



CDC International HIV Prevention Research Activities Among Injection Drug Users in Thailand and Russia

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ABSTRACT *The Centers for Disease Control and Prevention (CDC) has participated in collaborative HIV prevention research activities in injection drug users (IDUs) with the Bangkok Metropolitan Administration (BMA) in Bangkok, Thailand, from 1995 to the present and with the Orel AIDS Center in Orel Oblast, Russia, from 2001 to 2003. Studies in Bangkok have included an HIV prevention trial preparatory cohort from 1995 to 1998, a seroconverter cohort from 1998 to the present, a phase III trial of the AIDSVAX B/E gp120 HIV vaccine from 1999 to 2003, and a phase II/III HIV prophylaxis trial with tenofovir scheduled to begin in 2005. Activities in Orel included a review of HIV surveillance data in 2001, focus group discussions and a case-control study with HIV-infected and -uninfected IDUs in 2001, a cross-sectional study with the female sex partners of male IDUs in 2002, and a community outreach intervention in 2002–2003. In Bangkok, 1,209 IDUs were enrolled in the preparatory cohort which revealed an HIV incidence of 5.8% per 100 person-years; 133 HIV-infected IDUs have been followed in the seroconverter cohort with >85% follow-up and HIV and tuberculosis care provided; 2,546 IDUs were enrolled in the HIV vaccine efficacy trial which was successfully completed with a follow-up rate of >95%, although the vaccine was not shown to be effective at reducing HIV incidence; and 1,600 IDUs will be enrolled in the daily tenofovir HIV prophylaxis trial in 2005. In Orel, initial focus group discussions and epidemiologic studies revealed low HIV knowledge and high rates of unsafe injecting and sexual practices among IDUs and their female sex partners; and educational campaigns and the community outreach intervention were developed and implemented. A steady decline in new HIV infections in IDUs was then observed in Orel in 2002–2003. CDC has participated in the conduct of successful collaborative HIV prevention research activities in Thailand and Russia over the past decade. The establishment of long-term relationships with in-country public health and community partners has been instrumental in the success of these efforts.*

KEYWORDS HIV, IDUs, Research, Russia, Thailand.

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INTRODUCTION

The Centers for Disease Control and Prevention (CDC) has conducted HIV epidemiologic and prevention research in the international setting since 1985. The initial focus of this work was initially on the descriptive epidemiology of HIV in Africa and Asia, but in the past decade the focus has shifted to interventional studies to prevent HIV transmission and disease. For example, CDC has collaborated on antiretroviral trials to prevent mother-to-child transmission of HIV,^{1,2} has worked on both HIV microbicide and vaccine trials,³⁻⁵ has conducted studies to assess the efficacy of cotrimoxazole chemoprophylaxis to prevent opportunistic illness,⁶ and has helped to monitor the implementation of antiretroviral therapy in the developing world.⁷ In the past several years, CDC has greatly expanded its global programmatic role to contribute to the reduction of HIV transmission and to improve HIV care and treatment, initially through the establishment of the Global AIDS Program in 2001⁸ and more recently through participation in the President's Emergency Program for AIDS Relief.⁹

In two countries, Thailand and Russia, CDC has collaborated with local public health authorities to conduct a series of HIV prevention research activities among injection drug users (IDUs). In Thailand, HIV prevention research studies have been conducted with the overall objective of identifying biomedical interventions that could contribute to reducing HIV infections in this population. In Russia, CDC responded to a request for epidemiologic assistance in 2001 to help evaluate an dramatic increase from 1998 to 1999 in reported HIV cases in IDUs in Orel Oblast and to help design prevention interventions for this population. This report summarizes these activities.

METHODS

Bangkok, Thailand

In Bangkok, CDC has partnered closely with the Bangkok Metropolitan Administration (BMA) to conduct HIV prevention research studies since 1991, when a capture-recapture technique was used to estimate the number of opiate users in Bangkok.¹⁰ The BMA operates 17 outpatient methadone clinics for both detoxification and maintenance throughout the city (Fig. 1) that provide services for approximately 8,500 IDUs annually. In this article, we will focus on four longitudinal studies conducted through this collaboration (Table 1).

First, an HIV prevention research preparatory cohort was conducted from 1995 to 1998 in collaboration with the BMA, Mahidol University, WHO, and UNAIDS.¹¹ The objectives of this study were to assess the feasibility of conducting a phase III vaccine efficacy trial in this population, as well as the willingness of IDUs to participate in vaccine research. 3,643 IDUs were screened, of whom 30% were HIV positive; the 1,209 HIV-uninfected IDUs who were enrolled were then followed every 4 months with intensive HIV risk reduction counseling, questionnaires, physical examinations, and blood specimens collected for HIV testing at each visit.

Second, IDUs who became HIV-infected during the preparatory cohort were offered enrollment in the seroconverter cohort which has been ongoing since 1998.¹² Newly HIV-infected IDUs are followed every 4 months, with questionnaires administered and biologic specimens collected at each visit. Counseling to prevent HIV transmission is given, and information on HIV-related social services is available. HIV and tuberculosis therapy are provided by the BMA to cohort members, and the clinic, immunologic, and virologic progression of HIV disease in the population is monitored.

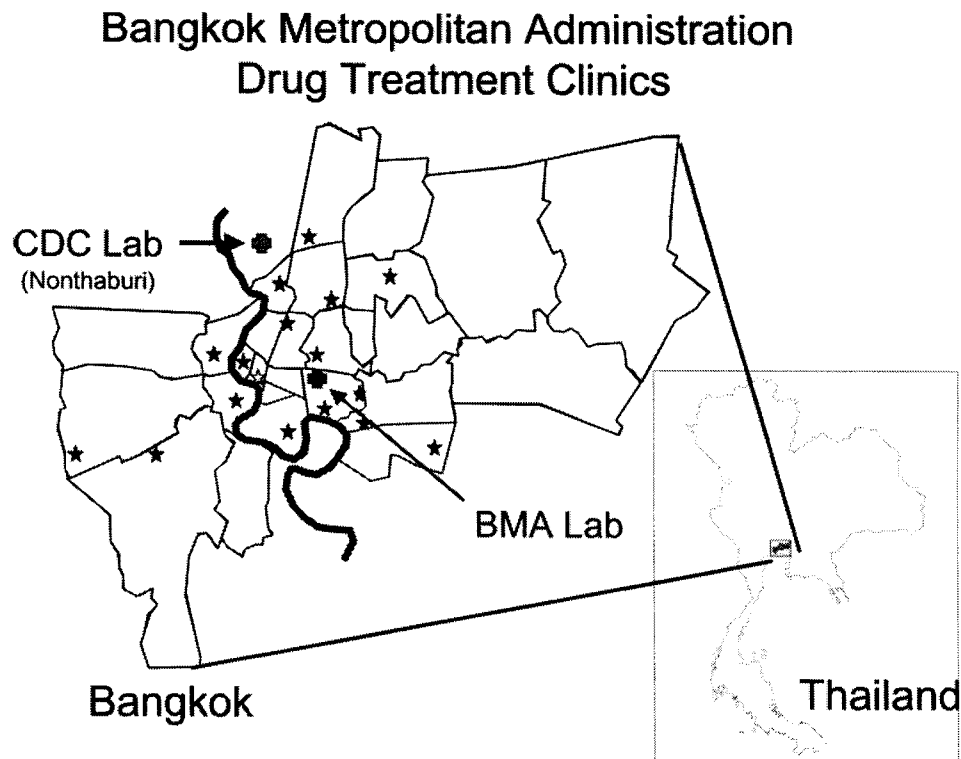


FIGURE 1. The 17 Bangkok Metropolitan Authority Drug Treatment Clinics, Bangkok, Thailand.

Third, a randomized, double-blind placebo-controlled HIV vaccine efficacy trial of the VaxGen rgp120 product (AIDSVAX B/E) was conducted among IDUs at the 17 BMA clinics from 1999 to 2003.¹³ This first HIV vaccine efficacy trial conducted in the international setting was conducted by a consortium, the Bangkok Vaccine Evaluation Group, which included the BMA, Mahidol University, VaxGen, and CDC. 4,983 IDUs were screened for the trial, of whom 2,546 HIV-uninfected IDUs were enrolled. Participants were randomized equally to vaccine or placebo arms, with seven injections administered at 0, 1, 6, 12, 18, 24, and 30 months.

Last, a randomized, double-blind placebo-controlled phase II/III combined safety and efficacy study of daily tenofovir as HIV antiretroviral prophylaxis is currently planned in IDUs at the 17 BMA clinics. 1,600 participants will be randomized equally to tenofovir or placebo arms, with an anticipated 12 months of enrollment followed by 12 months of follow-up. For the phase II safety study, a Data Safety Monitoring Board will review the safety data after 200 person-years of follow-up; if these safety data are acceptable, enrollment into the phase III efficacy trial will continue.

Each of these studies received Institutional Review Board Approval from the Thailand Ministry of Public Health and the CDC.

Orel, Russia

CDC's involvement in Russia began in 2001 in response to a request for epidemiologic assistance from Orel Oblast, a largely rural province located 400 km southwest

TABLE 1. Summary of Bangkok Metropolitan Administration and the Centers for Disease Control and Prevention (CDC) collaborative longitudinal HIV prevention research studies in injection drug users (IDUs) in Bangkok, Thailand

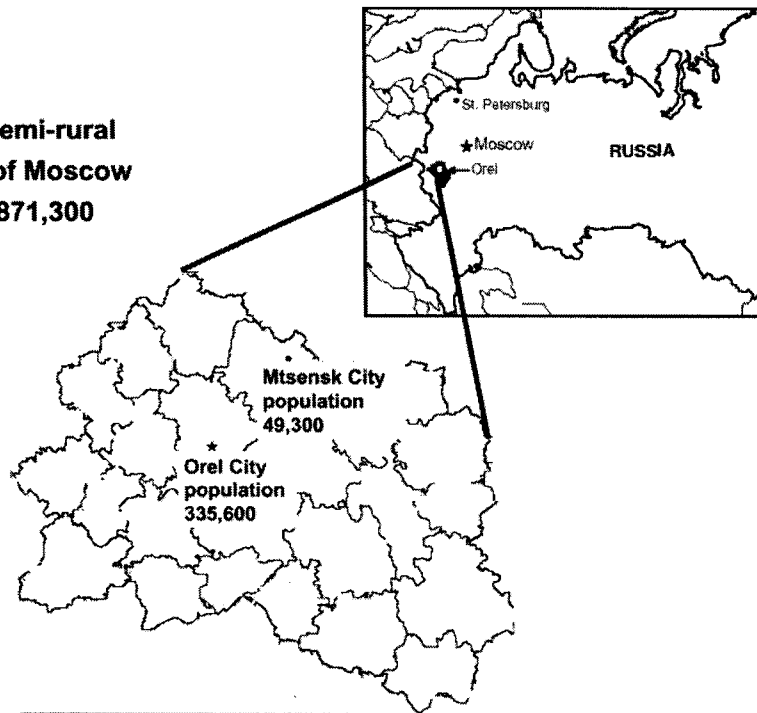
Study name	Year	Number of IDUs	Primary outcomes	Lessons learned
Preparatory cohort	1995–1998	1,209 HIV negative	HIV incidence of 5.8% per 100 person-years of follow-up, 76% retention rate at 24 months, and 71% at 36 months	A cohort of HIV-negative IDUs with high HIV incidence could be recruited and retained in Bangkok
Seroconverter cohort	1998–2004	133 HIV positive	>85% retention rate at 60 months and HIV and tuberculosis care provided	A cohort of HIV-positive IDUs could be followed and provided with high-quality HIV care and treatment
HIV vaccine trial	1999–2003	2,546 HIV negative	Trial successfully completed and vaccine not efficacious	A phase III HIV vaccine trial could be conducted successfully in IDUs in the developing world
HIV prophylaxis trial	2005	1,600 HIV negative	To begin in 2005	

of Moscow (Fig. 2), when a 30-fold increase in HIV cases in IDUs was observed.¹⁴ To address this request, CDC collaborated with the Orel AIDS Center to conduct a series of epidemiologic and HIV prevention activities (Table 2).

First, HIV surveillance data were reviewed and analyzed in 2001, and the computerized HIV surveillance system was enhanced to facilitate data entry and more rapid analyses. Second, focus group discussions with 18 HIV-infected and -uninfected IDUs were conducted at the Orel AIDS and Narcology Centers in 2001 to elicit information on HIV knowledge and information sources, drug use situations, HIV risk perception and prevention barriers, and access to HIV testing and drug treatment. Third, a case-control study was conducted at the Orel AIDS and Narcology Centers in 2001 with 50 HIV-infected and 100 HIV-uninfected IDUs who had been tested for HIV within the past year. An instrument consisting of 50 questions eliciting demographic information and injecting and sexual risk reduction behaviors was self-administered to each participant. Fourth, a cross-sectional study of HIV risk behaviors among female sexual partners of male IDUs was conducted in 2002. Eighty women who reported vaginal sex with a current or former male IDU in the past 2 months were recruited either through street outreach (58%) or through the Orel AIDS and Narcology Centers (42%). An anonymous, self-administered written questionnaire was used with questions on sexual, drug use, and HIV risk reduction behaviors. Last, a community outreach intervention was developed collaboratively by the Orel AIDS Center and CDC.

Orel Oblast

- Industrial, semi-rural
- 400km SW of Moscow
- Population 871,300

**FIGURE 2.** Orel Oblast, Orel, Russia.**TABLE 2.** Summary of Orel AIDS Center and Centers for Disease Control and Prevention (CDC) collaborative HIV prevention activities in injection drug users (IDUs) in Orel Oblast, Russia

Activity name	Year	Number of IDUs	Primary outcomes	Lessons learned
Surveillance review	2001	Not Applicable	Rapid increase in HIV cases in IDUs	HIV epidemic in IDUs in Orel was confirmed
Focus group discussions	2001	16 HIV positive and 2 HIV negative	Low levels of HIV prevention knowledge	HIV education urgently needed in this population
Case-control study	2001	50 HIV positive and 100 HIV negative	High rates of unsafe injecting and sexual behaviors	Behavioral interventions needed to be implemented rapidly in IDUs
Cross-sectional study	2002	80 female sex partners	High rates of unprotected sex with male IDU partners	Interventions needed to be directed at heterosexual partners of IDUs as well as IDUs themselves
Community outreach pilot	2002–2003	548	HIV prevention information disseminated	Peer outreach workers could effectively target HIV prevention messages to IDUs

RESULTS

Bangkok, Thailand

In the preparatory cohort,¹⁵ this largely male (93%) and young (median age 31 years) population was successfully followed with a retention rate of 76% after 24 months. Other pertinent findings included a high HIV incidence of 5.8% per 100 person-years of follow-up, despite intensive risk reduction counseling; the willingness of IDUs to participate in a phase III vaccine trial¹⁶; a baseline prevalence of Hepatitis B and C viruses of 48% and 96%, respectively; and that the majority of incident HIV infections were caused by HIV-1 subtype E (79%) with the remainder subtype B (21%). The information on subtypes led to the reformulation of the Vaxgen gp120 AIDS-VAX vaccine product to include both subtypes E and B for testing in Thailand.¹⁷

The seroconverter cohort demonstrated that a cohort of HIV-infected IDUs could be followed longitudinally in Thailand.¹⁵ There was a high follow-up rate of >85% after 60 months, and high-quality medical care was provided including anti-tuberculosis and antiretroviral therapy. Important scientific findings that resulted from the follow-up of this cohort included the description of one of the first cases of HIV-1 superinfection reported in the literature,¹⁸ differences in the viral load in IDUs infected with HIV-1 subtypes E and B,¹⁹ and new HIV-1 recombinant subtype E/B forms reported (HIV-1 CRF01_AE/B).²⁰

The HIV vaccine efficacy trial among IDUs was successfully conducted with >95% of participants receiving all scheduled injections and study visits.¹⁵ The effectiveness of HIV risk reduction counseling in this trial was demonstrated with statistically significant reductions in the rates of injecting (94% to 56%) and needle sharing (33% to 16%) during the course of the trial.²¹ The HIV infection rates between the vaccine arm (8.4%) and the placebo arm (8.3%) were not significantly different, resulting in a vaccine efficacy of only 0.1%⁵ which demonstrated that the vaccine did not prevent HIV infection.

Because of the conclusion of the HIV vaccine efficacy trial, the BMA and the CDC have continued epidemiologic follow-up of this IDU population. Unfortunately, despite continued risk reduction counseling, the HIV incidence rate has remained stable at 3.1% per 100 person-years of follow-up. To identify a biomedical intervention that could contribute to the reduction of this high incidence rate, the BMA and CDC will be studying the potential role of HIV antiretroviral prophylaxis as a supplement to continued risk reduction counseling. Accordingly, a randomized controlled trial of oral daily tenofovir as HIV preventative therapy will be initiated in 2005, and if successful, this intervention could provide a useful adjunctive prevention tool for this population.

Orel, Russia

The review of existing Orel surveillance data confirmed that there had been a dramatic increase in HIV case rates from 1998 to 2001 from 5 to 202 per 100,000 tests performed, whereas no changes in overall HIV-testing patterns were observed.²² The majority of persons reported with HIV from 1999 to 2001 were male (82%), young (90% <age 30), and IDUs (82%), although the proportion of cases among women increased from 12% to 22% during this period. HIV cases were identified through a large-scale HIV-testing program with approximately 150,000 tests done annually in Orel's population of 900,00 residents: 43% were routine, mandatory tests in groups such as antenatal women, blood donors, and persons tested for job requirements; 40% were in high-risk populations such as persons tested at an anon-

ymous HIV testing site, drug treatment centers, and tuberculosis and medical patients; and 19% were repeat tests in persons previously screened for HIV.²³ The predominant HIV-1 subtype throughout Russia is known to be subtype A.²⁴

The focus group discussions conducted with IDUs in 2001 revealed a generally low knowledge of HIV transmission patterns and high rates of unsafe injection and sexual risk behaviors. The case-control study demonstrated high levels of unsafe injection practices in both HIV-infected and -uninfected IDUs, with significantly higher rates of high-risk behaviors in HIV-positive compared with HIV-negative IDUs: multiple injecting partners in the past year (7 vs. 3), injecting with a used syringe (86% vs. 50%), and drawing drug from a shared container (100% vs. 62%).²⁵

The cross-sectional study among female sex partners of IDUs demonstrated that 41% had used injection drugs themselves, 18% were currently IDUs, 28% had a history of a sexually transmitted disease, 75% had been tested for HIV, and 12% reported that they had tested HIV positive in the past. Overall, 84% had a steady male partner, of whom 48% were currently IDUs and 24% were known to be HIV positive; 52% of the women had never used a condom with their steady partners. Moreover, 41% had one or more casual sexual partners in the past 6 months, of whom 81% were currently IDUs and 32% were known to be HIV positive.²⁶ These data demonstrated that female sex partners of IDUs in Orel were at substantial risk of HIV infection, largely through heterosexual contact but often through their own injection practices as well.

These surveillance and epidemiologic data, combined with a limited ability of the HIV program in Orel to reach out-of-system IDUs, led to the development of educational interventions for IDUs to help prevent further increases in HIV. The Orel AIDS Center and CDC trained peer outreach workers to identify key venues where IDUs congregated, such as in parks, apartment buildings, cafes, and on the streets and then to discuss HIV risk reduction strategies and to distribute HIV educational materials to IDUs in these settings. Referrals for HIV testing and care were made as well. 548 separate encounters were made in an initial community outreach pilot conducted from October, 2002, through May, 2003, with HIV educational materials distributed to 1,072 persons. These outreach activities, in addition to educational campaigns, are ongoing.²²

Last, from 2002 to 2003, a steady decline in the number of new HIV cases was documented in Orel during a period in which HIV-testing patterns were unchanged in the community (Fig. 3).

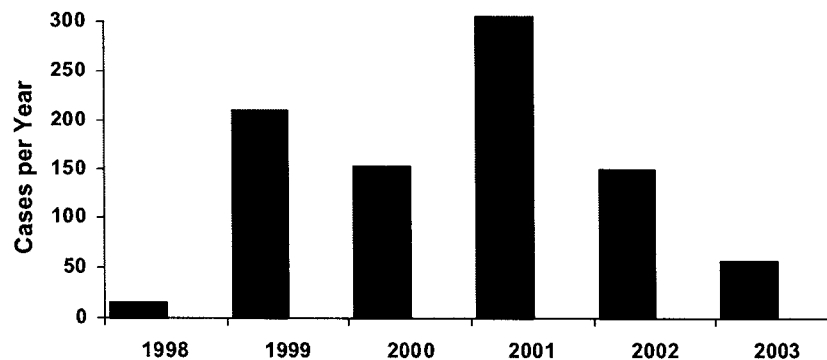


FIGURE 3. New HIV diagnoses, Orel Oblast, Orel, Russia, 1998–2003.

DISCUSSION

The activities described in this article provide important examples of how CDC has collaborated with in-country public health authorities to conduct HIV prevention activities with IDUs in the international setting. A number of common elements can be identified between the collaborations in Thailand and Russia, including the availability of considerable in-country expertise on HIV prevention among IDUs, established physical and personnel infrastructures on which new activities could be layered, local commitment to reducing HIV incidence in IDUs, and the establishment of close working relationships with the IDU communities themselves. There are also evident differences between the described activities in the two countries: in Thailand, the activities described in this article were longitudinal cohort studies and clinical trials, because prevention activities in IDUs are conducted through the CDC's Global AIDS Program; whereas in Russia, surveillance, epidemiologic, and prevention activities were conducted in response to a request for epidemiologic assistance.

Overall, the work in Thailand demonstrated that large cohorts of HIV-infected and -uninfected IDUs can be followed successfully and that a complex vaccine efficacy trial can be conducted in a high-risk IDU population in a scientifically and ethically rigorous fashion. The feasibility of providing high-quality medical care including preventative therapy for tuberculosis and antiretrovirals to this population was also shown. This work has demonstrated that intensive risk-reduction counseling for IDUs can be successful in reducing high-risk injecting practices; unfortunately, however, these interventions have not eliminated new HIV infections in this population. Accordingly, biomedical interventions are being sought to reinforce existing behavioral interventions—although the first HIV vaccine trial in this population failed to demonstrate efficacy, it is hoped that other interventions, such as antiretroviral prophylaxis and perhaps future HIV vaccine candidates, may prove effective in preventing HIV infections. In the meantime, the CDC Global AIDS Program is supporting a wide range of HIV prevention activities for IDUs in Bangkok, including voluntary HIV counseling and testing, treatment and care for HIV, screening and chemoprophylaxis for tuberculosis, immunization for hepatitis B, and community outreach activities to educate young IDUs about drug detoxification and available clinical care services. If tenofovir proves effective, CDC will work with the Thailand Ministry of Public Health as well and the BMA to discuss the optimal ways to implement this intervention.

In Russia, many valuable lessons were learned through the collaborative efforts described in this article. For example, the importance of the HIV surveillance system was critical both to the initial identification of the HIV epidemic in IDUs in Orel and to the documentation of the subsequent decline in HIV cases. In addition, the qualitative and quantitative research done through focus group discussions, case-control, and cross-sectional studies helped to highlight relatively low rates of HIV knowledge and high rates of high-risk injection practices that were then targeted with HIV prevention efforts. There are a variety of hypotheses that could explain the reduction in newly reported HIV cases in Orel in the past several years. Although it has been hypothesized that the decrease in HIV cases in IDUs in Orel was attributable to changes in national HIV-screening policies,²⁷ the number of HIV tests conducted annually in Orel has remained relatively constant for the past 5 years. In addition, other factors may have contributed to diminished HIV transmission, including the saturation of drug-sharing networks, a changing youth culture

which made it less “fashionable” to inject, the availability of 24-h pharmacies that supplied clean needles and syringes, and more permissive policing policies.²² However, the HIV prevention efforts of the Orel AIDS Center, including focused educational campaigns and innovative programs such as the street outreach peer education intervention, may have contributed to the observed declines in HIV cases as well.

In summary, these HIV prevention activities among IDUs in Thailand and Russia provide important examples of successful public health collaborations in the international setting. Valuable public health lessons were learned as well: in Bangkok, it was demonstrated that cohorts of both HIV-infected and -uninfected IDUs could be followed, high-quality HIV care and treatment for IDUs could be provided, and a phase III vaccine efficacy trial in this marginalized population could be conducted; in Orel, the existence of an HIV epidemic among IDUs was confirmed, the urgent need for HIV education and behavioral interventions for IDUs and their female sexual partners was demonstrated, and the effectiveness of peer-outreach workers in disseminating HIV prevention messages to IDUs was shown. The CDC Global AIDS Program is working to prevent HIV spread and to promote care and treatment for IDUs and has provided technical assistance for HIV programs for IDUs in Thailand, Brazil, Vietnam, Cambodia, China, and the Central Asia Republics.⁸ With a continued commitment to the development of effective HIV prevention programs and new biomedical interventions for IDUs, the incidence of HIV infection in this population on a global scale can be reduced.

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