

News and Views

## AIDS research in the NIDA Clinical Trials Network: Emerging results<sup>☆</sup>

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### Abstract

Prevention and treatment of HIV/AIDS among drug users continue to be vexing problems. Scientifically validated interventions have been developed to prevent and treat HIV/AIDS among substance users. The Clinical Trials Network (CTN) of the National Institute on Drug Abuse (NIDA) is conducting multi-site clinical trials, with emerging results that address both prevention and treatment of HIV/AIDS. This is a report of preliminary results from several of those trials, presented at a workshop of the College on Problems of Drug Dependence. Lawrence Brown surveyed over 120 CTN clinics and reports on the state of the clinics in treating HIV/AIDS and other infectious diseases. Robert Booth summarized preliminary data from over 600 participants in a multi-site trial of HIV and hepatitis C virus (HCV) interventions in drug detoxification settings. Donald Calsyn reported preliminary results from an effectiveness trial of a gender-specific, action-oriented, safer-sex group intervention for 575 men in drug treatment programs. Susan Tross reported on a similar study focusing on 515 women in 12 clinics. Yong Song presented the perspective of treatment programs in conducting clinical trials. Jacques Normand added comments from the perspective of the Director of the NIDA AIDS research program.

**Keywords:** HIV/AIDS; Drug abuse; Clinical trials; Substance abuse treatment

### 1. Introduction

It was June 1981, in *Morbidity and Mortality Weekly Report*, that Michael Gottlieb published observations on five gay men treated for pneumocystis carinii pneumonia (Gottlieb et al., 1981). An editorial note suggested “the possibility of

a cellular immune dysfunction related to common exposure” (Gottlieb et al., 1981, p. 252). This was the first appearance of acquired immunodeficiency syndrome (AIDS). Exactly 25 years later, the 2006 meeting of the College on Problems of Drug Dependence occurred. In the interim over 25 million people had died of AIDS, including 500,000 in the United States.

There have been major advances in the last decade in the fight against AIDS. Medications are effective in suppressing HIV to undetectable levels, and evidence-based prevention programs reduce HIV risk behaviors. Despite these advances, 40,000 Americans become infected with the human immunodeficiency virus (HIV) every year, and many of them are young people who do not know that they have the virus.

The CTN is conducting multi-site clinical trials with emerging results that address HIV/AIDS (Hanson et al., 2002). Altogether the CTN has begun about 25 studies on a wide range of topics. HIV issues are integral to this work. All studies address HIV risk behaviors using a common battery. A HIV/AIDS special interest group meets regularly to discuss study ideas and policy approaches, integrate results, and keep the organization informed with the timely issues. Several affiliated studies have been funded through external resources using the CTN “platform”. Most importantly, the CTN

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is conducting several studies specifically focused on HIV/AIDS and other infectious diseases.

## 2. HIV/AIDS-related services in substance abuse treatment settings

The CTN is comprised of 17 research nodes, with 116 Community Treatment Programs (CTPs) located in 26 USA States. The purpose of this study, led by Lawrence Brown, was to describe the range of infection-related services available in those CTPs, CTP characteristics (funding, staffing), clinician characteristics (training, knowledge, behavior), their opinions of barriers to providing infection-related services, and state regulatory guidelines. The study design involved three cross-sectional surveys, conducted with CTP Administrators, CTP Clinicians, and Administrators of State health departments and state substance abuse agencies. Of 319 CTP administrators approached, 269 responded (84% of those surveyed) from 95 CTPs in the CTN, 1723 clinicians returned surveys (78% of 2210 targeted), at least one substance abuse or health department administrator from 48 of the 50 states (96%) and the District of Columbia participated.

Some preliminary results were recently published (Brown et al., 2006). At the workshop Dr. Brown provided his impression of other recent findings. Most HIV/AIDS-related services were being offered by a substantial proportion of CTPs, although a significant number of programs offered no HIV-related services. As related to HIV services, it is interesting that 78.5% of the CTPs were private, not-for-profit agencies; funding came from diverse sources, the most common being the state; 20% had no medical staff; and 74–93% of CTPs (varying by treatment modality) offered HIV education to their staff. Regarding State administrators, 83% reported HIV-related guidance (policies, regulations, or guidelines) related to provider education. In comparison, 17% of the states reported such guidance for all four medical services (medical history and physical examination, biological testing, medical treatment, and medical monitoring), and 50% of the states

reported such guidance for all three non-medical services (patient education, risk assessment, and counseling).

Dr. Brown stressed that the study has limitations that include unknown generalizability (the CTP sample came from CTN clinics only) although the results seem consistent with previously published studies (Strauss et al., 2002; Substance Abuse and Mental Health Services Administration, 2004), lack of detailed description of services tailored for women and minorities, and the lack of information on utilization, cost, efficiency, or effectiveness of HCV-related services. For these reasons the study should be viewed as hypothesis-generating.

## 3. HIV/STD safer sex skills groups for men in methadone maintenance or drug-free outpatient treatment programs

The purpose of this study, led by Donald Calsyn, was to assess the efficacy of a safer-sex group intervention designed specifically for men in drug treatment programs. The study was conducted at seven methadone maintenance and seven psychosocial outpatient programs across the country. Regarding study design, participants in small cohorts were randomly assigned to a one-session HIV education group or a five-session gender-specific HIV prevention group, called Real Men are Safe (REMAS). Participants were reassessed prior to randomization, after the intervention and at 3 and 6-month follow-ups. The primary outcome was number of unprotected vaginal and anal sex events. Secondary outcomes focused on condom-related measures, combining of sex and drugs, number of sexual partners, and engaging in “outercourse” (engaging in sex to the point of orgasm without penetrating body orifices). In REMAS, most material came from either Project Light (NIMH Multisite HIV Prevention Trial Group, 1998), an HIV prevention intervention in STD clinics, or Time Out for Men (Bartholomew and Simpson, 1996), a workshop for men in substance abuse treatment.

Emphasizing that the study was ongoing, Calsyn noted that the research group

presented several posters at CPDD based on the baseline assessments. Calsyn et al. (2006) found that the majority of participants reported engaging in sex under the influence of drugs or alcohol in the prior 90 days and that combining sex and drugs was associated with sex with a casual partner and a higher likelihood of engaging in anal sex. Hatch-Maillette et al. (2006) focused on the overall sexual activity of the sample. Men in outpatient psychosocial programs were more sexually active than men in methadone programs, and had riskier sexual partners (non-monogamous or monogamous less than 6 months). Sterling et al. (2006) found that the only variable associated with attendance at sessions was being in methadone maintenance, as compared to psychosocial outpatient services. Song et al. (2006) examined condom possession, attitudes about condoms, acquisition of condoms and partner communications, with findings that support the efforts in the treatment groups to change attitudes about condoms and increase communication about sexual issues. Calsyn emphasized that study results are forthcoming from a collaborative team of researchers and clinicians.

## 4. HIV/STD safer sex skills groups for women in maintenance or drug-free outpatient treatment

Tross and co-workers used a parallel design to conduct and evaluate an HIV safer sex skills building group intervention, based on the work of El-Bassel and Schilling (Schilling et al., 1991; El-Bassel and Schilling, 1992), for women in methadone maintenance or drug-free outpatient programs. It was a sister study to the all-male investigation of Dr. Calsyn (above), using the same design involving random assignment of small cohorts to one versus five sessions of HIV education, and follow-ups post 3- and 6-month intervals).

The five-session intervention was labeled Women on the Road to Health (WORTH), an intervention that had been found to be efficacious in previous clinical trials (Exner et al., 1997). The study was conducted at seven methadone maintenance and five psychosocial outpatient programs around the country,

with over 500 participants randomized in cohorts. The primary outcome variable was unprotected penetrative (vaginal or anal) intercourse within the past 3 months. Secondary outcomes included drug-with-sex occasions, perceived self-efficacy to carry out safer sex, carrying condoms, and gender role beliefs. Only baseline data were available for analysis.

Inasmuch as heterosexual risk behavior is the primary mode of HIV transmission among US women, Generalized Linear Modeling (GLM) was used to identify predictors of baseline levels of unprotected vaginal and anal sex occasions (with primary and non-primary male partners) in the past 3 months. The sample had a mean of 19 occasions in the past 3 months. GLM identified highly significant predictors of unprotected behavior: younger age; frequency of sex-with-drug occasions; and being monogamous. At the same time, substantial percentages of monogamous (and non-monogamous) women reported that their partners had histories of risk factors (e.g. crack-cocaine use, jail time, injection drug use) in the past 10 years. For example, among monogamous women, for this period: 47% reported that their partners had spent time in jail; 46% reported that their partners had smoked crack cocaine; and 33% reported that their partners had injected drugs. Among non-monogamous women, for this period: 55% reported that their main male partners had spent time in jail; 52% reported that their main male partners had smoked crack cocaine; and 34% reported that their main male partners had injected drugs. These findings point to the importance of tailoring HIV prevention programs for female drug users who are monogamous and combine sex with drugs—who may not consider themselves at HIV risk.

In an interactive presentation, Dr. Tross posed several questions for the audience about the sustainability of a safer-sex intervention in clinics, including: What does it take to conduct the intervention in clinics, how does it fit in clinic life, what clinical problems might it open up, how do clients feel about it, and how do staff feel about it? These evoked spirited discussion among the audience.

## 5. HIV and HCV intervention in drug detoxification and treatment settings

This study, led by Robert Booth, is assessing participants in a multi-site trial of HIV and HCV interventions in drug detoxification settings. The study recruits adult injection drug users during residential detoxification treatment who are at risk for infection with HIV and HCV. While the primary aim is to reduce drug-related HIV and HCV risk behaviors, additionally the study aims to increase treatment entry and treatment retention, and decrease participants' sexual risk behaviors. The 646 participants (from eight different clinics) were randomly assigned to one of three conditions: two sessions of counseling and education, a therapeutic alliance intervention, or treatment as usual.

At present baseline characteristics are available for the study, indicating high levels of risk behaviors for acquiring or transmitting HIV or HCV. In the last 30 days: over 80% had used heroin and over 60% had used cocaine; over a third used "used" syringes, and over half had shared drug solutions (mean of 6.5 times); over half the men and nearly 80% of the women reported having sex.

## 6. Treatment program perspectives: Conducting HIV/AIDS research in the Clinical Trials Network

Yong Song explained the perspective of a treatment provider conducting studies at his clinic, which was in the study of safer sex for men. He emphasized that the study was a collaborative effort between research and clinical staff. As they carried out this protocol they learned several things about implementing a clinical trial in a busy county-hospital-based methadone program.

Training for a clinical trial can be lengthy and comprehensive. The counselor training consisted of a week-long intervention training in another city. Even though many counselors had been doing HIV prevention for years, they had to learn how to do things according to the established protocol, something they were not used to. Because the interven-

tion focused on sexual risk behaviors and communication issues, it also forced counselors to address their own comfort levels relating to explicit sexual material. At the end of the week counselors went through a certification process, and many found this anxiety-provoking, as most counselors were not accustomed to having their clinical work directly scrutinized in such a fashion.

Supervision also required adjustments. In some clinics counselors receive supervision only when their clinical work is sub-par, so supervision sometimes holds negative connotations. To ensure adherence to protocol, counselors received weekly supervision by a licensed clinician, and their intervention sessions were audio taped and reviewed. None of the counseling staff had prior experience with this level of clinical supervision, and they were not used to this level of feedback on their clinical performance. However, over time the counselors came to appreciate the supervision and viewed it as a benefit to being in the study, as they learned new content as well as alternative counseling skills and techniques.

There were other implementation issues from both the research and clinical perspectives. The groups in this protocol were co-facilitated, yet many counselors had not co-led groups before and found this to be useful. Clinical staff was instrumental in improving attendance for intervention sessions and helpful in finding participants for follow up interviews. Furthermore, counselors wisely advised that the study schedule intervention groups around the 1st and the 15th of each month . . . dates that were associated with increased no-shows and absences as many patients received entitlement checks. Other issues included balancing clinical and research resources and staff time, performance expectations, and need for mutual feedback. Song couched his conclusions in terms of "lessons learned" for clinicians and researchers.

## 7. Discussion

Discussant Jacques Normand, the Director of the AIDS research program at NIDA, added a perspective of the NIH and NIDA priorities for developing

knowledge in this vital area of research. HIV/AIDS issues have been imbued in the fabric of CTN activities through the AIDS special interest group, inclusion of risk behaviors in every study, and in the mounting of specific research projects studying HIV prevention and treatment services. The studies themselves show the potential of the CTN to contribute to our HIV drug-related knowledge base. The presentation of Dr. Brown indicated that barely a fifth of drug treatment programs in the CTN had any medical staff, which points out the traditional separation of medical from substance abuse services that can be a barrier to mounting HIV interventions in drug treatment programs. Moreover, soon to be released CDC guidelines for HIV testing will apply only to medical settings. This may introduce wider divisions between drug abuse treatment programs that are in medical settings and those that are not as far as HIV services are concerned. The sibling studies of Drs. Calsyn (with men) and Tross (with women) can be ground-breaking, in that their large scale will allow sub-analyses that can help the field better understand the interrelationships between HIV risk behaviors, treatment programs, and interpersonal relationships. Dr. Booth's study in detoxification programs can contribute to the understanding of ways that HIV educational programs, as well as the alliance between patient and provider, can help link drug users to needed ongoing care. During the workshop each presenter, and many in the audience, reflected on why they became involved in HIV research originally, and how their commitment has

endured in the 25 years since AIDS was first reported.

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### References

- Bartholomew, N.G., Simpson, D.D., 1996. Time Out! For Men: a Communication Skills and Sexuality Workshop for Men. Lighthouse Institute Publishing, 720 W. Chestnut St. Bloomington, IL 61701, USA, or on the Internet at [www.tcu.ibr](http://www.tcu.ibr).
- Brown Jr., L.S., Kritz, S.A., Goldsmith, R.J., Bini, E.J., Rotrosen, J., Baker, S., Robinson, J., McAuliffe, P., 2006. Characteristics of substance abuse treatment programs providing services for HIV/AIDS, hepatitis C virus infection, and sexually transmitted infections: the National Drug Abuse Treatment Clinical Trials Network. *J. Subst. Abuse Treat.* 30 (4), 315–321.
- Calsyn, D.A., Hatch-Maillette, M.A., Doyle, S.R., Cousins, S.J., Woody, G.E., 2006. Sex under the influence is common for substance abuse treatment patients. In: Poster Presented at the CPDD 68th Annual Scientific Meeting Program, Scottsdale, Arizona.
- El-Bassel, N., Schilling, R., 1992. 15-month follow-up of women methadone patients taught skills to reduce heterosexual HIV transmission. *Pub. Health Rep.* 107, 500–504.
- Exner, T., Seal, D., Ehrhardt, A., 1997. A review of HIV interventions for at-risk women. *AIDS Behav.* 2, 93–124.
- Gottlieb, M.S., Schanker, H.M., Fan, P.T., Saxon, A., Weisman, J.D., Pozalski, I., 1981. Pneumocystic pneumonia—Los Angeles. *Morb. Mortal. Wkly Rep.* 30, 250–252.
- Hanson, G., Leshner, A., Tai, B., 2002. Putting drug abuse research to use in real life settings. *J. Subst. Abuse Treat.* 23 (2), 69–70.
- Hatch-Maillette, M., Calsyn, D., Doyle, S., Woods, A., Coyer, S., Sillo, G., Woody, G., 2006. Sexual practices in methadone maintenance and outpatient psychosocial drug treatment samples. In: Poster Presented at CPDD 68th Annual Scientific Meeting Program, Scottsdale, Arizona.
- NIMH Multisite HIV Prevention Trial Group, 1998. The NIMH Multisite HIV Prevention Trial: reducing HIV sexual behavior risk. *Science* 280, 1889–1894.
- Schilling, R., El-Bassel, N., Schinke, S., Gordon, K., Nichols, S., 1991. Building skills of recovering women drug users to reduce heterosexual AIDS transmission. *Pub. Health Rep.* 106, 297–304.
- Song, Y., Calsyn, D.A., Doyle, S.R., Herr, S., Sorensen, J.L., 2006. Communication about condom use and reported condom use among participants enrolled in drug treatment. In: Poster Presented at the CPDD 68th Annual Scientific Meeting Program, Scottsdale, Arizona.
- Sterling, R., Weinstein, S.P., Calsyn, D.A., Doyle, S.R., Crits-Cristoph, P., 2006. Factors associated with HIV education attendance. In: Poster Presented at the CPDD 68th Annual Scientific Meeting Program, Scottsdale, Arizona.
- Strauss, S.M., Falkin, G.P., Vassilev, Z., Des Jarlais, D.C., Astone, J., 2002. A nationwide survey of hepatitis C services provided by drug treatment programs. *J. Subst. Abuse Treat.* 22, 55–62.
- Substance Abuse and Mental Health Services Administration 2004, National Survey of Substance Abuse Treatment Services (NSSATS), 2004. Data on Substance Abuse Treatment Facilities, DASIS Series: S-28, DHHS Publication No. (SMA) 05-4112. Rockville, MD 20850, United States.