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## NIDA's Clinical Trials Network: An Opportunity for HIV Research in Community Substance Abuse Treatment Programs

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**Background/Objectives:** HIV continues to be a significant problem among substance users and their sexual partners in the United States. The National Drug Abuse Treatment Clinical Trials Network (CTN) offers a national platform for effectiveness trials of HIV interventions in community substance abuse treatment programs. This article presents the HIV activities of the CTN during its first 10 years. **Results:** While emphasizing CTN HIV protocols, this article reviews the (1) HIV context for this work; (2) the collaborative process among providers, researchers, and National Institute on Drug Abuse CTN staff, on which CTN HIV work was based; (3) results of CTN HIV protocols and HIV secondary analyses in CTN non-HIV protocols; and (4) implications for future HIV intervention effectiveness research in community substance abuse treatment programs. **Conclusion/Significance:** While the feasibility of engaging frontline providers in this research is highlighted, the limitations of small to

medium effect sizes and weak adoption and sustainability in everyday practice are also discussed.

**Keywords:** Clinical Trials Network, effectiveness research, HIV/AIDS, substance abuse

### BACKGROUND AND OBJECTIVES

The National Institute on Drug Abuse (NIDA) National Drug Abuse Treatment Clinical Trials Network (CTN) (1) was a response to the Institute of Medicine's (IOM) (2) 1998 call for infrastructure to increase effectiveness research to facilitate widespread adoption of efficacious treatments into community-based treatment programs. Now in its 11th year, the CTN is a national network of partnerships between researchers and providers delivering substance abuse treatment – described in a 2010 Anniversary issue in the *Journal of Substance Abuse Treatment* (3).

The past decade spans a dynamic period in HIV epidemiology, prevention, testing, and treatment in which

the CTN has been an active participant. This article summarizes the HIV context and describes HIV-related research within the CTN in terms of collaborative process, HIV protocols, HIV-related secondary analyses, limitations, and implications for future HIV effectiveness research.

## HIV CONTEXT

Over the past 10 years, HIV has continued to be a significant problem among substance users. In 2006, substance use was a likely factor in 51.1% of infections due to heterosexual contact with a high-risk partner (often a drug user; 27.6%), injection drug use (IDU) (18.5%), or male-to-male sexual contact and IDU (5%) (4). There is potential non-injection substance use involved in another 48.1% of infections in men-who-have-sex-with-men. In substance abuse treatment programs, HIV prevalence ranges from 1% to 28% (5,6).

Significant progress has been made in educating substance abusers about the risks of sharing needles and injection paraphernalia. This is partly due to the growth and effectiveness of syringe exchanges (7,8) and harm reduction messages about needle-sharing and needle hygiene (9,10). Substance abuse treatment has also had a significant role in reducing drug use and HIV IDU risk behavior (11–14). However, sexual risk behavior has been slower to change. Unprotected sex, often under the influence of drugs, and especially stimulants (15–17), has become increasingly important in HIV transmission (18). Meta-analyses and reviews of controlled trials of HIV risk reduction interventions among substance users (19–22) suggest that HIV safer sex interventions with certain core features can be effective: gender-specificity; intensity of at least four sessions; and focus on skills building (23), compared to brief, informational sessions that are often standard-of-care (24). Without an HIV vaccine, substance abuse treatment and HIV behavioral intervention are the primary approaches for reducing HIV transmission among substance users.

The past decade has been a period of marked progress. The HIV prevention and treatment fields have become more integrated, for example, and embraced the “Seek, Test, Treat and Retain” paradigm (25–29). This paradigm involves reaching out to vulnerable and hidden populations such as substance users (*seek*), offering them HIV testing so they will become aware of their HIV status (*test*), then if confirmed HIV-positive linking them to HIV primary care so they can begin antiretroviral therapy (ART) (*treat*), and finally examining strategies to retain them in HIV medical treatment including ways to address their substance use (*retain*). One important component of this approach and national recommendation is that healthcare settings, including substance use treatment programs, offer HIV testing to their patients (30) and then have available linkage services to primary medical care when a person tests positive for HIV. However, surveys have shown that only about one-half of treatment programs provide HIV testing services, either on-site or outsourced (31–34). Additionally, significant obstacles

complicate ART effectiveness, especially among substance users. They are late testers (35), have poorer access to HIV care (36,37), and may have difficulty maintaining high adherence required for ART (38–41). This is concerning as it has been shown that substance users, if started on ART, can achieve the same clinical outcomes (e.g., increased survival) of their non-substance-using counterparts (42). Studies have also demonstrated the value of integrating substance use treatment into HIV primary care (43,44).

Within this context, CTN HIV partners set out to build a program of HIV research. Mindful of staffing, resources, and priorities of community drug treatment programs, these studies focused on needs assessment, prevention, testing, and linkage to HIV treatment, while targeting sustainable practices.

## ACTIVITIES AND RESULTS

### CTN HIV Protocols

Since 2000, five HIV protocols have been implemented in the CTN. All shared defining features, intrinsic to community research networks, like the CTN. They were (1) national in scope; (2) program-diverse; (3) large-scale; (4) developed in ongoing partnerships between providers and researchers; (5) implemented through national training; (6) focused on real-world utility; and (7) conducted by frontline program providers and monitored by program supervisors – suggesting feasibility and the potential for sustainability. Below, the collaborative processes that supported the CTN HIV protocols are described.

### *Collaborative Processes for CTN HIV Protocols*

Following the IOM’s (2) charge, CTN HIV protocol development and implementation was the result of shared decision-making among researchers, service providers, and NIDA CTN staff. This process covered every aspect of research, including crafting study aims, methods, and procedures; implementing the protocol; interpreting and drafting results; and presenting and publishing findings. For example, frontline providers advised researchers about how to adjust research tasks to fit within the daily schedule of core substance abuse treatment activities. Providers advised researchers about how to introduce new and candid HIV sexual risk reduction interventions to busy substance abuse treatment counselors who might feel awkward, or even judgmental, about sexual material. In a study exploring HIV rapid testing, researchers and providers problem-solved potential needs for crisis intervention and fast linkage to HIV primary care that might arise. After protocols were completed, debriefing about results and process took place between providers and treatment program staff. Activities included offering strategies for HIV risk assessment, demonstrating risk reduction interventions to clinicians who did not directly participate in study intervention delivery, and presenting and dialoguing about study outcomes and lessons learned. An article in *Counselor Magazine*, “Addressing Sexual Issues,” was authored jointly by a community program

director and the principal investigators of the men's and women's risk reduction trials (45).

The collaborative process was supported by a CTN-wide HIV Special Interest Group. This volunteer partnership was a central voice for HIV priorities within the CTN. It served as a venue for (1) CTN-wide networking and strategizing among HIV-concerned providers and researchers; (2) conducting a CTN-wide HIV needs assessment survey (24); (3) helping launch CTN HIV protocols; (4) developing other (e.g., R01) HIV risk reduction studies using the CTN platform; and (5) choosing an HIV risk behavior assessment for use in CTN studies (i.e., Risk Behavior Survey) (46).

It should be emphasized that in implementing this work CTN HIV investigators joined a well-established tradition of researchers and community partners collaborating in large-scale networks to rapidly conduct HIV research. Indeed, the seven HIV/AIDS CTNs of NIAID (e.g., HIV Prevention Trials Network, AIDS Clinical Trials Group, etc.; see <http://www.hanc.info/about/Pages/networks.aspx>) have contributed groundbreaking advances in HIV prevention and treatment. However, the CTN differs from these networks because it is not HIV-dedicated. Rather, the CTN HIV research experience more closely parallels the HIV work of the NIDA-supported Criminal Justice Drug Abuse Treatment Studies Network (CJ-DATS). Over the first wave of CJ-DATS, from 2002 to 2008, it was comprised of nine research centers and criminal justice partner agencies that carried out 13 protocols testing integrated approaches for the treatment of offenders with substance use disorders. Of these, three were HIV protocols. Unlike the CTN HIV work, CJ-DATS protocols targeted populations within or transitioning from the criminal justice system (47).

The five CTN HIV protocols are presented in Table 1. Their major features, results, and significance are described below.

*CTN0012: Characteristics of Screening, Evaluation, and Treatment of HIV/AIDS, HCV Infection, and STI in Substance Abuse Treatment Programs.*

CTN0012 was a health services research study using standardized surveys completed by program administrators, program clinicians, and state administrators to determine current availability of HIV, HCV, and STI services, and related program and patient characteristics. Findings showed an array of infectious disease-related services provided in substance abuse treatment programs, but with great variability. While about half of programs reported providing HIV testing, this was as likely to be off-site referral as to be on-site testing (31,48). Services also varied by type of setting, type of addiction treatment, and patient medical characteristics (48). Administrators and clinicians reported lack of funding or health insurance, lack of patient acceptance, and state regulations as barriers (49). Treatment programs in states with specific policy about infectious disease services did have more explicit service guidelines than programs in states without them (50) and programs with addiction treatment tailored to

African American and Latino racial/ethnic subgroups also were more likely to offer these services (51).

*CTN0017: Reducing HIV-Related Risk Behaviors among IDUs in Residential Detoxification*

CTN0017 was a trial of three interventions for injection and sexual risk reduction for IDUs in detoxification: (1) two-session HIV/HCV counseling and education, from the NIDA Cooperative Agreement model for out-of-treatment substance users (52), plus treatment as usual (TAU); (2) single-session Therapeutic Alliance intervention (53), plus TAU; and (3) TAU alone. Among 632 IDUs in 8 residential detoxification centers, rates of entry into ongoing treatment were higher for Therapeutic Alliance, versus TAU, and entry into treatment was faster in Therapeutic Alliance versus TAU (54). In all three interventions, detoxification significantly decreased injection and sexual risk behavior over 6 months; there were no differences between interventions (55). Participation in treatment 2 months post-detoxification was associated with reduction in injection risk behavior (55).

*CTN0018: HIV/STD Safer Sex Skills Groups for Men and CTN0019: HIV/STD Safer Sex Skills Groups for Women, in Methadone Maintenance or Psychosocial Outpatient Treatment Programs*

Two gender-specific protocols were developed as companion trials with a single protocol development team, combined training of research staff, and parallel design, assessments, procedures, and interventions. They incorporated features of successful HIV sexual prevention programs (e.g., gender specificity, sufficient intensity, and skills training) (56) and included psychosocial outpatient treatment programs, typically underrepresented in HIV clinical trials.

CTN0018's Real Men Are Safe (REMAS) intervention adapted materials from the NIMH Multisite HIV Prevention Trial Group's Project Light (57) and Bartholomew and Simpson's Time Out for Men (58). REMAS was a five-session group intervention targeting HIV/STI transmission and prevention information, risk assessment, male and female condom use, safer sex negotiation, and the interplay between substance use and sexual behavior, a primary factor in men's sexual risk (59,60). Single-session HIV education (HIV-Ed) served as a standardized TAU control condition. Among 590 men in 7 methadone and 7 outpatient psychosocial programs, REMAS participants had significantly fewer unprotected sexual occasions than HIV-Ed participants at both 3-month (effect size = .10) and 6-month post-treatment (effect size = .17,  $p < .001$ ) (61). This effect was heightened for REMAS completers (attending the majority of sessions) compared to HIV-Ed completers (3-month effect size = .21; 6-month effect size = .34). At 3-month follow-up, sex under the influence decreased in REMAS men, but increased in HIV-Ed men (60).

CTN0019 adapted a safer sex skills building (SSSB) intervention for women in methadone maintenance, shown to be efficacious by El-Bassel and colleagues (62,63). SSSB was a five-session group intervention

TABLE 1. NIDA Clinical Trials Network protocols with HIV/HCV outcomes.

CTN protocol number	Recruitment dates	Subjects: Sites	Study name	Study type	Main outcomes or HIV/AIDS-related outcomes
0010	7/2003–12/2005	152:6	Buprenorphine/Naloxone Facilitated Rehabilitation for Heroin Addicted Adolescents/Young Adults (aged 15–21)	Randomized trial of two outpatient regimens in addition to TAU: BUP: extended treatment consisting of 12 weeks of tapered treatment; and DETOX: short-term detoxification over 14 days	At week 12, BUP patients reported less injection drug use and, within the BUP group females had less injection use than males. Injection risk did not change for persistent injectors. Sexual activity decreased in both genders and conditions, but sexual risk did not.
0012	7/2003–1/2005	269 administrators, 1723 providers, 48 state administrators	Screening, Evaluation, and Treatment of HIV/AIDS, Hepatitis C Viral Infections, and Sexually Transmitted Infections in Substance Abuse Treatment Programs	Survey of treatment program administrators and providers, and state administrators regarding the availability of and factors associated with infection-related health services	There was wide variability in services depending on program type, revenue source, and patient characteristics. Perceived barriers were lack of funding, regulations constraints, and patient attitudes.
0015	1/2004–10/2005	353:7	Women's Treatment for Trauma and Substance Use Disorders: A Randomized Clinical Trial	Randomized trial of Seeking Safety and TAU versus Women's Health Education and TAU to reduce posttraumatic stress and substance use symptoms	Among women with higher sexual risk (at least 12 unprotected sexual occasions/month), those in Seeking Safety showed greater reductions in HIV sexual risk behavior versus Women's Health Education 12 months post-treatment.
0017	11/2004–2/2006	632:8	HIV and HCV Intervention for Injection Drug Users in Inpatient Detoxification	Randomized trial of (1) HIV/HCV testing and counseling (2) Therapeutic Alliance (TA), and (3) TAU to reduce HIV risk behavior and increase entry into ongoing substance abuse treatment	Rates of entry into ongoing treatment were higher for TA than TAU; entry into treatment was faster in TA than TAU. Treatment participation within 2 months after detox predicted reductions in injection risk. Participation in detox was followed by significant decreases in drug injection and risk behaviors for up to 6 months; interventions added to TAU offered no improvement in risk behavior outcomes.

0018	5/2004–10/2005	590:14	Safer Sex Skills Groups for Men: Real Men Are Safe (REMAS)	Randomized trial of a five-session safer sex skills group (REMAS) versus single-session standard HIV education (HE) to reduce sexual risk behavior	There was significantly greater decrease in sexual risk behavior in REMAS versus HE at 3 months and 6 months.
0019	6/2004–10/2005	515:12	Safer Sex Skills Groups for Women: Safer Sex Skills Building (SSSB)	Randomized trial of a five-session SSSB group versus single-session standard HE to reduce sexual risk behaviors	There was significantly greater decrease in sexual risk behavior in SSSB versus HE at 6 months.
0032	1/2009–5/2009	1281:12	HIV Rapid Testing and Counseling	Randomized trial of (1) on-site rapid HIV testing/counseling, (2) on-site rapid HIV testing only, and (3) standard referral to off-site HIV testing to increase rates of HIV testing acceptance and to decrease HIV sexual risk behavior	Primary outcomes pending

Note: NIDA, National Institute on Drug Abuse; CTN, Clinical Trials Network; TAU, treatment as usual.

consisting of HIV risk assessment, HIV safer sex problem-solving, condom use practice, and safer sex decision-making and negotiation skill-building, with additional focus on gender role constraints in sexual relationships, a primary factor in women's sexual risk (56). SSSB was enhanced with risk assessment and safety planning for potential partner abuse. Among 515 women in 7 methadone maintenance and 5 psychosocial outpatient treatment programs, a significant difference in number of unprotected vaginal/anal sexual occasions was obtained between SSSB and HIV-Ed over time (effect size = .42,  $p < .001$ ). At 3-month post-treatment follow-up, significant decreases were observed in both interventions. At 6-month follow-up, while SSSB women maintained this decrease, those in HIV-Ed returned to baseline levels of unprotected sex. The effect of SSSB was enhanced by intervention completion, increasing the effect size to .62 (64).

*CTN0032: HIV Rapid Testing in Drug Treatment Programs in the United States*

CTN0032 rolled out newly available, rapid HIV testing in community substance abuse treatment programs to evaluate the utility of recent CDC guidelines to forego pre-test HIV risk reduction counseling (65). CTN0032 compares three strategies: (1) referral to off-site testing (TAU), (2) on-site rapid testing, and (c) on-site rapid testing with evidence-based RESPECT counseling (from CDC STD clinic trials) (66,67). The primary outcomes are rates of HIV testing and HIV sexual risk behavior change. The trial also includes an ancillary economic study to determine cost and cost-effectiveness (68). In 12 outpatient, inpatient, or methadone treatment programs, 1281 participants were randomized. Primary analysis and publications are forthcoming.

**HIV Secondary Analyses in CTN Non-HIV Protocols**

Mindful of the HIV vulnerability of substance users, the CTN included HIV risk behavior measures in the Common Assessment Battery for all protocols. A CTN cross-protocol database (at [www.ctndatashare.org](http://www.ctndatashare.org)) presented the opportunity to identify predictors of HIV risk behavior and needs for future HIV interventions targeting subgroups. Examples of secondary analyses from these non-HIV protocols are given below.

*CTN0015: Women's Treatment for Trauma and Substance Use Disorders*

CTN0015 (69) examined whether a trauma-focused intervention reduced HIV sexual risk behavior among women with posttraumatic stress and substance use disorders. The study compared 12 sessions of Seeking Safety, a cognitive behavioral trauma-focused treatment (70), to a women's health education control condition. Seeking Safety focuses on safe coping skills, communication and boundary setting, and identifying and reducing unsafe behavior, including sexual behavior. Among 353 women attending 7 outpatient psychosocial treatment programs, those with higher sexual risk and who were in Seeking Safety showed greater decrements in HIV sexual risk

behavior than those with higher risk in health education at the 12-month post-treatment follow-up ( $p = .04$ ) (71).

*CTN0010: Buprenorphine/Naloxone-Facilitated Rehabilitation for Opioid-Dependent Adolescents/Young Adults*

Opioid dependence is a serious, increasing problem among adolescents and young adults (72). CTN0010 (73) evaluated two buprenorphine/naloxone outpatient regimens in addition to standard, weekly substance abuse counseling: (1) extended treatment consisting of 12 weeks of tapered treatment; and (2) short-term detoxification over 14 days. Participants were 152 patients from 2 adolescent programs and 4 methadone programs, aged 15–21 years. Primary outcome analysis at week 12 showed that BUP patients had fewer opioid-positive urine screens ( $p < .001$ ), reported less injection behavior ( $p < .02$ ), and had better retention in substance abuse treatment ( $p < .001$ ). However, after cessation of medication, high rates of opioid-positive urine screens were obtained across the entire sample. HCV prevalence of 18% and HCV seroconversion in 4 of 83 patients by 12-week follow-up highlighted the threat of HCV, HIV, and other infections. Findings suggested that prompt and careful use of buprenorphine/naloxone, for a potentially extended period, could be an effective deterrent to HCV and HIV infection.

*Gender Differences in Rates and Correlates of HIV Risk Behaviors among Drug-Dependent Individuals*

Using data from five studies ( $N = 1429$  substance users; 45% women), this study obtained different rates of risk behavior and identified different predictors of risk behavior by gender. Women exceeded men in sex with multiple partners, unprotected sex with regular partners, and overall high-risk sexual behavior. Men exceeded women in IDU. Among women, sexual risk behavior was positively associated with alcohol use and psychiatric problem severity. Among men, sexual risk behavior was negatively associated with impairment in social function. Among both men and women, sexual risk behavior was associated with sexual abuse history, drug use severity, and legal system involvement (74).

**HIV Studies Using the CTN as a Platform**

Three studies are using the CTN as a platform for multisite HIV research. One study is piloting a novel, multilevel Directly Administered AntiRetroviral Treatment intervention to improve long-term ART medication adherence and reduce HIV-1 RNA viral load in methadone maintenance patients (75). Another study is testing the efficacy of an on-site HIV and Hepatitis Care Coordination intervention to increase hepatitis vaccination and attendance at HIV and/or HCV medical care intake (76,77). The third study is testing a novel, low-cost, brief audio computer-assisted HIV risk assessment and prevention intervention for substance abuse treatment programs, including parallel client risk behavior feedback reports and counselor reports (78).



## CONCLUSIONS, SIGNIFICANCE, AND LIMITATIONS

HIV, HCV, and other infections present a widespread and serious threat to the health of substance users; it is imperative to bring proven HIV behavioral interventions to community substance abuse treatment programs. However, these interventions can only be useful if they are acceptable, feasible, and effective within the daily operations of programs. Over the past decade, within the CTN framework, five large-scale, multisite HIV/HCV protocols, conducted in community treatment programs have addressed questions about effectiveness and feasibility of HIV behavioral interventions. One protocol provided a national profile of existing HIV and HCV services and regulations from which to make strategic plans. Two protocols focused on sexual risk reduction in outpatient programs. One protocol focused on HIV testing, risk reduction, and linkage to ongoing treatment for IDUs in inpatient detoxification. Aided by the inclusion of HIV risk behavior assessments in every CTN protocol, other CTN investigators have tracked the effects of their non-HIV-centered interventions on HIV risk behavior.

A few conclusions should be emphasized from the CTN HIV experience. First, with focused training and support, brief evidence-based HIV interventions can be integrated into the daily substance abuse treatment work of frontline providers. All interventions were delivered by frontline providers. It is noteworthy that, in all three HIV protocols (i.e., CTN0017, CTN0018, CTN0019), rates of frontline counselor adherence to the intervention exceeded 80%. However, participant attendance was problematic. For example, in the HIV/STD Safer Sex Skills trials, intervention completion rates were slightly above 50% (men) and slightly below 50% (women). Second, within the CTN multisite trial infrastructure, the effectiveness of HIV interventions can be tested to address the question of whether results from community effectiveness trials can be as robust as those from original single site efficacy studies, an important empirical issue. For the women's Safer Sex Skills trial, it was possible to compare the effect size obtained for SSSB in this community trial with that of the original efficacy study. The CTN effect size ( $d = .42$ ) was very similar to that ( $d = .46$ ) of the original efficacy study (63), as reported in Prendergast and colleagues' meta-analysis (19). It is relevant that in both the SSSB and men's REMAS trials effect sizes exceeded those reported for sexual risk behavior by Prendergast et al. (19). However, these effect sizes are still only considered small to medium. Third, within the large and diverse samples of these trials, compelling clinical and/or scientific questions can be answered in secondary analyses. Fourth, while some trials demonstrated superiority of enhanced HIV interventions, other trials obtained equal effects for TAU and enhanced conditions. These mixed results raise questions about the durability of enhanced interventions in community programs, already facing resource and funding constraints.

The question of whether CTN HIV effectiveness research interventions became part of daily practice in

community substance abuse programs, especially those in which the research was conducted, is a crucial one. Multiple dissemination efforts of CTN HIV research findings, interventions, and materials have been made to providers in the CTN and general community. Dissemination efforts have included traditional methods such as publications in academic journals and presentations at national and international professional conferences and meetings. It has also included a publication in a trade journal that is popular among substance abuse treatment counselors (45). Representation on websites has also enhanced visibility and promoted dissemination. The REMAS and SSSB interventions were identified as promising, evidence-based HIV prevention interventions by the CDC, and listed on the CDC Diffusion of Effective Behavioral Interventions website (see <http://www.cdc.gov/hiv/topics/research/prs/>). An online course is now being developed with these two interventions that will enable substance abuse treatment providers to earn continuing education credits free of charge.

The CTN also supports a web-based dissemination library (<http://ctndisseminationlibrary.org/>). As of January 2011 there have been 574 visits to the REMAS manual webpage, 674 visits to the SSSB manual webpage, 247 visits to the Therapeutic Alliance Intervention manual webpage, and 128 visits to the HIV and HCV Counseling and Education manual webpage. SSSB is now being tailored for use with other community treatment populations, including pregnant women (79) and adolescent girls (80).

Despite these promising dissemination activities, uptake of CTN HIV protocol interventions in community treatment programs remains mixed and a crucial limitation of the work. In CTN0010 alone, uptake was robust; four of the five participating clinics are using buprenorphine/naloxone for opioid-dependent youth. However, for other CTN protocols, there is limited evidence of intervention uptake, wholesale, into host community treatment programs after the end of the research. A survey study conducted with host programs that participated in the Safer Sex Skills trials explored the issues of uptake, and barriers to and promoters of sustainability. While clinicians and administrators rated the interventions very favorably (81), none of the programs had adopted either intervention in entirety (82). However, a few programs reported using a subset of the modules that make up the interventions. The primary reasons given for low uptake were "lack of staff time," "competing treatment priorities," and "inadequate mechanism for reimbursement." While lack of uptake is an important limitation of the work, it is an ongoing challenge to HIV researcher and provider partners to develop strategies that will enhance adoption of research interventions as an integral part of their research program from the outset (83).

Taken together, the limitations of low-intervention completion rates, modest effect sizes, and lack of adoption would seem to beg for cost-effective, less-cumbersome intervention delivery methods in future HIV intervention effectiveness research. Thus,

technologically innovative interventions, using computers or cell phones as delivery platforms, and minimizing provider resource burden, might improve upon these findings (84). In addition, important gaps in the CTN HIV portfolio also press for future projects, in priority areas identified by the National HIV/AIDS Strategy for the United States ([www.WhiteHouse.gov/ONAP](http://www.WhiteHouse.gov/ONAP)), at the intersection of HIV and substance use. Future research is needed to (1) reduce new HIV transmission through tailored HIV risk reduction interventions with HIV high-risk populations, including stimulant-using men-who-have-sex-with-men, racial/ethnic minority substance users, and substance-using adolescents; (2) reduce new transmission through tailored HIV risk reduction interventions with HIV seropositive substance users; (3) reduce new transmission by implementing pre- and/or post-exposure medication among HIV high-risk populations; (4) improve health outcomes for people living with HIV by integrating substance abuse treatment into HIV primary care settings and integrating HCV, STI, and other infectious disease services into substance abuse treatment programs; and (5) reduce HIV health disparities by tailoring HIV risk reduction, outreach and linkage, and adherence programs to the racial/ethnic groups disproportionately impacted by the epidemic.

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#### Declaration of Interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this article.

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