

B. SIGNIFICANCE

1. Overview: Injection drug use continues to be a major risk factor for acquisition of HIV, the virus that causes AIDS. The Centers for Disease Control (CDC) reported that in the United States injection drug use directly or indirectly accounted for 36% of AIDS as of December, 1995. (1) Maryland AIDS cases attributed to injecting drug use is a major public health problem. The highest rates of IDU related AIDS cases continue to occur in the Northeast with 44% of the reported cases being from this region. (1) In Maryland, there are an estimated 50,000 IDUs of which approximately 35,000 - 45,000 reside in Baltimore city. The DAWN (Drug Abuse Warning Network) data for 1991-92 indicate that Baltimore was first in the nation for increases in heroin emergency room mentions and second for cocaine emergency room mentions. (2)

In Baltimore City, AIDS is the leading cause of death among persons aged 25-44 years. Recent studies indicate that the age groups with the most rapid increases in HIV infection are the adolescent and young adult populations. (3) The ALIVE study demonstrated a 9.7% seroprevalence rate among participants injecting 12 months or less between 18-25 years of age. (4) About 20% of those in treatment programs in Maryland indicated that their first noninjection use of cocaine and heroin occurred between the ages of 14 and 17. Another 30% initiated cocaine or heroin use between the ages of 18 and 21. Although treatment data may not be reflective of the entire drug using community, this data is compatible with increasing injection drug use in Maryland and a pattern of first cocaine and heroin use often occurring during adolescence and young adulthood. In fact, the ALIVE Study demonstrated the median age of initiating injection drug use to be 20 years old. (5) These disturbing trends in HIV infection coupled with the trends in injection practices and sexual behaviors among young people indicate the need for more intensive research in this population.

According to CDC, the proportion of cases among persons who reported injection drug use increased from 17% during 1981-1987 to 27% during 1993 to 1995.(6) Recent studies have shown that the risk of HIV infection among IDUs is high during the early stages of an injecting career (4,5,7,8,). It is hypothesized that at the first injection, 'harm reduction' measures such as using bleach to disinfect needles and syringes, may not be employed and residual blood in the needle or syringe used by the recent initiate may be contaminated with HIV. An association between injection drug use and sexual risk-taking also is possible.(9) This may lead to higher levels of unprotected sex among IDUs and increased exposure to HIV.

Data to document the risks associated with recent initiation into injecting drug use are sparse. It is speculated that a person will begin injecting drugs when sniffing, snorting or smoking the drug no longer provides the same high, as a result of pharmacologic tolerance or low potency of the street drug, or when the amount of drug needed to satisfy a dependency becomes expensive. **In this proposed study, risk factors instigating a young person to become an injector will be determined.** Ethnographic research has shown that IDUs will usually begin to inject within his/her own peer group. In fact, typically, a member of an individual's social group or a sexual partner will help an initiate inject drugs the first time. (10) This person will serve as the "teacher" and must prepare and inject the drug into the vein of the initiate. The role of the teacher in relation to the new injector, and the point of entry of the teacher into the initiates social network has not been well documented. Additionally, density of the social network, including the drug subnetwork, and family and /or partner membership of the social networks which has been important in studies of adult IDUs, has not been adequately examined in young adult initiates.

2. Established Correlates of HIV infection Across Cross-sectional Studies. Certain **injecting practices**, which increase opportunities for parenteral exposures to HIV, are strongly associated with HIV infection. For example, sharing of injection equipment, or frequency of injection, are important correlates of HIV infection.(11,12,13,14) Attending shooting galleries, clandestine spots where sharing with anonymous injecting partners can occur, is an independent risk factor across many studies. (12,14,15) Injecting cocaine and number of needle sharing partners are also associated with HIV infection.(11,16) One study found "booting" or "kicking" (when blood is drawn into the syringe and then injected) to be 2 to 3 times greater for both cocaine and speedball than heroin which may explain one mechanism contributing to cocaine's association with HIV infection (17). Some studies have found an association between 'frontloading' (i.e., one person will draw up liquefied drug into a potentially contaminated first syringe and inject half of the drug into the barrel of a second syringe) and risk of HIV whereas, others have not. (18,19,20).

Rates of HIV infection tend to differ by *duration of drug use*. Cross-sectional surveys noted rising seroprevalence by age with a leveling off after five to ten years of injecting drug use. (13,21) This suggests that HIV infection is related to cumulative exposure. Friedman also suggests that longer duration IDUs may circulate in injection networks that are at greater risk of HIV infection or that have an elevated seroprevalence. In contrast, Vlahov and colleagues noted a trend of higher seroprevalence among more recent initiates who persistently attended shooting galleries and who shared needles. (15) Data from

Milan, Amsterdam and Baltimore support Vlahov's findings that more recent initiates, defined as those injecting for less than 2 years, have higher seroincidence rates than longer duration IDUs. (7,8,3) Other factors associated with HIV infection among recent initiates **injecting** 12 months or less were *sexual variables* (men having sex with men, and never being married) and not high risk injecting variables. (4) This could possibly suggest a stronger effect of high-risk sexual practices on HIV infection than high-risk injection practices given the reduced chance of using a contaminated needle because of the shorter period of injection use among young recent initiates. Although this hypothesis has yet to be adequately explored, this proposal has the potential of elucidating such a linkage through comparisons of high-risk injection practices and high-risk sexual practices.

Early in the HIV epidemic, *heterosexual transmission* of HIV did not appear to be an important mode of infection among injecting drug users. (22) It was suspected that injection practices were the predominant source of viral transmission and heterosexual transmission could occur but at negligible rates. (23). However, more recent data indicate that sexual behaviors are correlated with HIV in IDUs, despite the fact that parenteral transmission is considered more efficient than heterosexual transmission. (12,24) Again, this may support the previous findings that recent initiates may have a higher risk of HIV infection primarily because of high-risk sexual practices and that high-risk injection practices may be secondary.

The phenomena of '*sex for money or drugs*' and '*survival sex*' are related to HIV transmission among IDUs. (25) Crack is a smokable form of cocaine that has a short half-life in the body. Its appearance on the streets resulted in an increase in sex for money or drugs behaviors. Because crack and injectable cocaine require many 'hits' each day, an addict may quickly develop an expensive habit, thus leading some to barter sex for the drug. (26). Several studies indicate that cocaine injection (11,16) and smoking crack cocaine (27,28,29,30) are independently associated with HIV infection. Ethnographic studies also indicate that drugs can affect one's sex drive differentially; cocaine and amphetamine use may act as sexual stimulants while heroin or opiate use may not enhance sexual desire. (31,32) **In this proposed study, an examination of trading sex and drug type used during the pre- and post-initiation period and how these events relate to HIV will be done.**

HIV seroprevalence has also been strongly associated with race/ethnicity in the United States. (12,33) The high odds ratios for Black or Hispanic groups reflects higher prevalence of HIV infection in such communities, and is usually considered to be due to unmeasured exposure opportunities rather than race/ethnicity *per se*. In one study, low income as a surrogate for socioeconomic status was also associated with HIV prevalence. (12)

3. Risk Factors for HIV Seroconversion: Incidence Data. Age is identified as a risk factor for HIV seroconversion. Nelson noted a two fold increase in seroincidence among younger drug users. (3) In Milan, a strong incidence rate ratio of 3.3, [95% CI (1.4-7.5)] was found in IDUs younger than 20 years compare to IDUs older than 20 years. Increased risk was also reported for those injecting for less than 2 years and those sharing syringes. (7) Considering that the median age of initiating injecting drug use is 20 years across different studies, age and duration of injecting drugs are probably highly correlated. Of particular interest in this proposal is not only why HIV incidence is high early after initiation of drug use, but why rates decline after the first couple of years of initiating drug use. One avenue to explore is the role of social networks over time - does network size and density (defined as the actual number of network ties among individuals in a social network divided by the number of ties) decrease as the injector becomes more experienced? **Is the social network that is established during the pre-initiation period predict a safe or unsafe injecting behavior?**

Solomon and colleagues (1993) conducted a nested case-control study of risk factors for HIV seroconversion among injecting drug users part of the ALIVE study in Baltimore. This analysis showed that seroconversion among females was only associated with having three or more sex partners [OR=5.11, 95%CI (1.62-16.1)], whereas, among males, seroconversion was associated both a history of syphilis and presence of an abscess **which is** a marker of risky injection, [OR=6.32, 95%CI (2.48-16.14)]. Solomon also noted an association between younger age and increased seroconversion and concluded that young age may be related to particularly risky behaviors engaged in during the first few injections or young age may simply be a marker for riskier sexual behavior. (25)

It is interesting to note that Solomon reported the presence of an abscess rather than sharing or attending shooting galleries as a drug use risk factor for HIV seroconversion. This may indicate that sharing and shooting gallery use become less important over time or that participants who are counseled of HIV risks, when enrolled in prospective studies, will under-report their high risk behavior. We will be sensitive to methodological issues such as validity of self-reports, as we have detailed elsewhere. (34)

The reported risk factors outlined above explain a portion of the trends in HIV acquisition among IDUs. However, new

risk correlates of HIV infection need to be explored to assess the differential trends in HIV prevalence and incidence by social network changes, previous or current abuse status, and mental health status among young initiates **and NIUs at risk of becoming injectors.**

4. Patterns of Transition and Initiation into Injecting Drug Use. In 1969, de Alarçon made an attempt to apply infectious disease epidemiology methods to the spread of heroin injection in a community. Recruiting all the injectors in an area, he identified the initiates and the "initiators" (we refer to initiators as "teachers"). Mapping the teachers as point sources of the injection outbreak over calendar time, network patterns of initiation emerged. The results showed that two individuals were central to the outbreak as they introduced heroin injection to the majority of the new injectors. Such patterns of initiation may exist today, but are very difficult to trace due to pervasiveness of **injection drug use** in certain communities. However, identification of trends in initiation and the roles of the teacher(s) will help in the development of public health interventions to reduce high risk first injection experiences.

a) The New Injecting Drug Users: New injectors have been defined in the literature by duration of injecting drugs. Various investigators have defined new users as having injected less than 2 years, less than 5 years and less than 10 years. These definitions have come about more for statistical purposes as opposed to a firm definition of a "new injector". Originally, it was assumed that new injectors would have lower HIV seroprevalence due to a shorter duration of exposure. It was hypothesized that they may be less likely to share injection equipment with older users preferring to share with primarily younger less experienced users. (21) Supporting this hypothesis, among street users in New York City, newer injectors were significantly less likely to rent (typically in a 'shooting gallery') previously used injection equipment. In contrast, in another study of street recruited injectors, Kleinman found that primarily the longer-term injectors were following harm reduction procedures to reduce their risk of HIV infection. (35) Of those who had been injecting for less than two years, only 16% had adopted harm reduction procedures while 66% of those injecting for more than 10 years had altered risky injection practices. (35) Among 421 IDUs reporting their first injection between 1982 and 1987, the use of sterile needles increased while both the proportion of those who always used equipment previously used by another and the number of needle-sharing partners decreased. (5)

The social dynamics surrounding the first injection are not well documented. Usually, a new IDU is introduced to injection by a friend or a relative. (21,36,37) This person may also be a sexual partner. Since the first injection may not be planned, the new injector does not usually have his/her own equipment and will borrow from the "teacher". Although there is little data characterizing the teacher, he/she may not be experiencing problems due to drug injection and may be relatively new to injection practices him/herself. (36) Newer injectors may continue to inject within their newer network and only slowly move into the networks of older injectors. Some speculate that this practice would protect them from HIV infection. However, as the newer groups mix with older users, their knowledge of the risks of HIV and AIDS increase, and they may begin to adopt safer injection practices despite the fact that they will have greater risks of exposure. (21) In the REACH Study, Doherty et al. found younger initiates (≤ 19 vs ≥ 20) were more likely to have 2 or more people present at initiation, had 2 or more actual trainers before **being** able to self-inject, and be initiated by a someone of the opposite sex. (39) Yet, these same findings did not find young women to be initiated by an opposite sex initiator than young men. These hypotheses have not been corroborated by data collected in a systematic way. Considering the enormous impact injection drug use has had on the spread of HIV, it is important to better document the experience of initiation and HIV seroprevalence of new injectors so timely interventions can be designed.

b) Factors Associated with Transition into an Injecting Career: Recently, attention has been given to factors associated with a transition **from noninjection drug use to injection of drug use.** van Ameijden et al. found current use of heroin, ethnicity, and current sexual relationship with an IDU to be significantly associated with a transition into **injecting or resuming an injecting career.** The main draw back with this study is that those who reported last injection ≥ 1 year ago were included with the "never injected" group. Thus, the "never injected" group actually contained initiates. These same authors also conducted a case-control study and found a transition rate (going from a noninjecting drug status to an injecting drug status) of 30% over a 5-year follow-up period. (105) Such a rate has not yet been determined in an out-of-mainstream US population of adolescent and young adult drug users (heroin/cocaine sniffers and crack smokers). One other cross-sectional study conducted by Irwin et al. found that crack smokers were more likely to initiate injecting if they had ever snorted heroin (PR = 3.4, 2.0-5.9) or snorted heroin while smoking crack (PR = 2.3, 1.3-4.0). (106) In this proposed study, transition rates will be estimated in addition to unveiling risk factors (e.g. childhood abuse, depression, network changes over time) associated with a transition into an injecting career.

5. Role of Physical/Sexual Abuse. The revised estimates of sexual assault against women and children by the Bureau of Justice Statistics more than doubled the previous annual estimates with now approximately one half million self-reports of sexual assault (39). It has also been demonstrated that women who report rape during childhood are at increased risk for repeat assault. (40)

One study randomly sampled U.S. adult women and found 33% to 68% of survivors of childhood sexual abuse experienced at least one rape in adulthood, a recurrence risk that was 1.9 - 4.0 times higher than the risk among women without previous sexual victimization. (41) Among IDUs, HIV seroincidence is greater among women. (3,24) Some studies have reported that women may have a higher sexual role than men which could be due to higher levels of trading sex for drugs. (25) At the root of this, Zierler's 1991 landmark article suggested that childhood sexual abuse was associated with higher rates of HIV. (42) While most studies have exclusively looked at women with regard to abuse, we are also interested in men. Although Zierler found higher prevalence rates of childhood sexual abuse among women (71%), both men and women showed strong associations with high risk behaviors such as prostitution, multiple sex partners, and sex with strangers with prevalence ratios of 2.8 and 7.6, 1.7 and 2.4, and 1.5 and 1.2 for women and men, respectively. (42) Among young men and women, Doherty et al. found an association between those reporting previous sexual assault and HIV seroprevalence during the REACH study. (39) In the HERS Study, Vlahov found no significant association of childhood or adult abuse by HIV serostatus. (43) Although the women were older, no association with HIV was found in another study of younger women. (44) This discrepancy in results needs to be clarified. In this proposal, we plan to examine and elucidate the role of childhood and young adult physical/sexual abuse in both young women and men as it relates to risk of HIV infection and its interrelationship with psychiatric condition, social networks, social support and circumstances surrounding initiation.

a) Risk Factors for HIV and Sexual Abuse: Specific conditions which enforce violence against women may also be the same conditions that increase women's susceptibility to HIV infection. (45) Conditions of social inequality such as social economic status, gender, and ethnicity not only serve as risk factors for HIV, but also as risk factors for sexual/physical victimization (46) thus, creating an overlap of the HIV and violence epidemics among women. This overlap has been further demonstrated by a high prevalence of rape and physical assault among women at risk for HIV. (27,42,47,48) Some studies have found early sexual abuse to be associated with HIV risk behaviors such as sex work and addiction to alcohol and other drugs. (49,50) Although similarity of risk factors suggest an overlap between HIV and violence epidemics among women, the specific linkage between the two still remains loosely defined.

b) Linking Physical/Sexual Abuse with HIV among Recent Initiates: Given that research linking violence with HIV is scant, there continues to be a gap in research on HIV and violence among young female initiates. Differences and similarities in a recent study demonstrated adolescent girls to have higher prevalences of prior consensual sexual activity, 79%, use of drugs and/or alcohol just prior to the assault, 47%, less frequent use of weapons and physical force when assaulted, 36%, and reported previous assault, 19%, compared to older women. (51) Another found that a history of physical abuse, sexual abuse or rape to be related to engaging in a variety of HIV risk behaviors between adolescence and young adulthood in a stratified random sample of 602 youths from public health clinics across 10 U.S. cities. (52) Conversely, women interviewed on lifetime experiences of rape and HIV-related risk exposures found a 43% lifetime prevalence of sexual abuse but, with over half occurring during adulthood. (45) In the same study examining only women with HIV, adult rape experiences were associated with earlier age of first sex, more sexual partners, unprotected sex with drugs, earlier age of injection drug use, teen pregnancy, STDs, and serious gynecologic surgery than those reporting they were never raped. (45) It has been further suggested that the abuse and HIV connection has been partially linked to the high risk among IDUs which is a setting that carries its own risk for violence in sexual relationships, whether in a context of trading sex-for-drugs, or of intimacy. (53,54,55,56) Irwin (1995) found 13.7% of the 1104 surveyed women age 18-29 years old to self-report recent rape (≤ 1 year) of whom were more likely to report smoking crack, being homeless, having a recent sexually transmitted disease (STD), and to be infected with syphilis and HSV-2. (44) Yet, rape was not independently associated with HIV after adjustment. This may suggest that rape is unlikely to play a direct role in HIV seropositivity but, its potential indirect role still remains unclear. This suggested linkage will be clarified within the proposed study.

In addition to the relationship between HIV seroconversion and history of abuse, this proposed study will also examine the risk of abuse as a result of HIV seroconversion (e.g., disclosure of HIV seropositivity). A recently published study that surveyed 136 health care providers reported 45% having at least one patient who expressed fear of physical violence resulting from her disclosure to a partner, 56% had patients who expressed fear of emotional abuse, and 66% had patients who expressed fear of abandonment. Warren (57) noted that among HIV seropositive IDUs, women were significantly less likely than men to inform partners of their HIV serostatus, possibly due to fear of violence. It has been suggested that reasons for excess mortality in HIV positive women may include such factors as domestic violence (58), yet comprehensive data reporting the prevalence of abuse in HIV seropositive women and the extent to which partner notification adds to the severity and frequency of abuse has been rarely seen in published literature. Given the prospective nature of the design, abuse patterns can be **assessed prior to initiation, prior to HIV seroconversion and after among young female initiates.**

Given these findings, history of childhood, adolescent and/or young adult abuse may serve as a circumstance of a young adults likelihood of injection drug use initiation. If injection drug use is the main risk factor for HIV seroconversion, are women more prone to initiate injection drug use upon leaving an abusive living arrangement (i.e., change in social network), or initiating injection drug use to better cope with an abusive living arrangement (i.e., lack of social support)? In examining the role of abuse among women initiates, what role does partner notification of HIV results play within abuse patterns (e.g., does notification of seropositivity trigger a violent response from partners)? In describing the link between abuse and HIV, one pathway that may be hypothesized that early childhood abuse may lead to an increased risk of psychiatric distress. Such nontreated conditions could in fact play a significant role in a young adults injection drug use initiation. An association between untreated childhood traumatization and HIV risk behaviors among clinic and non-clinic populations has been reported in a few studies. (42,59,60) The characteristic abuse symptoms of chronic depression, sexual compulsivity, revictimization, and substance abuse were identified as barriers to HIV education and intervention for survivors. (60) A study conducted among injection drug using HIV seropositive women found significant high levels of depression, prior physical abuse and lack of social support systems. (61) Such studies have neither sufficiently addressed out-of-mainstream communities of young adult injection drug users nor adequately assessed HIV seroprevalence and seroincidence status which will be examined in this proposed cohort.

6. Prevalence of Psychiatric Co-morbidity in Substance Abusers. Several population based studies have examined the prevalence of psychiatric disorders among drug-dependent individuals. Base rates from the Epidemiologic Catchment Area (ECA) Study showed a 22.5% lifetime prevalence rate of any psychiatric condition other than alcohol or other drug use disorder and 16.1% lifetime prevalence rate of any substance abuse disorder in the general population. Among individuals with any lifetime psychiatric diagnosis, 22.3% had a lifetime prevalence of alcohol abuse-dependence, 14.7% drug abuse-dependence, and 28.9% of either addictive disorder. (62) Among those with no lifetime psychiatric diagnosis, the rates for alcohol abuse-dependence, other drug abuse-dependence and either alcohol or other drug abuse dependence disorder were 11.0%, 3.7% and 13.2%, respectively. (62) These results demonstrate that having a lifetime psychiatric condition is associated with more than twice the risk of having an alcohol disorder, and over four times the risk of having an other drug abuse disorder. The National Co-morbidity Survey (NCS) found similar results (63) and both studies have shown a higher rate of psychiatric co-morbidity among drug users as compared to non-drug users. Specifically, the Epidemiologic Catchment Area (ECA) landmark study found that among those with a lifetime history of a drug (other than alcohol) use disorder, over half were affected by a psychiatric condition and were at more than four times the risk of having such psychiatric disturbances (OR=4.5). (62) In drug users, having a co-morbid psychiatric condition was associated with younger age (15-24) and lower socioeconomic status. Consistent with these findings, the ALIVE study demonstrated a 3-fold higher rate of psychiatric distress (assessed by General Health Questionnaire scores) than community counterparts after adjusting for age, sex, and census tract among IDUs. (63) **We plan to examine hypotheses such as higher prevalence rates of anxiety, depression and psychiatric distress among young adult initiates as compared to the previous population based studies. Other hypotheses we plan to examine are whether a particular psychiatric condition is a risk factor for a high risk first injection.**

a) Drug Type and Psychiatric Conditions: Individual drugs of abuse were found to be associated with lifetime prevalence rates of psychiatric co-morbidity ranging from 50.1% for marijuana and 76.1% for cocaine. (62) The ECA study found cocaine and opiate abusers to have an 11.1 and 6.7 increased odds of having a psychiatric condition compared to non-abusers. (62) Although epidemiologic evidence on suspected associations between cocaine use and psychiatric condition has been documented (66), specific use of crack cocaine among young initiates in non-clinic or noninstitutional settings has not been studied. In this study, we will determine co-morbidity rates of psychiatric condition (psychiatric distress, anxiety and depression) by drug type at pre- and post-initiation, and further explore these relationships of co-morbidity with HIV.

b) Gender and Psychiatric Condition: Excluding other drug and alcohol disorders, anxiety and depression are two of the most common psychiatric conditions observed in association with drug dependence. The pattern of psychiatric co-morbidity varies between men and women. For instance, women exhibit more depression and anxiety disorder in association with drug dependence compared to men (63). Such gender differences with respect to co-morbidity, specifically among young, recent initiates, will be examined in the proposed study.

c) Interactions Between Gender, Abuse and Psychiatric Condition by HIV Status: Several studies have linked early post-traumatic stress disorder to later alcohol and drug problems. Individuals who have been victims of or witnesses to violence appear to have an increased vulnerability to anxiety disorders. It has also been suggested in the literature that victims of crime, especially women, are at higher risk for developing drug dependence. In the current REACH Study, young women initiates were found to be at higher risk for HIV compared to young men after adjusting for injection practices. (38) In an effort to further explain these results, we hypothesize that abuse or exposure to a violent event in childhood and/or adolescence results in an

increased risk for a particular psychiatric condition (psychiatric distress, anxiety and/or depression), which in turn, places young women at higher risk for initiation and/or drug dependence which in turn places one at high risk for HIV. We plan to explore this hypothesis in the current proposal and consider it to be one of several causal pathways toward drug dependence among HIV seropositive and seronegative initiates.

7. Influence of Social Networks on HIV Risk Behaviors. Many epidemiologic studies have examined the role of individual levels of behavior on rates of HIV infection to construct risk factors. However, it is not only “how much” by “with whom” and “under what circumstances” a behavior is performed that needs to be known in order to understand risk of being or becoming infected. There is ample evidence that HIV risk behaviors in IDUs are influenced by social factors. Several studies have examined correlates of needle sharing and self-reported reasons for needle sharing (67,68) and the role of injection settings (69). It has been found that sharing injection equipment is associated with economic status and living conditions (67) and that attending shooting galleries and other HIV risk behaviors are correlated with factors such as age, race, and peer's HIV risk behaviors. (70)

The observed difficulty IDUs have in changing their needle sharing behavior have led investigators to postulate that the sharing of injection equipment is embedded in social processes that promote and reinforce this HIV risk behavior. (71,72) Research on drug use patterns has demonstrated the relationship between adolescent drug usage and the use pattern of friends. (73,74) Several social factors have been identified as influencing HIV infection risk behaviors. Friedman et al. found that friends' HIV risk behaviors were the strongest predictors of behavioral change; perception of friends' risk behavior was a stronger determinant of risk reduction than was knowledge about AIDS, education level, or personal knowledge of somebody with AIDS. (75) Magura et al. also report that friends' attitudes are associated with needle sharing. (67) The observed variations in HIV risk behaviors by social environmental factors and the persistence of high risk behaviors among IDUs suggest the need to systematically assess the relationship between social influence on initiation of injection drug use and HIV.

Social influence, especially by friends, has been found to affect numerous drug use and other health related behaviors. (76) One method of studying social influence is through social network analysis. Social networks are conceived as patterns of stable interactions among people. These interactions may be categorized as instrumental, psychologically supportive, disruptive, burdensome, or neutral. Analyses of these processes allow for the study of both individuals and their social environments. Social networks can be analyzed from the **individual's perspective** (egocentric or personal) and from within **multiple perspectives in a defined social field** (e.g., sociograms). For this study, we will utilize the egocentric methodology because it is logistically efficient for population based studies and appropriate to use to find associations before application of the considerably more time-intensive approach of social field analysis.

a) Social Networks and Substance Abuse: Previous research indicates that social network characteristics can be reliably measured (77,78), are associated with adoption of health behaviors (76,79), buffer against psychological stress, and differentiate drug use behaviors (79). In a study of friendship networks, intimacy, and illicit drug use in young adults, Kandel and Davis (1991) found that illicit drug use was positively associated with intimacy among male friendship networks. (80) One interpretation of this finding is that the illegal nature of drug use reinforces ties among drug users. Social network characteristics may also be used as an index of daily routine for IDUs. Specifically, research addressing the social network characteristics surrounding initiation of injection drug use in young adults has not been done. Although not specific to injection drug use or young adults, some studies have explored the early influences of the family origin on initiation of drug abuse, disruptions in family dynamics that occur prior to drug use and after, and the role of family in drug treatment. (74,80) Westermeyer and Neider (1988), in a treatment sample of 168 substance abuse patients, found that size of social networks was negatively associated with psychiatric symptoms but was not associated with years of substance use or periods of drug abstinence. (81) Although determining factors associated with initiation is beyond the scope of the proposed design for lack of a control group, factors surrounding initiation as a method of measuring initiation is in part a way of looking at social networks. For example, in this study we can address issues surrounding how long it takes an initiate to get to the point of self-injection (if in fact such a period is reached), and its relationship to network characteristics and HIV infection.

b) Social Networks and HIV: There is relatively little published literature on social networks and HIV. The majority of research to date on social networks and HIV has used network methodology to map the transmission of HIV through and among personal networks. (82) There are a few extant studies on HIV risk behaviors and social networks. Frey, et al. in a pilot study of 20 male African American IDUs found that IDUs' networks were hyper centric and that the proportion of kin in the social network was associated with drug-use pattern, as was the pattern of drug use in the index IDUs' network members. (83) Trotter, et. al identified four types of drug user networks: closed, kinship, longstanding friendship, and open. (84) Closed networks reported the highest drug use and kinship networks the second highest. In New York City, Neaigus, et al. found that there was a

high degree of concordance in the reports of HIV risk behaviors among network dyads. (85) In a follow-up study of network characteristics as antecedents of drug-related HIV risk behaviors, Latkin (1995) found a higher total network density and larger drug subnetwork size to be positively associated with size of positive feedback network (those identified by the participant as “people you could expect to let you know when they liked your ideas or the things that you did”) and negatively associated with size of material aid network (those identified by the participant as “people you could borrow \$25 or something valuable from”). (86) Latkin (1995s) further found in a sample of the same study population that although most participants reported at least one family member in their social network, the presence of family members in their personal networks was not related to patterns of drug use and those who reported a partner in their personal social network injected significantly less often than those who did not report a partner. (86) Further analysis showed that network density and size of drug subnetworks were positively associated with frequency of drug injection. (87) These findings suggests that social network analysis is a potential useful tool for comprehending the social context of HIV risk behaviors. To date, there have been no studies [with the exception of Doherty’s (1996) cross-sectional REACH Study findings-see preliminary reports section C.2.] examining the role of social networks on HIV seroprevalence and seroincidence among recent initiates. We are particularly interested in the role of networks at initiation into drug use, and by duration of drug use, specifically to see if network characteristics change over time in a way that is associated with differences in prevalence and incidence of HIV infection during this vulnerable period of drug abuse. In this study, this role will be examined.

8. Role of Social Support and HIV Risk Behaviors. The results of numerous cross-sectional and longitudinal studies consistently indicate that social support can reduce morbidity and mortality. Prospective cohort studies have confirmed the direct beneficial effect of social support on global mental health, depressive symptoms, and psychological distress. In a sample of IDUs, social support was found to predict sexual risk reduction. Abdul-Quader, et al. interviewed IDUs (African American 24%, white 39%, and Hispanic 35%) in New York City to assess their HIV-related risk behaviors and possible behavior changes (88). Specific health beliefs and general social support, "having someone to talk to", were significant predictors of sexual risk reduction. Specifically, studies addressing the social support characteristics surrounding injection drug use initiation and its relationship with HIV among recent initiates has not been done. This study will address these issues.

a) Components of Social Support: Several theoretical frameworks have been developed to characterize the components of social support. Models presented by Hall and Wellman (1985) and House, Umberson, & Landis (1988) consider both structural and relationship characteristics. (89,90) The three major proposed support characteristics are: 1) the *existence or quality of social relationships*, including types, frequency of contact and density; 2) *network structure*: the relationship between the index person and another person regarding factors such as reciprocity, multiplexity, and durability; and 3) *relationship content*: the function and quality of a relationship, which is usually described in terms of source or role, e.g., spouse, friend, co-worker. Density is defined as the actual number of network ties among individuals in a social network divided by the number of possible ties. Multiplexity is the number of relationships between the participant and the network member and is indexed by the number of network members named in two or more functional network domains (e.g., material and physical assistance). These components will serve as the framework in elucidating social support as it relates to initiation and HIV.

b) Negative Relationships: Many social support instruments measure supportive ties but ignore disruptive or harmful relationships. However, for health behaviors a negative content of relationships may be more consequential than positive ties. (91,92) Individuals who engage in high levels of HIV risk behaviors, such as IDUs or persons with multiple sex partners, may have some social relationships that militate against positive social support and instigate initiation of injection drug use.

c) Social Control: A potentially important and often overlooked aspect of social support is social control. Social control may influence health behaviors through self-regulation in conformity to norms or through others' health promoting behaviors. (93) These controls may constrain HIV risk behaviors. Intimates and other social network members may be a source of social control for young adults deciding on whether or not to initiate injection drug use.

9. Summary of Proposed Study. This proposal has two designs: *cross-sectional* and *prospective*. Given the cross-sectional design of the baseline data, there are limitations in terms of causal inferences because of the uncertainty of temporality. The prospective (i.e. follow-up) component of this study will serve to overcome this limitation by helping assess specific pathways that lead to **initiation of an injecting career** and HIV infection. Therefore, in a single example, if there is an association of psychiatric condition and HIV, we cannot say if psychiatric condition leads to HIV, or if people develop a psychiatric condition by virtue of being or knowing that they have HIV infection. Thus, we will first examine our variables of interest (**e.g., sex practices, injection practices, abuse, psychiatric condition, social networks, etc.**) using a cross-sectional design of data collected at baseline. Then, as prospective data and/or HIV seroconversion data become available over the 5-year proposed

study, we will examine associations of relevant variables by whether initially 1) HIV seronegatives convert to seropositivity, and 2) noninjectors become injectors. Although, we may suffer from insufficient power to detect significant differences among all the proposed variables of interest, we may be able to elucidate some pathways, and through database linking with our recent study (REACH II), we will have the improved power to sufficiently address these prospective pathways and others. Given what we already know about HIV risk factors, this study will establish independent risk factors and correlated individual drug and sex practice

interrelationships of HIV infection and begin to examine other variables as to how they impact on HIV infection.

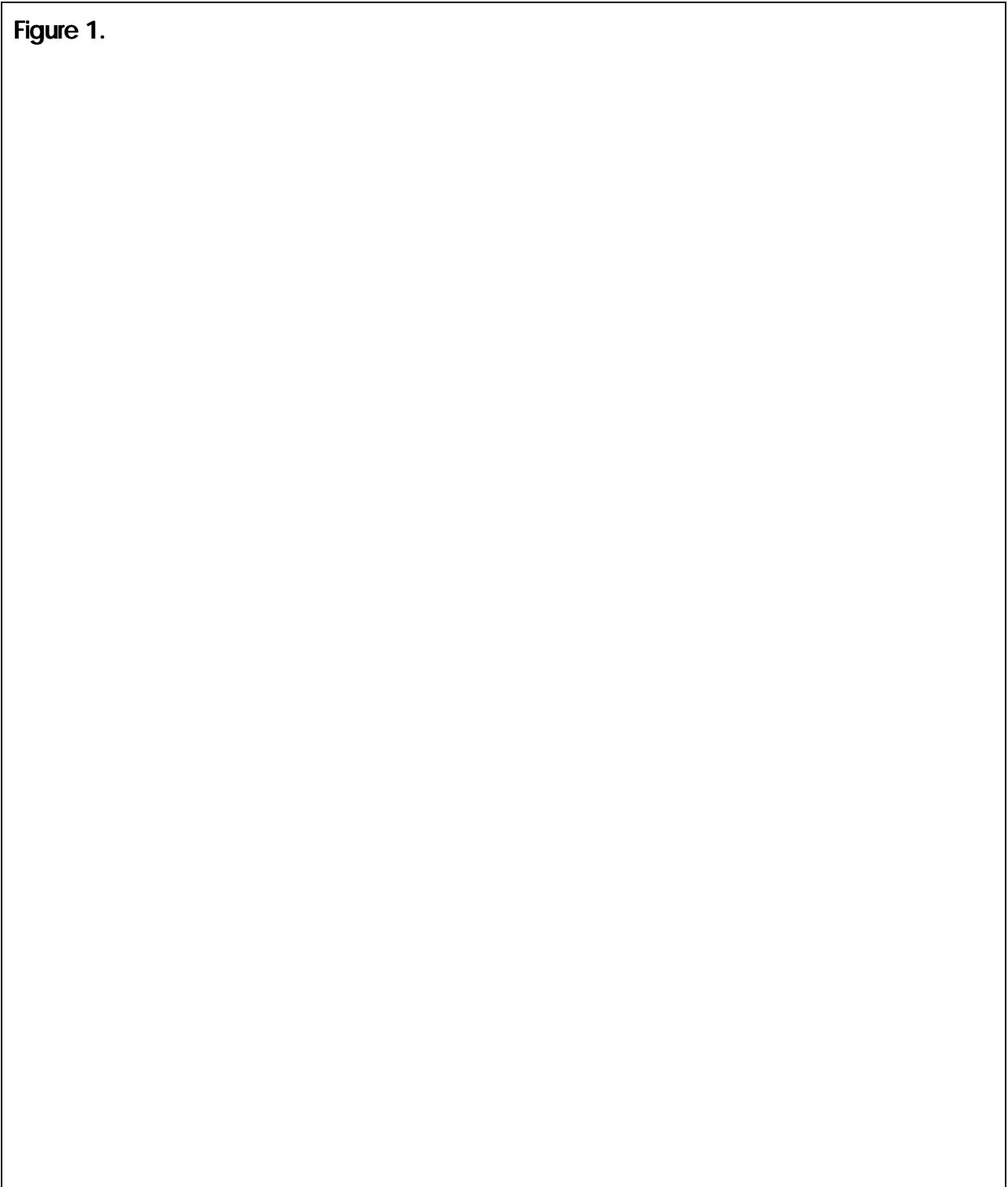
Through the proposed study, we will thoroughly examine six sequential areas of germane interest as depicted in **Figure 1**. The overall plan for considering the proposed variables is as follows:

First, many studies have identified behavioral factors such as unsafe injection and sexual practices which lead to HIV infections (**A C1**, and **B C2**). We will describe these factors among NIUs as well as recent initiates because they both play an integral part in HIV infection, as well as, in the following eight areas of this study (**D1, D3, E1, E3, F1, F3, G1, G2**).

Second, we will consider the first and third sets of factors,

circumstances of initiation, abuse, psychiatric condition, social networks, and social support in Figure 1 (**D1, D3, E1, E3, F1, F3, G1, G2**) as they relate to HIV infection, independently and through adjustment for the previously identified risk factors (A and B) because the primary design is cross-sectional where temporality cannot be definitively established. We will also assess same factors (**D1, E1, F1, G1, and D3, E3, F3, G2**) as they correlate with the risk behaviors of box **A** and box **B**, respectively.

Figure 1.



Third, we will examine the interrelationship of each of the eight factors (**D1, E1, F1, G1, and D3, E3, F3, G2**) with each other while ignoring the previously identified risk factors (**A** and **B**, respectively). The examination of these interrelationships will include the interactions between risk factors (**A** and **B**) and factors (**D1**), (**E1**), (**F1**), (**G1**) and (**D3**), (**E3**), (**F3**), (**G2**), respectively.

Fourth, we will look further at the right-hand side of Figure 1 and cross-sectionally determine if HIV seropositive NIUs (**C1**) and initiates (**C2**) are more likely to be abused (**D2**, and **D3**), have a psychiatric condition(s) (**E2, E3**), possess certain social network and social support characteristics (**F2, F3**), and have particular circumstances surrounding their initiation (**G1, G2**). We will further examine the role of disclosure of HIV status (**H1**, and **H2**) as a result of HIV seroconversion (left-side of Figure 1) and whether this leads to abuse in young, female NIUs and young female initiates, either during follow-up or in the past (i.e. in the case of HIV prevalent NIUs and initiates).

Five, in understanding the relationships between the above mentioned factors and HIV given the limitations of cross-sectional analysis, we will prospectively examine the temporal nature of these factors as they relate to a first injection and HIV seroconversion. Such examples will include, but not be limited to, the changing status of social networks and persistence of psychiatric condition(s) on or about the period of a first injection or the period of seroconversion. In the event of insufficient power (even after database linking of previous studies), the well studied risk factors (**A** and **B**) above will provide as proxy outcome measurements for HIV infection given the event of limited numbers of HIV seroconverters. As a second alternative to small numbers of seroconverters, we could use an additional surrogate measurement such as Hepatitis C virus. In regard to insufficient power among the NIUs first injection, one alternative could be to add those who have either “tried to inject and failed” and/or “considering injecting but have not injected”. (In both cases, these two groups must report the alternative at baseline to be considered an outcome.) These alternatives lead us to the final area of our proposed study.

The sixth area of interest will include a) HIV risk reductions and, b) the behavioral correlates of risk reduction both of which will be measured at baseline, 6-month and 12 month follow-up. Although this is not a primary aim of this study, it is a benefit due to the nature of prospective design.