponding to increased likelihood.

Substance use. Substance use was assessed using a 1-item novel measure of frequency of use in the past 3 months for each of the following substances: methamphetamine, cocaine or crack, other stimulants, opiates, hallucinogens, phencyclidine or ketamine, tranquilizers or sedatives or hypnotics, poppers, other inhalants, and any other substance. Participants indicated the frequency of use of each substance on a 6-point Likert-type scale from 0 (*didn't use*) to 5 (*several times a day*). Responses indicating at least once daily use (i.e., 4 [*about once a day*] and 5 [*several times a day*]) were combined. Also, across substances, only the maximum value for frequency of use of any substance was retained, resulting in one 5-point categorical measure of frequency of substance use in the past 3 months, such that increasing values indicate increasing frequency of substance use.

Injection drug use. Injection drug use (IDU) was measured using a 1-item novel measure of frequency of use via injection in the past 3 months for each of the following substances: methamphetamine, cocaine or crack, other stimulants, opiates, phencyclidine or ketamine, and any other injected substance. Participants indicated the frequency of IDU of each substance on a 6-point Likert-type scale from 0 (*didn't use*) to 5 (*several times a day*). Responses indicating a frequency of at least once per week were combined. Only responses for the most frequently used substance were retained, creating one 3-point categorical measure of the frequency of IDU in the past 3 months. Larger values correspond to more frequent IDU.

Heavy drinking. Heavy drinking, defined as 5 or more drinks on one occasion, was assessed using a 1-item novel measure of frequency in the past 3 months. Participants indicated the frequency of engaging in heavy drinking on a 6-point Likert-type scale from 0 (*didn't use*) to 5 (*several times a day*). Responses indicating heavy drinking several times per week or daily were combined. Responses were retained as a 4-point categorical measure of frequency of heavy drinking in the past 3 months, such that increasing values indicate increasing frequency of heavy drinking.

Childhood sexual abuse. Childhood sexual abuse (CSA) was measured via a 3-item measure that assesses for the experience of various events as a child, following the Finkelhor definition (Finkelhor, 1994). Items assessed for a history of ever having a wanted or unwanted, with or without contact, sexual experience with an individual 5 years older or more when 12 years old or younger, and/or, with an individual 10 years older or more when 13-16 years old (Lenderking et al., 1997). Endorsement of any of these items was retained as a dichotomous measure of presence of CSA.

Intimate partner violence. Intimate partner violence (IPV) was assessed using a 4-item measure, which was adapted from a measure used in the HPTN061 study (Williams et al., 2015). Participants indicated responses to items assessing frequency of having experienced stalking, emotional, physical, and/or sexual abuse from an intimate partner on a 5-point Likert-type scale from 0 (*No*) to 4 (*Yes, this always happened*). Responses indicating a frequency of *often* or *always* were combined and the maximum value for frequency of IPV of any type was retained. A 4-point categorical measure of IPV was retained and higher scores indicated greater frequency.

Statistical Analysis Plan

All analyses were conducted in R, version 3.3.2 (R Development Core Team, 2016). The following packages were used in analyses: qgraph (Epskamp et al., 2017), ggplot2 (Wickham & Chang, 2016), dplyr (Wickham, Francois, Henry, & Müller, 2017), mgm (Haslbeck, 2017), bootnet (Fried, 2017), NetworkComparisonTest (C. D. van Borkulo & Millner, 2016), IsingFit (C. van Borkulo, Epskamp, & Robitzsch, 2016), readr (Wickham, Hester, & Francois, 2017), polycor (Fox, 2016), foreign (R Core Team et al., 2017), stats (R Development Core Team, 2016), magrittr (Bache & Wickham, 2014), psych (Falissard, 2012), nFactors (Raiche & Magis, 2011), sem (Fox et al., 2017), psych (Revelle, 2018), GPArotation (Bernaards & Jennrich, 2014), and Hmisc (Harrell Jr., 2018).

Preliminary analyses. Correlations between syndemics were computed first. Polychoric correlations were employed to estimate associations between psychosocial syndemic conditions. Polychoric correlations are appropriate when examining relationships between dichotomous variables, categorical variables, and mixed data in which one or more variables is categorical (Holgado-Tello, Chacón-Moscoso, Barbero-García, & Vila-Abad, 2010). Correlations were tested for statistical significance.

Exploratory factor analyses. EFA was conducted to examine potential factor structure solutions for these psychosocial syndemic conditions. An oblique rotation (promax) was used to examine these data because oblique rotations allow for investigation of correlation between factors, whereas orthogonal rotations do not allow for such correlation (Costello & Osborne, 2005; Kline, 2011). Given the synergistic nature of syndemic conditions, as specified in syndemic theory, it was assumed that

factors may be correlated. Additionally, as there are a number of methods for determining which factor solution to choose (Ledesma & Valero-Mora, 2007), several different methods for evaluating factor solutions were employed: Horn's (1965) parallel analysis, which suggests a number of factors for a solution based on the number of components with eigenvalues greater than that of the parallel analysis; the number of factors at which the scree plot of the eigenvalues elbows (Cattell, 1966); and Kaiser's (1960) rule, which suggests a factor solution given the number of eigenvalues greater than one.

Consideration was given to following the EFA with a confirmatory factor analysis (CFA). However, in the ideal scenario, if a clear EFA solution emerged, conducting a CFA would involve collecting new data and conducting the CFA using this new sample (Kline, 2011).

Network analysis. In the network analysis of the present study, edges represent bidirectional partial polychoric correlations between nodes, which represent psychosocial syndemic conditions. Partial polychoric correlations were employed to investigate edges that may provide evidence for potential direct causal relationships between syndemic conditions because partial polychoric correlations statistically control for all other syndemic conditions in the network, thus resulting in information about only the relationship between two syndemic conditions that remains after such statistical control is applied (Borsboom & Cramer, 2013). In addition, the use of partial polychoric correlations allows for investigation of edges in the network that may indicate information regarding possible direct causal relationships (Borsboom & Cramer, 2013). The exploratory, regularized, partial polychoric correlation network analysis utilized the graphical LASSO (glasso algorithm; Mazumder & Hastie, 2012), as well as an Extended

Bayesian Information Criteria (eBIC) hyperparameter of $\gamma=.5$ to produce a graphically parsimonious yet sensitive network (Epskamp & Fried, 2016). Employing glasso regularization and setting the eBIC hyperparameter to $\gamma=.5$ produces a network with higher specificity (i.e., fewer spurious connections are estimated) and higher sensitivity (i.e., fewer true connections are estimated), as compared with a smaller hyperparameter (e.g., .1 or 0; Epskamp & Fried, 2016). Edge weight significance testing was determined by examining the 95% confidence intervals, which were estimated using bootstrapping techniques. The network was also examined for clusters of disorders. In addition, as *node strength* is the main indicator of centrality, it was examined to determine the most central nodes.

Missing Data. On measures in which 75% or more of the data were present, the average score for items with responses was calculated and multiplied by the total number of items in that measure to calculate an imputed total score. If data were missing for more than 25% of items on a measure, that measure was considered missing. There were 10 cases for which the total score for the measure of social anxiety was imputed. With respect to missing data that could not be imputed, there was one case for the measure of social anxiety and two cases for the measure of suicidal ideation that were considered missing and excluded from the analyses.

Chapter 3: Results

Descriptive Statistics (Table 1)

Participants were 197 men with available baseline data. However, 194 cases were used in the analyses, as there were no missing data on the measures of syndemics for these individuals. The average age of the participants was 36.6 (SD = 11.64). With respect to race, participants were predominately White (71.6%), and the next largest racial group in the sample was Black/African-American (20.6%). Additional participant characteristics are presented in Table 1, as are descriptive statistics for the syndemics. For example, the mean depression score was 4.26 (SD = 5.16) and the mean social anxiety score was 11.32 (SD = 12.75). The majority of participants had no suicidal ideation in the past 2 weeks (90.2%) and had no IDU in the past 3 months (90.2%). Additionally, many participants had no substance use in the past 3 months (45.9%), though most had used substances in the past 3 months with varying frequencies (see Table 1).

Preliminary Analyses: Correlations (Table 2)

We first computed polychoric correlations between syndemics. Polychoric correlations were employed to estimate associations between dichotomous variables, categorical variables, and mixed data in which one or more variables is categorical (Holgado-Tello et al., 2010). The polychoric correlation matrix is presented in Table 2, revealing multiple significant correlations between the syndemic conditions. For example, there were large correlations between suicidal ideation and IDU, suicidal ideation and depression, depression and social anxiety, suicidal ideation and social anxiety, as well as IDU and substance use. However, not all syndemics were correlated.

For example, CSA was only correlated with depression, and of low magnitude, and with substance use. Similarly, heavy drinking was only correlated with substance use.

Exploratory Factor Analyses (Table 3)

Overall, factor analyses revealed the 1-factor solution as the only admissible option for the factor solution. Given the number of methods for determining the factor solution to choose, other factor solutions were examined. In Horn's (1965) parallel analysis, correlation matrices were generated from randomly selected variables from the observed data, and these correlation matrices were used to generate average eigenvalues. The average random eigenvalues were compared to the observed eigenvalues, and parallel analysis suggests that factor solutions with observed eigenvalues that are greater than the randomly generated eigenvalues should be retained (Hayton, Allen, & Scarpello, 2004). Results of the parallel analysis suggested only the 1-factor solution as a potential choice, as the first component had an observed eigenvalue greater than that of the parallel analysis (see Figure 1), but the second component did not (Ledesma & Valero-Mora, 2007). However, the scree plot of the eigenvalues (Figure 1) elbowed at two factors, suggesting both the 1- and 2-factor solutions as potential choices (Cattell, 1966; Ledesma & Valero-Mora, 2007), with two factors as the maximum number of components that should be retained (Ledesma, Valero-Mora, & Macbeth, 2015). Although examination of the scree plot suggested that the 2-factor solution was a potential choice, the 2-factor solution was inadmissible because it contained a factor loading greater than 1.0 with uniqueness near zero (Kline, 2011). In contrast, per Kaiser's (1960) rule, there were three eigenvalues greater than 1.0, suggesting the 3-factor solution as an additional potential choice. However, the 3-factor solution was also inadmissible due to a factor loading

greater than 1.0 with uniqueness near zero. Given the inadmissibility of the 2- and 3-factor solution, despite the suggestion that they may be potential options, only the 1-factor solution is presented. The full 1-factor solution is shown in Table 3. However, for clarity, only factor loadings with an absolute value $\geq .30$ are reported in text (Costello & Osborne, 2005).

The 1-factor solution yielded a factor that suggests substantial loading onto one factor for many of the syndemics, but several were not included. Specifically, the 1-factor solution returned a factor consisting of substantial loadings ($\geq .30$) for suicidal ideation, IDU, depression, social anxiety, IPV, substance use, and sexual compulsivity, which accounted for 28.1% of the total variance. Heavy drinking and CSA did not have substantial loadings in the 1-factor solution. Accordingly, this factor solution does not yield much information about how different syndemics might be associated with each other.

Network Analysis (Figure 2)

The results of the network analysis are depicted in Figure 2, which revealed a pattern of interconnectedness among syndemic conditions. In the current network analysis, as previously stated, edges represent bidirectional partial polychoric correlations between syndemics. Overall, 24 edges are represented in the network out of a total of 36 possible edges. Thus, the network appears relatively dense. No clusters of syndemics were apparent, as eight of the nine nodes each have four or more edges. Significance of edge weights was determined by evaluating the bootstrapped 95% confidence intervals, and those 95% confidence intervals that did not contain zero were considered to be significant (95% confidence intervals for all edges are presented in Figure 3). The results

of the network analysis suggest four specific significant positive bivariate associations (absolute edge weights) between syndemics: suicidal ideation—IDU ($b=.52$, $SD=.22$, 95% CI[.17, .93]), IDU—substance use ($b=.41$, $SD=.18$, 95% CI[.18, .85]), social anxiety—suicidal ideation ($b=.30$, $SD=.36$, 95% CI[.06, .77]), and depression—suicidal ideation ($b=.27$, $SD=.14$, 95% CI[.05, .62]). With respect to the 20 non-significant non-zero edges represented in the network, because the estimation using an (eBIC) hyperparameter of $\gamma=.5$ ¹ is designed to obtain a sparse solution, non-significant edges do not necessarily indicate that these relationships are not present. In contrast, the evidence suggests that the edges not represented in the network were not present in this sample.

In addition to the graphical representation of the network, we also computed centrality measures (depicted in Figure 4). Correlations between the three measures of centrality (i.e., betweenness, closeness, and strength) were computed. Results suggest that correlations between centrality measures were highly correlated: strength and closeness ($r = .93$), strength and betweenness ($r = .91$), and closeness and betweenness ($r = .91$). As all three measures of centrality (i.e., betweenness, closeness, and strength) were highly correlated and generally followed a similar pattern in the current analysis, and as node strength is the primary measure of centrality, the node strength index was used to identify the most central nodes. Accordingly, the results of the node strength centrality measure

¹ A hyperparameter of $\gamma=.5$ was employed to produce a network with higher specificity and sensitivity than that of a smaller hyperparameter, such as .25 or .1. Sensitivity analyses using hyperparameters of $\gamma=.25$ and $\gamma=.1$ were conducted, though are not reported here, to determine the appropriateness of a hyperparameter of $\gamma=.5$. Network analyses using hyperparameters of $\gamma=.25$ and $\gamma=.1$ revealed a pattern of results that were not ostensibly different than that of the network analysis presented in the current study, using a hyperparameter of $\gamma=.5$. Because the hyperparameter of $\gamma=.5$ is more a conservative estimate than that of smaller hyperparameters, and the pattern of results between all three hyperparameters tested were nearly identical, the network analysis using a hyperparameter of $\gamma=.5$ is presented to produce a network with higher specificity and sensitivity.

suggest that suicidal ideation, IDU, substance use, and depression were the most central nodes. However, none of these nodes were significantly more central than the others (all 95% CIs crossed zero).

Chapter 4: Discussion

The present study is the first to examine interrelationships between syndemic conditions, comparing network analysis to EFA. The results suggest that network analysis is a feasible approach to investigate interrelationships among syndemic conditions. Whereas EFA reveals latent variables, of which observed variables (indicators) are measures (Kline, 2011), network analysis treats observed variables (nodes) as interacting and reinforcing elements of the overarching concept that is examined (Borsboom & Cramer, 2013; Cramer et al., 2010). In other words, in the present study, network analysis examines psychosocial conditions as aspects of a syndemic that interact with and reinforce one another, rather than measures of a syndemic, as is the case in EFA. Given this difference in assumptions underlying the two approaches, network analysis may be more consistent with syndemic theory and a more methodologically preferable approach than EFA for examining patterns of interrelationships among psychosocial conditions that comprise a syndemic. The syndemic conditions included in the present study were psychosocial problems that theoretically could be related to one another and/or related to poor health behavior that were selected from available data. Indeed, the results of the present study demonstrate the feasibility of network analysis to examine psychosocial syndemic conditions and provide more information than EFA regarding the interrelationships of these conditions.

Four significant partial polychoric correlations between psychosocial syndemic conditions were revealed in the network analysis (Figure 2). Significant edges were found between depression and suicidal ideation, social anxiety and suicidal ideation, suicidal ideation and IDU, as well as IDU and substance use, all of which were positive

associations. The positive association between IDU and non-intravenous substance use was not unexpected given the theoretical overlap between non-intravenous substance use and IDU, as well as the overlap evidenced in these data, which showed that 18 of the 19 (9.3% and 9.8% of the sample, respectively) participants in this sample who engaged in IDU also engaged in non-injection substance use in the past 3 months. Similarly, the positive relationship found between depression and suicidal ideation is consistent with depressive symptomatology, as suicidal ideation is a symptom of depression (American Psychiatric Association, 2013). Therefore, one would expect a positive association between the eight other symptoms of depression, as measured in the depression node, and suicidal ideation to be present in the current network analysis. Suicidal ideation was included in the network as a separate node due to its clinical importance and severity.

Two significant positive edges were also identified between suicidal ideation and other psychosocial conditions (i.e., IDU and social anxiety). However, a relationship between depression and IDU was not found in this network, and the relationship between depression and social anxiety did not reach statistical significance, which may suggest that suicidal ideation should be examined separately. The positive association found between suicidal ideation and social anxiety is consistent with previous research on the relationship between social anxiety, as well as other anxiety disorders, and suicidal ideation. Specifically, social anxiety was found to be related to Joiner's (2005) concept of thwarted belongingness (Davidson, Wingate, Grant, Judah, & Mills, 2011), and anxiety disorders more broadly, including social anxiety, were found to be a risk factor for suicidal ideation (Sareen et al., 2005). Similarly, the positive association identified between suicidal ideation and IDU is also consistent with extant literature. Suicidal

ideation was found to be a risk factor for IDU (Fuller et al., 2002; Miller, Strathdee, Kerr, Li, & Wood, 2006), and those who engage in IDU were more likely to report suicidal ideation compared to those who do not (Havens, Sherman, Sapun, & Strathdee, 2006). Suicidal ideation and IDU may have a significant relationship due to the common feature of escape behavior that underlies both IDU and suicide. Indeed, the relationship between IDU and suicidal ideation was the strongest significant edge in this network analysis ($b=.52$).

Network analysis not only provides empirical information regarding relationships between nodes, but also provides information on centrality, a measure of how interconnected nodes are in the network (Figure 3). Results of the network analysis revealed that the four most central nodes, according to their relative *node strength*, were suicidal ideation, then IDU, followed by non-intravenous substance use, and then depression. In the current network analysis, suicidal ideation appeared to be the node with the greatest relative interconnectedness. In addition, suicidal ideation and IDU were the nodes with the strongest relationship in the network analysis, and with the two highest centralities, despite having relatively low base rates compared to other nodes in the network (Table 1). Notably, suicidal ideation had three significant edges with other nodes, despite only 19 (9.8%) participants endorsing having experienced any suicidal ideation in the past two weeks. Similarly, IDU also evidenced a base rate of only 19 (9.8%) participants in the past 3 months. The strong relationship found between suicidal ideation and IDU, as well as the high degree of centrality for both, despite both nodes having relatively low base rates, indicates that although fairly uncommon, both suicidal ideation and IDU may have important down-stream effects on other syndemic conditions.

In addition, as this sample was comprised of MSM at high risk for HIV, suicidal ideation and IDU may also have implications for HIV acquisition risk behavior.

Given the cross-sectional nature of the present study, examination of temporality and causality is not possible. However, the significant positive relationships between suicidal ideation and depression, social anxiety, and IDU suggest that suicidal ideation may be an important psychosocial condition in the HIV syndemic among high-risk, HIV-negative MSM. Suicidal ideation is of obvious clinical importance, though the relationships found in the present study suggest that, among a sample of high-risk, HIV-negative MSM, the presence of suicidal ideation may indicate additional psychopathology beyond depression, such as a social anxiety or IDU. And, conversely, clinicians working with this population should be aware of the potential for suicidal ideation among those with IDU or social anxiety, even in the absence of comorbid depression.

Recent research points out that centrality should be interpreted with caution (Fried et al., 2018). A node has high centrality in a cross-sectional network because it has a relatively large total weight of undirected associations, and although high centrality may suggest that a node is clinically important, merely being highly central is not sufficient to conclude that a node should be a target of intervention (Fried et al., 2018). In other words, nodes with high centrality may provide further evidence, in the context of extant literature, that a specific node may be a relevant intervention target but should not be taken as the sole evidence for clinical importance. However, in the present study, the four nodes with the highest centrality (i.e., suicidal ideation, IDU, substance use, and depression) are indeed all highly clinically relevant psychosocial conditions and/or have

been shown to be related to HIV risk among MSM (e.g., Koblin et al., 2006; Safren, Reisner, Herrick, Mimiaga, & Stall, 2010; Stall et al., 2003; Strathdee & Sherman, 2003). Given both the extant literature on IDU, non-intravenous substance use, and depression and suicidal ideation, as well as the findings of the current network analysis that suggest the high degree of interconnectedness of these psychosocial syndemic conditions with the other conditions in the network that comprise a syndemic, suicidal ideation, IDU, substance use, and depression may be important targets of intervention for syndemics among high-risk, HIV-negative MSM.

Notably, the pattern of interrelationships found in this network analysis may be different in other samples, and is indeed different from the pattern of interrelatedness found in a sample of young Latino MSM in Southern California (Lee et al., Under Review). However, among the current sample, the significant edges in this network, in the context of the low base rate of suicidal ideation and IDU, suggest that, when present in an individual, suicidal ideation and IDU may have important relationships with other syndemic psychosocial conditions. Suicidal ideation and IDU are severe presentations of depression and substance use, and therefore may be especially important intervention targets, in addition to depression and non-intravenous substance use, to reduce the effects of syndemics on HIV acquisition risk.

Another noteworthy feature of the network analysis are the non-significant non-zero edges that were found. Edges that are depicted in the network (Figure 2) are non-zero edges. However, as previously discussed, only four edges reached statistical significance. The remaining 20 edges in this network analysis did not achieve statistical significance due to a 95% confidence interval that contained zero. However, in a

regularized network, as in the current network analysis, the conventional interpretation of a confidence interval is not applicable because the estimates in a regularized network have been penalized or “shrunk” (Fried & Haslbeck, 2018). Owing to this regularization of the network, parameter estimates are biased toward zero, and subsequently, the bootstrapped confidence intervals of these parameters are also biased toward zero. As such, there is some evidence that edges containing zero in the 95% confidence interval may still be present in the true network of these psychosocial syndemic conditions. A number of edges are depicted in the network (Figure 2) that contain zero in the bootstrapped 95% confidence intervals, which suggest that IPV, CSA, sexual compulsivity, and social anxiety may also have important interrelationships with other psychosocial syndemic conditions among high-risk HIV-negative MSM. However, future research is needed with larger sample sizes to further examine these associations.

In addition to the findings of the network analysis of the patterns of interrelationships among psychosocial syndemic conditions, the EFA revealed a 1-factor solution as the only admissible factor solution (Table 3). Based on the various methods for determining potential factor solutions, the 1-, 2-, and 3-factor solutions were examined. However, both the 2- and 3-factor solutions contained a factor loading greater than 1.0, with uniqueness near zero, rendering the 1-factor solution the only admissible solution. Upon further inspection, the 1-factor solution is not easily interpretable with respect to the relationships between psychosocial syndemic conditions. Of note, heavy drinking and CSA did not have substantial loadings ($< .30$), indicating they are weak measures of a syndemic in this sample. However, in the network analysis (Figure 2), CSA had a number of non-zero edges with other psychosocial syndemic conditions,

including with heavy drinking, and heavy drinking also appeared to have a relatively substantial, though non-significant, relationship with non-intravenous substance use. Additionally, among this high-risk HIV-negative sample of MSM, the findings that CSA and heavy drinking are not related are not consistent with prior research, which suggests that CSA (Mimiaga et al., 2009) and alcohol use (Woolf & Maisto, 2009) are related to increase HIV risk, as well as appear to be significantly related to other psychosocial syndemic conditions (e.g., Mimiaga et al., 2015; O’Cleirigh et al., 2018). Indeed, another network analysis of the relationships among psychosocial syndemic conditions and with condomless anal sex among Latino MSM found that alcohol use and CSA were significantly related, and alcohol use was also significantly related to condomless anal sex (Lee et al., Under Review).

Moreover, the 1-factor solution provides little information regarding the ways in which these psychosocial syndemic conditions are interrelated. Results of the EFA suggest that one latent variable created the association between the observed variables (Kline, 2011), but it is difficult to discern, from the EFA alone, the ways in which psychosocial syndemic conditions are related to one another, and which would be potentially important targets of intervention. However, it should be noted that there are some similarities between the results of the EFA and the network analysis.

Suicidal ideation followed by IDU were found to have the largest factor loadings in the EFA, and as stated previously, these were the two most central nodes and had the strongest significant relationship in the network analysis. Also, the four psychosocial syndemic conditions with the highest factor loadings were, in order, suicidal ideation, IDU, depression, and social anxiety, all three of which were significantly related to

suicidal ideation in the network analysis. Although these similarities appear to support the findings of the network analysis and the notion that network analysis is a feasible and theoretically appropriate statistical method for examining the patterns of interrelationships among psychosocial syndemic conditions, the information provided by the EFA would have been less meaningful outside of the context of the information provided by the network analysis. It is also notable that only the 1-factor solution was admissible in this EFA. Prior research using structural equation modeling (Mustanski et al., 2017), partitioned psychosocial syndemic conditions into theoretically-derived groups of conditions: mental health, violence, and substance use. However, the results of this EFA, which contained conditions in all three of those categories, suggest only that a 1-factor solution was most appropriate for these data. Future research is warranted to examine the number of latent variables that should be used to examine psychosocial structural syndemic conditions.

Additional research to replicate and extend these findings in other samples is warranted, as the patterns of interrelationships may be different among different samples and populations. Indeed, future research should also consider the intersectionality of minority status to examine the relationships between syndemic conditions across various risk groups and minority statuses (e.g., Bowleg, 2012). Given the use of network analysis to examine symptomatology of one or more conditions (Choi et al., 2017; Cramer et al., 2010; Epskamp & Fried, 2016; Rhemtulla et al., 2016), future research should also examine networks of each of the symptoms of syndemic conditions to better determine which symptoms may be important in the relationships between syndemic conditions. Future research should also investigate interaction effects of syndemics on HIV

acquisition risk behavior. Additionally, due to the significant associations and the relatively high degrees of centrality in the current network, additional research on the role of depression and specific depressive symptoms, such as suicidal ideation, on the interrelationships between syndemic conditions is needed. Similarly, the role of substance use, especially IDU, on these interrelationships also merits additional research. Also, given the prevalence of stimulant use in high-risk combinations of syndemic conditions, as discussed previously (Mimiaga, O’Cleirigh, et al., 2015), and the relative importance of IDU and non-intravenous substance use in the current network analysis, future research should examine the effects of stimulant use in syndemic effects on negative health behaviors. Lastly, future research should also examine causal relationships among syndemic conditions.

The present study was not without limitations. As this study was cross-sectional in design, the current analyses were not able to examine temporality and causality, and only associations were analyzed and discussed. However, the results of the present study suggest that network analysis is indeed a feasible methodology to examine interrelationships among syndemic conditions, and may be methodologically preferable to EFA. Additionally, this study investigated associations using self-reported data, which may introduce bias in reporting. Future research should attempt to utilize clinician-administered measures of syndemic conditions whenever possible to reduce such bias. Another limitation of the present study was sample size, and the study would have benefited from greater statistical power to detect associations. In addition, several dichotomous measures were used in these analyses. In the network analysis, dichotomous nodes with low base rates may not be as expected. Future research should also strive to

use categorical or continuous data whenever possible. Lastly, non-intravenous substance use and IDU were analyzed by examining the substance with the greatest frequency of use in the past 3 months. This methodology does not account for polysubstance use, nor any differences among substances.

In summary, the present study is one of the first network analyses, and the first to compare network analysis to EFA, to examine patterns of interrelationships among psychosocial syndemic conditions. The network analysis and EFA were conducted among a sample of high risk HIV-negative MSM. The results of the present study suggest that network analysis is statistically and theoretically appropriate for examining associations between psychosocial syndemic conditions, and may be methodologically preferable to EFA for such analyses. Results of the network analysis revealed four significant positive associations between depression and suicidal ideation, social anxiety and suicidal ideation, suicidal ideation and IDU, as well as IDU and substance use. Additionally, the network analysis suggested that suicidal ideation, IDU, non-intravenous substance use, and depression were the four most central nodes. These results were also compared to those of the EFA, which suggested that the 1-factor solution was the only admissible solution. In addition, several similarities were found between the EFA and the network analysis, suggesting that network analysis is indeed feasible and appropriate, and may provide more information on the pattern of interrelationships between syndemic conditions. Thus, the results of the present study suggest that symptoms of depression, especially suicidal ideation, as well as substance use, especially IDU, are particularly important psychosocial syndemics to investigate and intervene upon among high risk HIV-negative MSM.

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Figures

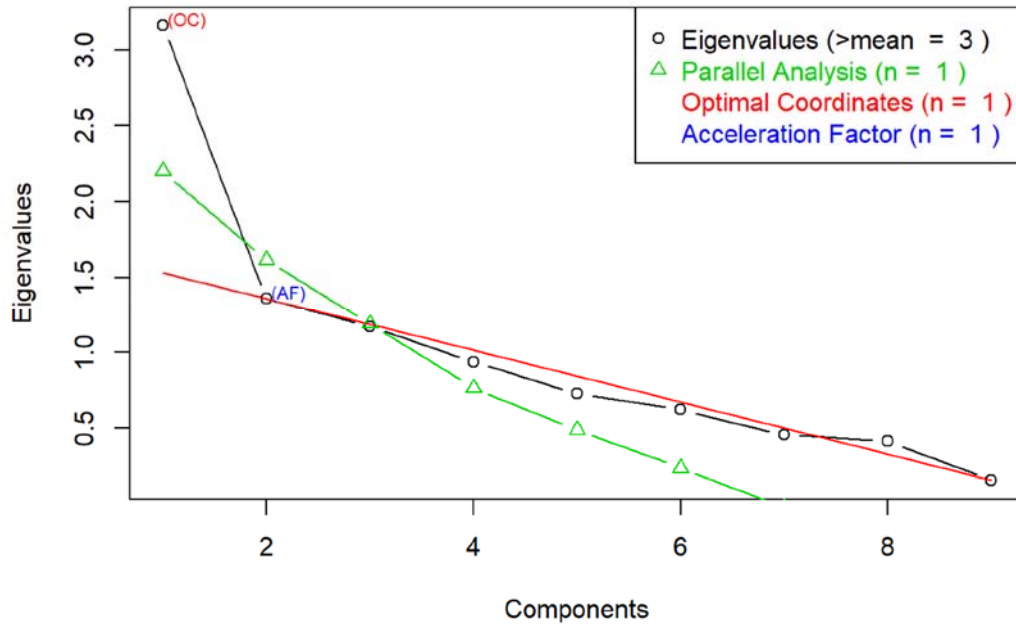


Figure 1. Exploratory factor analyses scree plot of the eigenvalues.

Note. The acceleration factor (AF), above in blue, indicates the point at which the scree plot elbows.

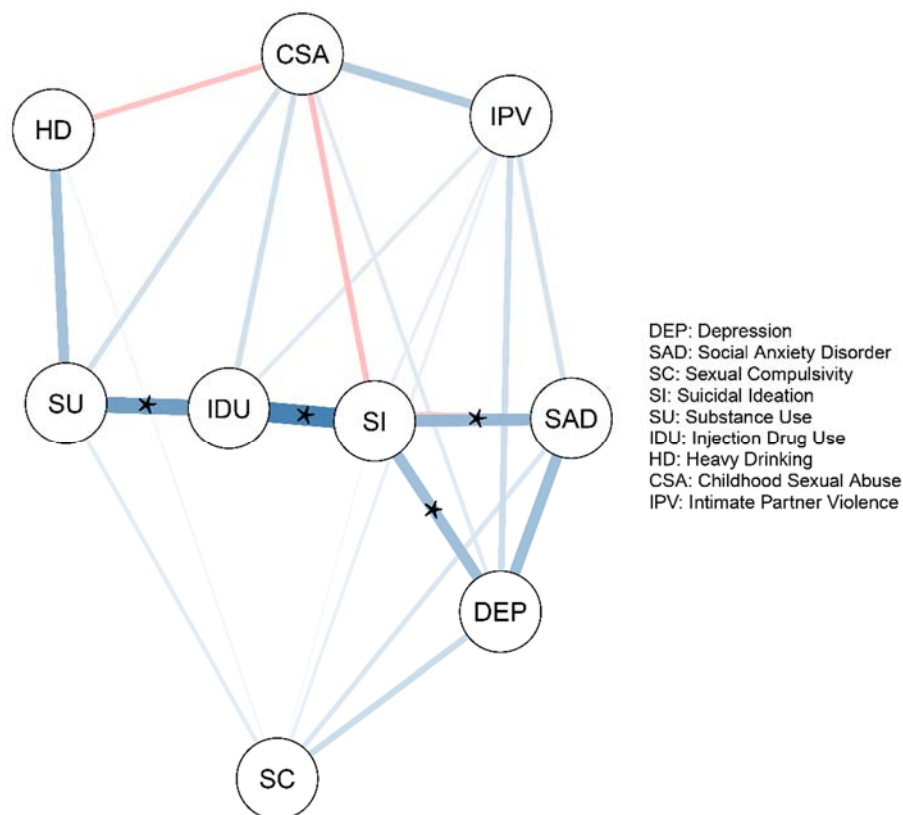


Figure 2. Network analysis of nine syndemic conditions.

Note. Blue edges represent positive associations, whereas red edges represent negative associations. Thicker and darker edges indicate stronger associations than do thinner and lighter edges. * Indicates a significant edge (pairwise association) between two nodes (i.e., SI—IDU, SU—IDU, SAD—SI, DEP—SI). For full node names, refer to the legend in the figure.

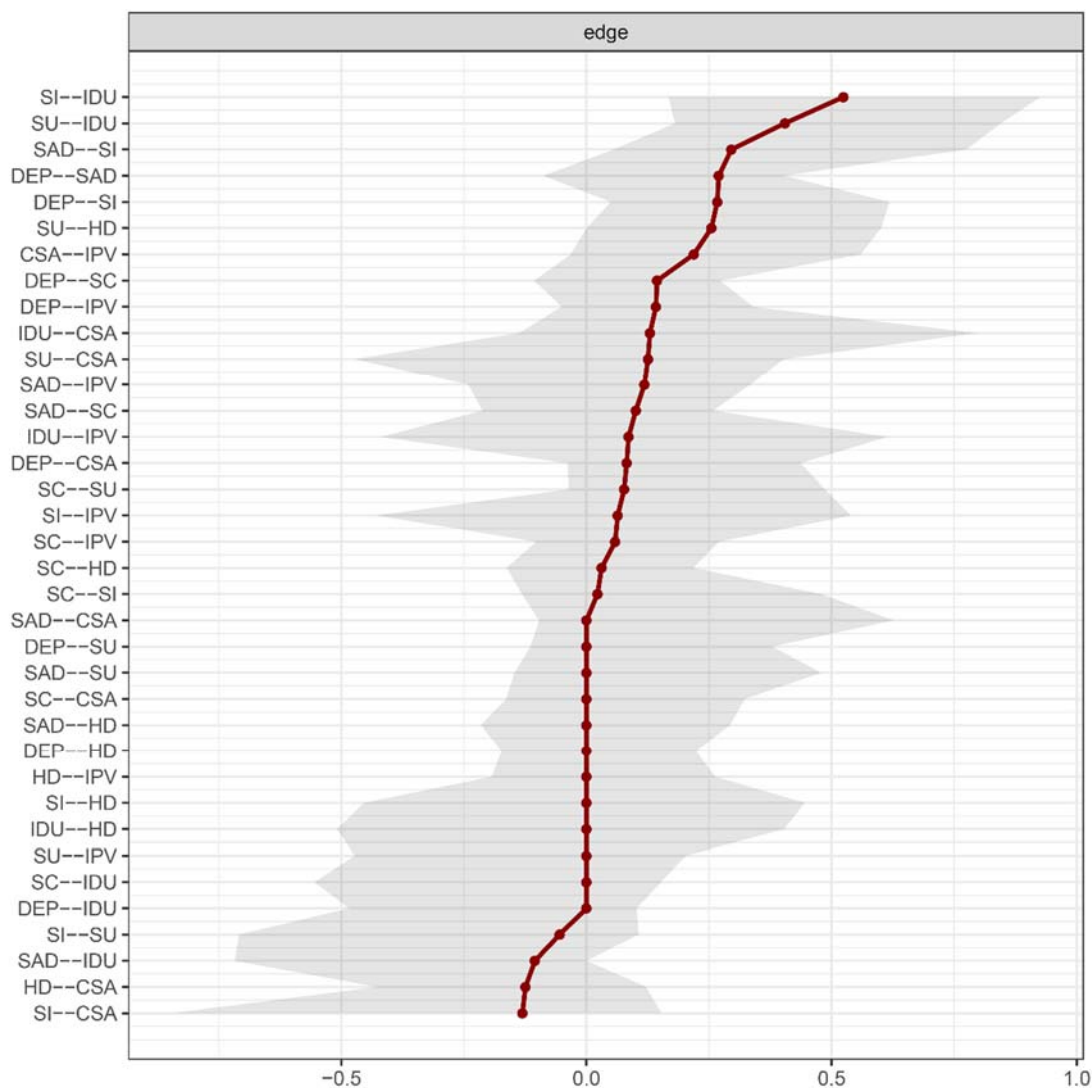


Figure 3. Parameter estimates and 95% confidence intervals for edges in the network.
Note. Red dots represent the parameter estimates of the edge weights. Grayed out areas represent the bootstrapped 95% confidence intervals for the edge weights. Full node names are: substance use (SU), suicidal ideation (SI), sexual compulsivity (SC), social anxiety (SAD), intimate partner violence (IPV), injection drug use (IDU), heavy drinking (HD), depression (DEP), childhood sexual abuse (CSA).

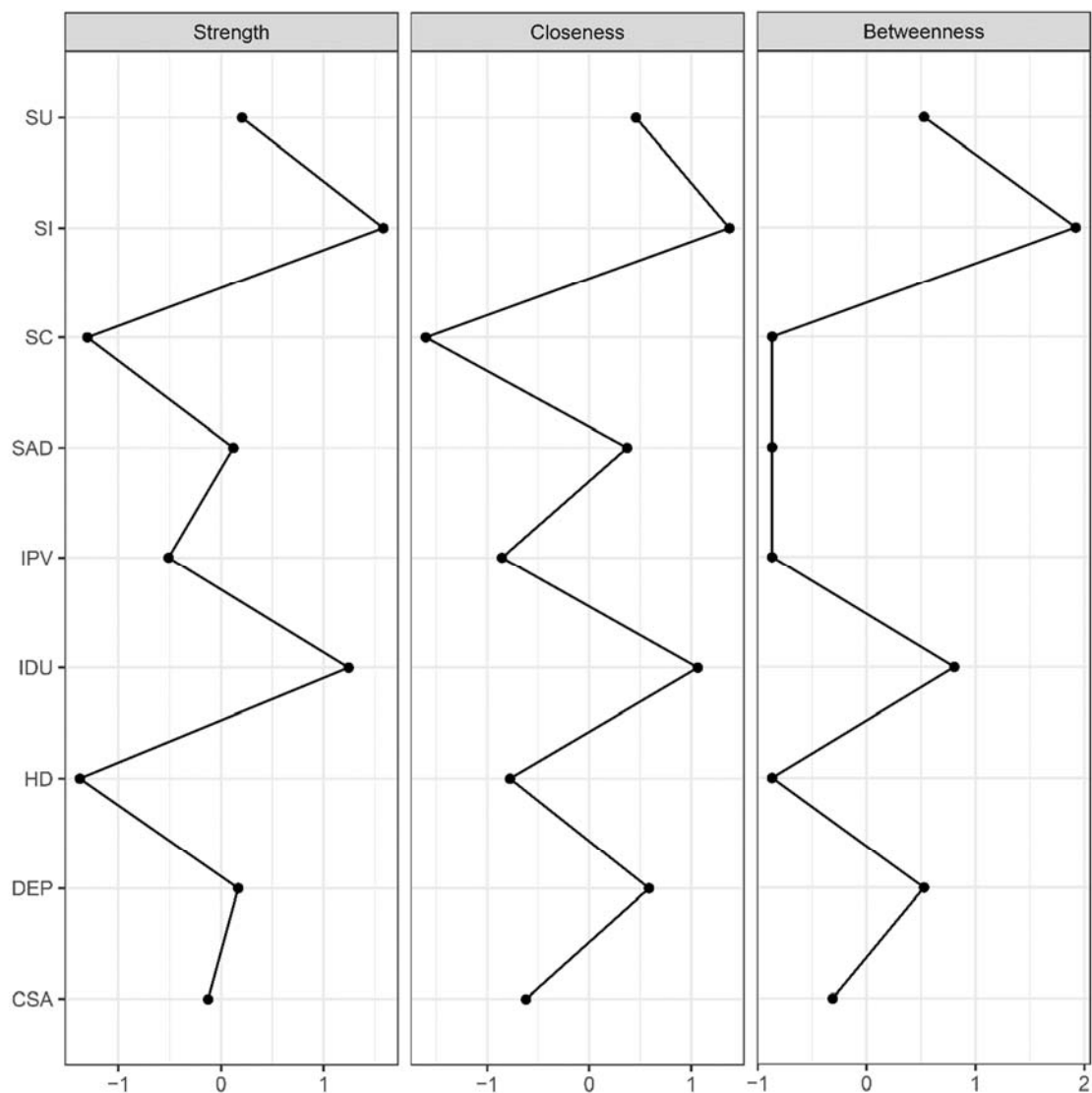


Figure 4. Centrality measures of each node in the network analysis.

Note. z-Scores are presented on the x-axis for each centrality measure. Full node names are: substance use (SU), suicidal ideation (SI), sexual compulsivity (SC), social anxiety (SAD), intimate partner violence (IPV), injection drug use (IDU), heavy drinking (HD), depression (DEP), childhood sexual abuse (CSA).

Tables

Table 1. *Descriptive Statistics*

Variable	Mean (SD) [Range]	Variable	Mean (SD) [Range]
Age	36.6 (11.64) [19 – 67]	Depression	4.26 (5.16) [0 – 24]
	<u>N (%)</u>	Social Anxiety	11.32 (12.75) [0 – 60]
Gender		Sexual Compulsivity	15.88 (5.52) [10 – 40]
Cisgender Male	190 (97.9%)		<u>N (%)</u>
Transgender	4 (2.1%)	Suicidal Ideation	
Sexual Orientation		Not at all	175 (90.2%)
Homosexual/Gay	151 (77.8%)	Several days or more	19 (9.8%)
Bisexual	35 (18.0%)	Substance Use	
Heterosexual/Straight	4 (2.1%)	Did not use	89 (45.9%)
Don't know	1 (0.5%)	Once a month or less	48 (24.7%)
Other	3 (1.5%)	About once a week	30 (15.5%)
Race ¹		Several times a week	16 (8.2%)
Asian	7 (3.6%)	Once a day or more	11 (5.7%)
Black/African-American	40 (20.6%)	Injection Drug Use	
White	139 (71.6%)	Did not use	175 (90.2%)
Alaskan Native/ American Indian	4 (2.1%)	Once a month or less	13 (6.7%)
Native Hawaiian/ Other Pacific	2 (1.0%)	Once a week or more	6 (3.1%)
Islander		Heavy Drinking	
Multi-racial/Other	6 (3.1%)	Did not use	77 (39.7%)
Ethnicity		Once a month or less	62 (32.0%)
Hispanic/Latino	29 (14.9%)	About once a week	38 (19.6%)
Non-Hispanic/Latino	165 (85.1%)	Once a week or more	17 (8.8%)
Education		Childhood Sexual Abuse	
High School Diploma or less	44 (27.7%)	No	117 (60.3%)
Some college or AA/ Vocational/Tech degree	70 (36.1%)	Yes	77 (39.7%)
4-year college degree or greater	79 (40.7%)	Intimate Partner Violence	
Missing data	1 (0.5%)	No	97 (50.0%)
Income		Yes, but this has rarely happened	49 (25.3%)
Less than \$10,000	53 (27.3%)	Yes, this has sometimes happened	30 (15.5%)
\$10,000-29,999	56 (28.9%)	Yes, this has happened often	18 (9.3%)
\$30,000-49,999	34 (17.5%)		
50,000 or more	50 (25.8%)		
Missing data	1 (0.5%)		

Note. ¹Totals for race may not equal 194 as participants could select more than one response option.

Table 2. *Polychoric Correlation Matrix*

	DEP	SAD	SC	SI	SU	IDU	HD	CSA	IPV
DEP	1	-	-	-	-	-	-	-	-
SAD	0.53***	1	-	-	-	-	-	-	-
SC	0.33***	0.29***	1	-	-	-	-	-	-
SI	0.56***	0.52***	0.27**	1	-	-	-	-	-
SU	0.18**	0.08	0.20**	0.23	1	-	-	-	-
IDU	0.30**	0.19	0.16	0.66***	0.55***	1	-	-	-
HD	0.04	0.04	0.11	0.04	0.32***	0.08	1	-	-
CSA	0.19*	0.13	0.10	0.04	0.25**	0.26	-0.11	1	-
IPV	0.39***	0.35***	0.23**	0.37**	0.14	0.34**	-0.01	0.32**	1

Note. Full variable names are: depression (DEP), social anxiety (SAD), sexual compulsivity (SC), suicidal ideation (SI), substance use (SU), injection drug use (IDU), heavy drinking (HD), childhood sexual abuse (CSA), intimate partner violence (IPV).

*** $p < .001$

** $.001 < p < .01$

* $.01 < p < .05$

Table 3. *Exploratory Factor Analyses Results*

Eigenvalues	3.156	1.357	1.174	.939	.728	.620	.456	.414	.157
	1-Factor Solution								
	<i>Factor 1 Loadings</i>								
	Suicidal Ideation	.849							
	Injection Drug Use	.687							
	Depression	.657							
	Social Anxiety	.583							
	Intimate Partner Violence	.498							
	Substance Use	.369							
	Sexual Compulsivity	.361							
	Childhood Sexual Abuse	.212							
	Heavy Drinking	.087							
	SS Loadings	2.531							
	Proportional Variance	.281							
	Degrees of Freedom	27							
	Model Fit	1.109							

Note. Factor loadings with an absolute value $\geq .30$ are presented in bold, corresponding to the factors reported in text.