Summary

Drug dependence is a complex, chronic, relapsing condition that is often accompanied by severe health, psychological, economic, legal, and social consequences (IOM, 1990; 1995). It is manifested by a complex set of behaviors including compulsive drug craving, seeking, and use that interferes with an individual's physical, mental, and social functioning (IOM, 1997; McLellan et al., 2000). Similar to other chronic conditions, such as heart disease or diabetes, individuals with drug dependence can stabilize their condition by making behavioral changes and with the use of appropriate medications (WHO et al., 2004). Drug-dependent individuals have high rates of medical and psychiatric comorbidity and increased risk of pre-mature mortality (DHHS, 2006). Injecting drug users are particularly vulnerable to HIV and other bloodborne infections (such as hepatitis C) as a result of sharing contaminated injecting equipment. All drug dependent individuals, including injecting drug users (IDUs), may be at increased risk of HIV infection because of high-risk sexual behaviors.

There are an estimated 13.2 million injecting drug users worldwide—78 percent of whom live in developing or transitional countries (Aceijas et al., 2004). The sharing of contaminated injecting equipment has become a major driving force of the global AIDS epidemic and is the primary mode of HIV transmission in many countries throughout Eastern Europe, the Commonwealth of Independent States,1 and significant parts of Asia (UNAIDS, 2006). In some cases, epidemics initially fueled by the sharing of contaminated injecting equipment are spreading through sexual transmission from IDUs to non-injecting populations, and through perinatal transmission to newborns. Reversing the rise of HIV infections among IDUs has thus become an urgent global public health challenge—one that remains largely unmet.

STUDY GOALS AND APPROACH

In response to this challenge, in 2005 the Joint United Nations Programme on HIV/AIDS (UNAIDS) and the Bill & Melinda Gates Foundation commissioned the Institute of Medicine to undertake an expedited review of the scientific evidence on strategies to prevent HIV transmission through contaminated injecting equipment, with a specific focus on high-risk2 countries—namely in Eastern Europe, the Commonwealth of Independent States, and significant parts of Asia—where injecting drug use is, or is on the verge of becoming, the primary driver of the HIV epidemic.

The charge to the Committee included five questions. They are listed here in the order in which they are addressed in the chapters. The Committee found it most helpful to first discuss the evidence on the intermediate outcomes of drug-related risk (question one) and sex-related risk (question two) prior to examining the impact on HIV transmission (question three).

(1) What impact do needle and syringe exchange, disinfection programs, drug substitution programs, drug treatment programs, and counseling and education on the extent and frequency of drug injection?

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1 The Commonwealth of Independent States includes Azerbaijan, Armenia, Belarus, Georgia, Kazakhstan, Kyrgyzstan, Moldova, Russia, Tajikistan, Turkmenistan, Uzbekistan, and Ukraine.

2 In this report, such countries are labeled as “high-risk,” indicating that injecting drug use is, or is on the verge of becoming, the primary driver of the HIV epidemic.
(2) What evidence is there on the extent to which these prevention strategies help reduce HIV transmission from IDUs to their sex partners and through maternal-to-child transmission to their offspring?

(3) How effective are such programs in reducing HIV transmission among IDUs?

(4) To what extent do such programs also increase the use of health and social services and drug treatment?

(5) What evidence is there that programs aimed at reducing the risk of HIV transmission among IDUs are more effective when they are part of a comprehensive array of services, which include outreach, HIV prevention education, counseling, referral to drug substitution treatment, drug rehabilitation services, and medical and psychosocial support?

In response to this charge, the Committee convened a public workshop in Geneva, Switzerland, in December 2005 to gather information from experts on IDU-driven HIV epidemics in the world’s most affected regions (see Appendix A for the meeting agenda). The Committee also conducted a comprehensive search of the English language peer-reviewed scientific literature, and evaluated previous systematic reviews and reports prepared by international organizations. (See Appendix B for further detail on the Committee’s review methods.) To assess this evidence, the Committee held a closed meeting in Washington, DC, in March 2006, and also conducted numerous conference calls.

Although the report focuses on HIV prevention for IDUs in high-risk countries, the Committee considered evidence from countries around the world. The findings and recommendations of this report are also applicable to countries where injecting drug use is not the primary driver, but in which injection drug use is nevertheless associated with significant HIV transmission.

**HIV PREVENTION STRATEGIES FOR IDUs**

This report focuses on programs designed to prevent the transmission of HIV among IDUs. These programs range from efforts to curtail non-medical drug use to those that encourage reduction in high-risk behavior among drug users. The term “harm reduction” is often used to describe programs such as sterile needle and syringe access, because their primary aim is to reduce the harms related to drug use among those who are unable or unwilling to stop using drugs. However, because the term has a wide range of interpretations, the Committee refers to all interventions in this report as HIV prevention programs for IDUs.

The Committee grouped the wide range of HIV prevention strategies for IDUs into three categories: (1) drug dependence treatment, which include both pharmacotherapies and psychosocial interventions; (2) sterile needle and syringe access; and (3) outreach and education programs (see Box S.1). Other HIV prevention strategies, such as voluntary counseling and testing, antiretroviral therapy, and prevention and treatment of sexually transmitted infections, are important for IDUs but also apply to broader populations. While there is a large body of evidence evaluating the effectiveness of these interventions, the Committee’s review was limited to those prevention interventions specific to IDUs. Therefore, Chapter 1 includes only a brief overview of these broader interventions.

The most effective way to reduce the risks of HIV transmission among injecting drug users is to stop drug use. However, not all drug users are ready or able to take this step. An individual IDU’s risk of HIV infection is mediated by both individual-level factors (such as severity of dependence and co-existing psychiatric disorders) and structural-level, or environmental, factors.
(such as drug laws and law enforcement and socioeconomic stability) (Rhodes et al., 2005). The vast majority of HIV prevention efforts target the risk behavior of individual drug users (Rhodes et al., 2005), for example, through drug treatment or outreach. Structural-level interventions, which attempt to create an environment supportive of individual behavioral change, have received less attention from researchers and policymakers (Rhodes et al., 2005; Burris et al., 2004). Examples of structural-level interventions include legal reform and programs to reduce stigma and discrimination against HIV-infected people and drug users.

BOX S-1 Key HIV Prevention Interventions for IDUs

**Drug treatment—pharmacotherapies**

Two primary types of pharmacotherapies are available for treating opioid dependence: agonist agents and antagonist agents. No pharmacotherapies have been found to be consistently efficacious in treating stimulant dependence.

Opioid agonist maintenance medications work by preventing withdrawal symptoms and reducing opioid cravings—and therefore the need to use illicit drugs—and also by diminishing the effects of opioid use by creating cross-tolerance to their effects (IOM, 1995). Agonist medications have two primary clinical applications: they can be used on a limited basis to facilitate opioid detoxification, or they can be administered over a longer period as a maintenance treatment (IOM, 1995). This report focuses on the latter application. In maintenance therapy, the agonist agent is administered at higher doses for a sustained period. The goal of maintenance treatment is to reduce illicit drug use and high-risk behavior by building cross-tolerance to the effects of other opioids, thereby allowing patients to stabilize physiologically and psychologically, so they can reengage in normal life activities (IOM, 1990; WHO et al., 2004). Due to their long half life and resulting steady state, opioid agonists are not intoxicating and do not impair function when used at clinically appropriate and stable doses over time (IOM, 1990; IOM, 1995). Methadone, a full opioid agonist, is the most widely used and researched agonist maintenance medication for the treatment of opioid dependence (WHO et al., 2004). Buprenorphine is a partial opioid agonist that is used increasingly as an alternative to methadone. Both methadone and buprenorphine are classified as psychotherapeutic medicines for substance dependence treatment programs on the WHO list of essential medicines (WHO, 2005c). Other pharmacological agonist agents have been studied in limited settings, but are not widely used and are not reviewed in this report (MacCoun and Reuter, 2001; WHO et al., 2004).

An alternative to opioid agonists are antagonist agents that block the effects of opioids. Naltrexone, the most widely used opioid antagonist, helps patients maintain long-term abstinence from opioids (WHO, 2005a). Oral naltrexone provides a relatively long-lasting blockade (one to three days, depending on the dose) of euphoric or rewarding effects of heroin or other opioids, and thus may help prevent resumption of opioid use (O’Brien and Kampman, 2004). New long-acting, injectable formulations of naltrexone produce adequate opioid blockade for up to one month (Dunbar et al., 2006). Before beginning naltrexone treatment, patients must be detoxified (medically withdrawn from heroin or other opioids), because naltrexone will precipitate severe withdrawal symptoms in people physically dependent on opioids (O’Brien and Kampman, 2004).

**Drug treatment—psychosocial**

A second major approach to drug treatment involves psychosocial interventions, which include a broad range of psychological and behavioral strategies, used either alone or in combination with pharma-

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3 Detoxification refers to medically-supervised withdrawal to a drug-free state over a short period of time (typically 5-7 days, but up to several months). When used to assist with detoxification, the agonist agent helps to relieve patient discomfort during withdrawal and the dosage is slowly tapered over time until the person reaches a drug-free state (IOM, 1990; 1995). Detoxification alone is not considered an effective treatment (IOM, 1990). Studies show users have high rates of relapse to drug use when detoxification is not followed by further therapeutic intervention (IOM, 1990).
cotherapies and other medical or social interventions (Mayet et al., 2004). These interventions may be provided with varying levels of intensity, frequency, and duration, using different approaches including outpatient, partial hospital, hospital, or residential-based programs. Psychosocial interventions may be delivered in individual or group settings, and may also include family members in order to address family functioning (e.g., through behavioral family therapy). Examples of psychosocial interventions include specific behavioral interventions (e.g., cognitive behavioral therapy, contingency management) as well as collection of program models (e.g., therapeutic communities, 12-step programs) (see Chapter 2, Box 2.2 for a description of these interventions).

Sterile needle and syringe access

Sterile needle and syringe access may include needle and syringe exchange; the legal, accessible, and economical sale of needles and syringes through pharmacies, voucher schemes, physician prescription programs, or vending machines; supervised injecting facilities or rooms; and disinfection programs.

In most cases, needle and syringe exchange (NSE) is part of a multi-component HIV prevention effort. The Committee uses the term “multi-component HIV prevention programs that include needle and syringe exchange” to refer to programs that combine NSE with one or more of the following services: outreach, health education in risk reduction, condom distribution, bleach distribution coupled with education on needle disinfection, and referrals to substance abuse treatment and other health and social services.

Outreach and education

Outreach and education rely on peers and local health workers to identify IDUs and provide education on preventing HIV infection, and to serve as guides to health and social services (WHO, 2004a). Outreach workers may distribute information on HIV/AIDS, bleach kits for disinfecting injection equipment, and condoms. While some programs are linked to needle and syringe exchanges or drug treatment clinics, outreach efforts often occur outside clinical settings and separate from other interventions.

**CONCLUSIONS ON THE EFFECTIVENESS OF HIV PREVENTION INTERVENTIONS**

The Committee’s major conclusions and key recommendations regarding the five questions in the charge follow (see Box S.2 for a complete list of recommendations):

**Question 1: What impact do intervention programs have on the extent and frequency of drug injection?**

The Committee interpreted this question as asking about the extent to which these interventions affect drug-related HIV risk behavior, including frequency of drug use, injection, and sharing of contaminated equipment.

**Drug Treatment**

**Pharmacotherapies:** Strong and consistent evidence from a number of well-designed, randomized controlled trials shows that opioid agonist maintenance treatment—including methadone and buprenorphine—is effective in reducing illicit opioid use and increasing retention of opioid-dependent patients in drug abuse treatment (Mattick et al., 2003a; Mattick et al., 2003b; Gowing et al., 2004; 2005). There is also strong evidence that this treatment reduces drug-related HIV risk behavior, including frequency of injecting and sharing of equipment (Gowing et al., 2004; 2005). Given the strong evidence of its effectiveness, opioid agonist maintenance treatment should be made widely available, where feasible. The medication should be provided in
sufficiently high doses and for a sufficient duration for therapeutic effects to occur (Sees et al., 2000; Vanichseni et al., 1991; Strain et al., 1993; Faggiano et al., 2003). Programs should be scaled up enough to exert a public health impact, provide adequate public health infrastructure, include a plan for sustainability, and balance strategies to decrease potential diversion of treatment drugs with strategies to disseminate them.

Despite strong pharmacological evidence and theoretical potential for naltrexone—an opioid antagonist (see Box S.1)—evidence regarding its efficacy in controlled clinical trials is inconclusive. Efficacy and effectiveness studies of naltrexone treatment have been limited by problems with high patient attrition and the limited patient appeal of naltrexone (Johansson et al., 2006; Minozzi et al., 2006). However, naltrexone may be effective when used in circumstances where patients’ adherence to medication and retention in treatment can be closely monitored and facilitated (Cornish et al., 1997; Tennant et al., 1984; Washton et al., 1984; Krupitsky et al., 2004; Krupitsky et al., 2006). Given its potential benefits and lack of harmful effects, naltrexone should be made available, where feasible, as part of a multi-component drug treatment strategy. However, more research is needed on the effectiveness of naltrexone for various patient populations and settings.

No pharmacotherapies have been found to be consistently efficacious in treating stimulant dependence. More research is urgently needed to identify effective pharmacotherapies for stimulant dependence, particularly for amphetamine-type stimulants, which have emerged as a major problem in many parts of the world.

**Psychosocial:** While opioid agonist maintenance therapy has been shown to be very effective in treating opioid dependence, no psychosocial intervention alone—without additional pharmacotherapy—has been shown to be efficacious in treating opioid dependence. Research shows that adjunctive psychosocial interventions may improve outcomes for individuals enrolled in opioid agonist treatment (McLellan et al., 1993), but more research is needed on the benefit and cost-effectiveness of adding psychosocial interventions to such treatment in high-risk countries, and the effectiveness of those interventions in particular cultural contexts and patient subgroups. More research is also needed to determine the relative effectiveness of various psychosocial interventions in treating opioid dependence in places where opioid agonist maintenance therapy is not available or accessible.

Because proven pharmacological interventions are available only for opioid addiction and not for stimulants or other classes of injectable drugs, psychosocial approaches are the primary treatment option for individuals dependent on these substances. One such approach—contingency management—entails consistently rewarding patients (with monetary vouchers or other reinforcers) who remain abstinent or fulfill other verifiable treatment objectives, and withholding rewards when patients do not abstain (or successfully accomplish other specified objectives). A number of randomized controlled trials have found that contingency management is associated with longer retention in treatment, and time abstinent from stimulants, among individuals who are primarily dependent on stimulants (Higgins et al., 1991, 1993, 1994, 2000; Petry et al., 2004), and among individuals who are dependent on both stimulants and opioids and enrolled in agonist maintenance therapy (Piotrowski et al., 1999; Schottenfeld et al., 2005; Peirce et al., 2006). While most studies have examined the efficacy of contingency management for cocaine users, two randomized clinical trials show that it is efficacious in reducing methamphetamine use (Shoptaw et al., 2005; Shoptaw et al., 2006). More research is needed to develop cost-effective and feasible alternatives to voucher-based contingency management for treating stimulant dependence that can be implemented outside research settings.
There is also modest evidence of effectiveness for several additional psychotherapeutic approaches to treating stimulant abuse. These include combined individual drug counseling and intensive group drug counseling, cognitive behavioral therapy, and the community reinforcement approach combined with contingency management (Crits-Christoph et al., 1999; Maude-Griffin et al., 1998; Monti et al., 1997; McKay et al., 1997; Carroll et al., 1994; Higgins et al. 2003; Roozen et al., 2004) (see Chapter 2, Box 2.2 for definitions of these interventions).

There is relatively weak evidence regarding the effectiveness of therapeutic communities, chemical dependency programs, and drug anonymous treatments, but these are an important treatment options for opioid-dependent individuals who will not accept or cannot access opioid agonist maintenance treatment, or for individuals dependent on other classes of drugs (IOM, 1990; Hubbard et al., 2003). Studies have found that length of time in treatment in these programs is the strongest predictor of positive treatment outcomes.

Given the potential benefits and lack of harmful effects, the following treatments should also be made available as part of a multi-component treatment system, where feasible, but should be accompanied by rigorous evaluation: (1) specific behavioral interventions (contingency management, cognitive behavioral therapy, community reinforcement approach, and individual drug counseling for treating stimulant dependence); and (2) chemical dependency treatment, therapeutic communities, and Drug Anonymous groups for patients dependent on any drug class who are interested in abstinence-oriented treatment.

**Sterile Needle and Syringe Access**

**Multi-component programs that include needle and syringe exchange:** A large number of studies and review papers—most from developed countries—show that participation in multi-component HIV prevention programs that include NSE is associated with a reduction in drug-related HIV risk behavior, including self-reported sharing of needles and syringes, unsafe injection and disposal practices, and frequency of injection. Although many of the studies have design limitations, this finding is consistent across a large number of studies.

One concern that has been raised is whether HIV prevention programs that include needle and syringe exchange leads to unintended consequences. The few studies that have examined the unintended consequences of programs that include NSE found no evidence that they lead to more new drug users, more frequent injection among established users, expanded networks of high-risk users, changes in crime trends, or more discarded needles in the community. However, few studies have specifically focused on these outcomes, and this issue could benefit from further study.

Given consistent evidence that multi-component HIV prevention programs that include sterile needle and syringe is associated with reductions in drug-related HIV risk behavior, such programs should be implemented where feasible.

**Alternative access to needles and syringes:** Eliminating criminal penalties for possessing needles and syringes—and enhancing legal access via pharmacy sales, voucher schemes, and physician prescription programs—are alternative avenues for making sterile needles and syringes available to IDUs. Evaluations of these strategies have primarily been conducted in the United States and have focused on the acceptability of such programs by drug users, pharmacists, and physicians. A few studies have examined the impact on drug-related HIV risk behavior, and found suggestive evidence of a reduction. Evidence regarding supervised injecting facilities and vending machines—while encouraging—is insufficient for drawing conclusions on their effectiveness in reducing drug-related HIV risk among IDUs.
**Outreach and Education**

Several studies and reviews from the developed world—most with weak designs—show a degree of consistency in finding that outreach reduces self-reported drug-related risk behavior. A review by Coyle et al. (1998) included studies that consistently reported that after an outreach intervention, significant declines occurred in self-reported injection drug use (10 of 11 studies), injection frequency (17 of 18 studies), reuse of needles and syringes (16 of 20 studies), and reuse of other equipment such as cookers, cotton, and rinse water (8 of 12 studies). A later review article by Needle and colleagues (2005) updated the 1998 review and confirmed findings that outreach results in self-reported reduction in HIV-related risk behavior. Outreach services should be made available to provide education on risk reduction and links to sterile needle and syringe access programs, drug treatment, and medical and social services for hard to-reach IDUs.

**Question 2: What evidence is there on the extent to which these prevention strategies help reduce HIV transmission from IDUs to their sex partners, and through maternal-to-child transmission to their offspring?**

**Sexual Transmission**

Because the primary objective of drug treatment is to reduce or stop drug use, and the goal of sterile needle and syringe access is to reduce exposure to bloodborne infections through contaminated injecting equipment, one would not necessarily expect to see an effect of these interventions on sex-related HIV risk behavior, unless they are combined with additional risk reduction efforts targeting sexual behavior. And indeed, evidence of such an impact is lacking.

**Drug Treatment**

Evidence from observational studies is weak and inconclusive on whether opioid agonist therapy alone is associated with reductions in high-risk sexual behavior (Gowing et al., 2004; 2005). Some studies suggest that methadone maintenance therapy is associated with small reductions—compared with pre-treatment baseline measures—in the number of sexual partners and exchanges of sex for money or drugs, but that it has virtually no effect on reported rates of unprotected sex (Gowing et al., 2004; 2005). One study assessed the impact of naltrexone on self-reported high-risk sex behavior (Krupitsky et al., 2006). While patients who remained in treatment reported declines in high-risk sex behavior, none of the changes were statistically significant. Some evidence shows that targeted psychosocial interventions are effective in reducing sex-related HIV risk behavior among stimulant-dependent individuals (Prendergast et al., 2001; Gibson et al., 1998; Shoptaw et al., 2005). Efforts should be made to combine effective programs that address sex-related HIV risk behavior with drug treatment programs.

**Sterile Needle and Syringe Access Programs**

Few studies have evaluated the effect of NSEs on sex-related HIV risk behavior. In two early prospective cohort studies, participants in needle and syringe exchange reported decreases in sex-related risk behavior (Donoghoe, 1989; Hart, 1989). However, this issue has not been well studied, and the existing evidence is insufficient to determine the effectiveness of NSE in reducing sex-related risk. Sterile needle and syringe access programs should focus additional efforts on reducing sex-related HIV risk behavior.
Outreach and Education

There is limited evidence that outreach influences self-reported sex-related risk. A review by Coyle et al. (1998) found that 16 of 17 studies showed an increase in self-reported condom use, or a decrease in self-reported unprotected sex, after outreach. The review authors note, however, that a large percentage of IDUs continued to practice high-risk sexual behavior. A review by Needle et al. (2005) showed that outreach can increase condom use, but found smaller reductions in sex-related HIV risk behavior than in drug-related HIV risk behavior.

A meta-analysis by Semaan et al. (2002) showed that some interventions have lowered sexual risk among IDUs, including outreach based on multiple theories and strategies, peer interventions, and skills training. A study of network-oriented peer outreach suggests that interventions that focus on social roles and identity can reduce injection risk behavior and increase condom use with casual sex partners (Latkin et al., 2003).

Outreach and education programs should focus more on reduction of sex-related HIV risk behavior.

Perinatal Transmission

Perinatal transmission from HIV infected female IDUs and infected female sex partners of IDUs to their children is a growing concern. The magnitude of IDU-associated perinatal transmission has not been systematically examined, but some studies suggest that it is a major problem. For example, according to one report, most HIV-infected infants born in the Russian Federation between 1996 and 2001 apparently had mothers who were either IDUs or sexual partners of IDUs (UNODC, 2005). The risk of mother-to-child transmission can be greatly reduced by providing antiretroviral drugs to women during pregnancy and labor, and to infants during the first weeks of life (WHO, 2004b). The World Health Organization provides recommendations on using antiretroviral therapy to prevent mother-to-child transmission (WHO, 2004b).

Question 3: How effective are drug treatment programs, sterile needle and syringe access programs, and outreach in reducing HIV transmission among IDUs?

Drug Treatment

Pharmacotherapies: Evidence from prospective cohort and case-control studies shows that continuous opioid agonist maintenance treatment is associated with protection against HIV seroconversion (Moss et al., 1994; Serpellini and Carrieri, 1994; Williams et al., 1992). These studies also show that the risk of HIV seroconversion is inversely related to the length of time in treatment. However, the possibility of bias in these findings from self-selection cannot be ruled out: that is, patients who resist treatment or engage in risky behaviors may be more likely to leave treatment, while patients who engage in fewer HIV risk behaviors may be more likely to stay in treatment longer. No studies have examined the impact of naltrexone on HIV incidence.

Psychosocial: No studies have examined the impact of individual (i.e., not in conjunction with opioid agonist maintenance treatment) psychosocial interventions for substance abuse treatment on HIV incidence.
Sterile Needle and Syringe Access Programs

Multi-component programs that include needle and syringe exchange: The Committee found that virtually all evaluated programs combined NSE with other prevention strategies, such as outreach, risk reduction education, condom distribution, bleach distribution and education on needle disinfection, and referrals to substance abuse treatment and other health and social services.

Evaluation studies of such multi-component HIV prevention programs have primarily examined their impact on HIV risk behavior rather than HIV incidence. While such studies consistently show that these programs reduce drug-related HIV risk behavior (see the response to Question 1), questions remain about their impact on HIV incidence (Bruneau et al., 1997; Strathdee et al., 1997; Schechter et al., 1999; Patrick et al., 1997).

Although not specifically within its charge, the Committee identified five studies that found that multi-component HIV prevention programs that include NSE have significantly less impact on transmission and acquisition of hepatitis C virus than on HIV (Hagan and Thiede, 2000; Hahn, 2001; Sarkar et al., 2003; Taylor et al., 2000; Mansson et al., 2000). This is possibly because NSEs do not always provide other clean equipment (such as cookers and cotton) that, when contaminated, may lead to hepatitis C infection.

While evidence shows that multi-component prevention programs are associated with reductions drug-related HIV risk behavior, questions remain about the specific contribution of individual elements to reductions in risk behavior and HIV incidence. Elements of these multi-component prevention programs can be resource intensive. Further research is needed to identify the most effective and cost-effective combination of programs that are feasible to implement in high-risk countries. While these questions could be addressed in several ways, one approach would be a trial randomized at the community level (community randomized trial) to evaluate the effectiveness and cost-effectiveness of multi-component programs of increasing complexity. Such a trial could specifically assess the impact of needle and syringe exchange and outreach components on the primary outcome measure—incidence of HIV infection (and, as feasible, hepatitis C infection)—as well as important secondary outcome measures. (See Appendix E for further details.)

Disinfection programs: Laboratory studies show that undiluted bleach can inactivate HIV in injecting equipment, and that undiluted bleach is more efficacious than other tested disinfectants (NRC and IOM, 1995). However, although bleach disinfection works in the laboratory, field studies show that, in practice, drug users do not correctly follow disinfection procedures, and that they fail to disinfect syringes effectively (Carlson et al., 1998; Gleghorn et al., 1994; McCoy et al., 1994). As a result, concerted effort should be made to increase the use of effective procedures for disinfecting shared equipment. IDUs should rely on disinfection to prevent infection with HIV and hepatitis C virus only when they cannot stop injecting or do not have access to new, sterile injecting equipment. While undiluted bleach is the most effective disinfectant, bleach may not be available or acceptable in some settings, and alternative disinfectants may be used or needed.

Outreach and Education

Evidence is very limited regarding the impact of outreach on HIV incidence. The Committee found only one study that directly examined that impact (Wiebel et al., 1996). This study found...
that HIV seroconversion fell from 8.4 to 2.4 per 100 person-years among IDUs receiving street-based outreach in Chicago from 1988 to 1992 (Wiebel et al., 1996).

**Question 4: To what extent do these programs also increase the use of health and social services and drug treatment?**

This issue has not been well-studied across interventions. Drug treatment services are not always well integrated with other health and social programs (WHO, 2004). Few studies have examined whether participation in drug dependence treatment leads to increases in the use of health and social services. Studies in the United States show that providing basic primary care as part of drug treatment reduces emergency department use and hospitalization among IDUs (Friedmann et al., 2006; Samet et al., 2001). Providing directly administered antiretroviral therapy to HIV-seropositive IDUs can also improve adherence and treatment outcomes (Lucas et al., 2006; Moatti et al., 2000). However, it is important to monitor potential interactions between antiretroviral medications and opioid agonist maintenance drugs (Iribarne et al., 1998; McCance-Katz et al., 2001; McCance-Katz et al., 2003; McCance-Katz et al., 2006). Studies indicate that IDUs can benefit from integrated drug treatment, HIV care, and other health and social services, but that further research is needed on optimal strategies for linking or coordinating drug dependence treatment with health and social services.

The few studies of multi-component HIV prevention programs that include needle and syringe exchange and link drug users with health and social services showed a moderate uptake of these services (Porter et al., 2002; Riley et al., 2002; Strathdee et al., 1999). However, none of the studies included comparison or control groups, so the overall use of such services among drug users who do not rely on NSE is unknown.

**Question 5: What evidence is there that programs aimed at reducing the risk of HIV transmission among IDUs are more effective when they are part of a comprehensive array of services?**

While definitions vary, many health policy and research organizations recommend a comprehensive HIV prevention strategy for IDUs. For instance, the World Health Organization (WHO) recommends a comprehensive HIV prevention program for IDUs that includes outreach, information, education, and communication, risk reduction counseling, HIV testing and counseling, disinfection programs, sterile needle and syringe access programs, disposal of used injecting equipment, drug treatment services, agonist pharmacotherapy programs, HIV/AIDS treatment and care, primary health care, and peer education (WHO, 2005b). Similarly, the U.S. National Institute on Drug Abuse (2002) recommends comprehensive programs that encompass three approaches: community-based outreach, drug abuse treatment, and sterile needle and syringe access. These three approaches include a voluntary HIV counseling and testing component and may include many components cited by WHO.

As noted, the Committee found that most prevention programs have multiple components. However, there are few, if any, examples of true “comprehensive” programs. As such, the evidence does not exist to fully answer this question.

**CONSIDERATIONS FOR POLICYMAKERS**

High-risk countries should act now to prevent the growing problem of HIV infection among IDUs, their partners, and children. The design of approaches to respond to the HIV epidemic
among injecting drug users depends on many factors. Scientific evidence should provide the foundation of the policymaking process. However, any programmatic strategy must factor in the local context, and local programs must be tailored to that context.

Economics in resource-constrained countries is one key factor that can influence the choice of programs and the strategy and pace with which they are implemented. Cost-effectiveness and cost-benefit analyses are standard economic techniques used to guide resource allocation decisions. Models and empirical data from the United States and other resource-rich countries show that methadone maintenance treatment is associated with lower expenditures for injection-related events, such as co-morbidity, crime, and transmission of HIV infection to others (Gerstein et al., 1997; Pollack and Heimer, 2004). Some recent studies—mostly mathematical models of the costs of HIV transmission among injecting drug users—also suggest that programs that include needle and syringe exchange are cost-effective (e.g., Laufer, 2001; Cabases and Sanchez, 2003). While there is notable evidence that both NSE and methadone maintenance therapy are quite cost-effective in resource rich countries, these studies are not themselves strong evidence for cost-effectiveness in high-risk countries. Thus, while savings can be similarly anticipated in developing countries, both program costs and the magnitude of these savings will vary by country, establishing the question of cost-effectiveness as an important research topic.

For HIV prevention efforts to exert a public health impact, they need to be scaled up to provide adequate coverage of the target population(s). Scaling up prevention programs imposes certain infrastructure requirements. These include the availability of a sufficient pool of trained treatment providers, pharmacists, outreach workers, drug and alcohol counselors, infectious disease specialists, and other professionals to carry out the chosen programs, as well as the physical infrastructure, commodities, and funding to enable them to do so. In some places, broad scale-up of intervention packages will require a parallel scale-up of training and accreditation programs for health care workers. Similarly, countries creating or expanding pharmacotherapy programs for opioid dependence may need to adopt or enhance clinical guidelines (regarding patient eligibility criteria, dosage levels, and contraindications with other drugs, for example) and regulations. Information systems will be needed to track and ensure a consistent supply of commodities such as medications and needles. Some high-risk countries may have limited public health, drug treatment, and overall medical infrastructure and operating capacity. These countries must make pragmatic decisions regarding which approaches they can realistically pursue.

Public perceptions also help shape the choice of strategies to prevent HIV transmission and reduce illicit drug use. Some view public health interventions that provide access to sterile injecting equipment or opioid agonist treatment negatively because these interventions aim to reduce the harms related to drug use rather than prevent drug use itself (NRC and IOM, 1995; Gostin, 1991). These groups may see such harm reduction efforts as condoning rather than condemning illegal drug use. Local communities may also object to programs that include needle and syringe exchange and opioid agonist maintenance treatment because they fear that these programs will attract drug users who may commit crimes and discard needles and other drug paraphernalia in their neighborhoods (NRC and IOM, 1995).

Several studies suggest that the involvement and education of key stakeholders, such as community members, government agencies, nongovernmental groups, public health officials, and law enforcement officials are critical to the success of HIV prevention programs for IDUs. Consultation with community leaders before the initiation of needle and syringe exchange in Thailand and Vietnam was key to their success (Gray, 1995; 1998; Quan et al., 1998). A key realization when such communication occurs is that many disagreements over priorities and strate-
gies stem from a lack of information about the focus, methods, and evidence base of the competing factions. A common understanding that each domain wishes to prevent the needless human suffering of an emerging HIV epidemic is essential. The Committee recommends that public health and criminal justice officials, key community leaders (religious, educational), and community members work together at international, national, regional, and local levels to develop interventions that balance their respective missions in fighting both HIV/AIDS and drug epidemics.

Concerted national efforts to limit the transmission of HIV among IDUs must begin now. Nations must approach these efforts with both immediacy, to break the cycle of HIV transmission, but also with a longer-term view, to sustain progress.

Although reviewing the evidence on primary programs for preventing drug use was beyond the scope of its charge, the Committee believes that programs to prevent the initiation of injecting drug use—and drug use in general—can and should be part of a comprehensive, sustained approach to preventing HIV transmission among IDUs. Broader population-based efforts at HIV awareness and prevention can provide a foundation for sustaining such efforts for IDUs.

Similarly, investments in the infrastructure to deliver clinical and supportive services to the general population will be needed and will have benefits beyond the IDU population. Maintaining infrastructure and sustaining funding is central to ensuring continuous services. Programs that do not have sustainable funding are at risk of interruption. Service interruptions could have serious implications for individuals receiving medication for opioid dependence and other IDUs receiving treatment or preventive services.

As part of a sustained effort, the Committee repeats its recommendation that such approaches be monitored and evaluated, and modified based on such evaluations. Scale-up of prevention efforts should include staggered program designs or other approaches that permit the evaluation of effectiveness, alongside more rigorous efforts to experiment with different implementation choices to see which ones work best.

CONCLUSION

Nations where the HIV pandemic is newly emerging can and should take effective action now to stem the tide of this tragic and preventable illness. In countries where injecting drug use is the primary source of HIV infection, national programs must address the challenges of both drug use and HIV. The Committee has reviewed the evidence regarding interventions for injecting drug use and HIV among IDUs, and hopes it has provided policymakers a knowledge base regarding what works. The Committee recognizes though that each country will pursue a different combination of interventions, reflecting its economic circumstances and legal, ethical, and cultural traditions. However, these policy decisions should not be based on erroneous understanding if scientific truth is available. The Committee believes that the evidence-based conclusions and recommendations in this report can provide an important foundation for governments and communities engaging in economic, legal, and ethical debates about these issues.

Evidence on effective interventions provides a solid basis for action now. The experiences of other nations with extensive HIV epidemics underscore the urgent need for an immediate response. As policy unfolds into programmatic action, nations should also evaluate their implementation, to inform the next generation of responses to drug dependence and HIV.
Recommendations Regarding Treatment for Drug Dependence (Chapter 2)

Recommendation 2-1: Given the strong evidence of its effectiveness in treating opioid dependence, opioid agonist maintenance treatment should be made widely available where feasible. Such programs should include:

- The necessary infrastructure to make treatment widely available (e.g., clinics, trained health workers) and a strategy to ensure sustainability.
- Assurance of adequate dosage and treatment duration.
- A balance between strategies to decrease diversion of treatment medication and strategies to disseminate the treatment. An evaluation component to monitor treatment implementation, quality, and outcomes.
- Monitoring of potential drug interactions between antiretroviral medications and opioid agonist maintenance drugs for HIV-infected IDUs.

Recommendation 2-2: Given the potential benefits and lack of harmful effects, the following treatments should also be made available as part of a multi-component treatment system, where feasible, but should include a rigorous evaluation component:

- Specific behavioral treatments (contingency management, cognitive behavioral therapy, community reinforcement approach, motivational interviewing, and individual drug counseling) for treating stimulant dependence.
- Chemical dependency treatment, therapeutic communities, and Drug Anonymous groups for patients dependent on any drug class who are interested in abstinence-oriented treatment.

Recommendation 2-3: Given the relative weakness of the evidence, further research should occur on the following issues related to treatment for drug dependence:

- The additional benefits and cost-effectiveness of adding psychosocial interventions to opioid agonist maintenance treatment for opioid-dependent people in high-risk countries, and the relative effectiveness of those interventions in particular cultural contexts and for particular patient subgroups.
- Pharmacotherapies for stimulant abuse, particularly amphetamine-type stimulants which have emerged as a major problem in many parts of the world.
- The effectiveness of naltrexone for different patient populations and in different settings.
- The relative effectiveness of various psychosocial interventions in treating opioid dependence in places where opioid agonist maintenance therapy is not available or accessible.
- Developing cost-effective and feasible alternatives to voucher-based contingency management approaches for treating stimulant dependence.
- Optimal strategies for linking drug dependence treatment with health and social services.

Recommendations Regarding Sterile Needle and Syringe Access and Outreach and Education (Chapter 3)

Recommendation 3-1: Given consistent evidence that multi-component HIV prevention programs that include sterile needle and syringe access reduce drug-related HIV risks, such programs should be implemented where feasible.

Recommendation 3-2: Multi-component HIV prevention programs that include sterile needle and syringe access should:
- Maximize their accessibility to the largest number of IDUs by using multiple access points and methods of delivery.
- Focus on reducing sex-related HIV risk behavior.
- Actively refer IDUs to other services, such as substance abuse treatment, HIV voluntary counseling and testing and, if appropriate, antiretroviral treatment for HIV.
- Focus additional efforts on preventing hepatitis C infection, such as by providing sterile cotton swabs, alcohol wipes for cleaning injection sites, sterile water, cookers, and other disinfection supplies.
- Incorporate strong program and component evaluations, and where feasible, include comparison populations or regions.

Recommendation 3-3: Because field studies have shown that drug users often fail to properly disinfect injecting equipment, concerted effort should be made to increase the uptake of effective procedures for disinfecting shared equipment. IDUs should rely on disinfection to prevent HIV and HCV infection only when they cannot stop injecting or do not have access to new, sterile injecting equipment.

Recommendation 3-4: Outreach services should be made available to provide education on risk reduction and links to sterile needle and syringe access programs, drug treatment, and medical and social services for hard to-reach IDUs.

Recommendation 3-5: The Committee recommends that additional research focus on:
- The impact of outreach and education and multi-component programs that include sterile needle and syringe access on sexual risk reduction.
- Integration of effective strategies for reducing sexual risk behavior and sexual transmission of HIV into multi-component programs that include sterile needle and syringe exchange and outreach and education.
- The potential unintended consequences of HIV prevention programs that include needle and syringe exchange, such as increases in new drug users or in discarded needles in the community, and strategies to address such problems, if they are found.
- Identifying the simplest, most acceptable effective disinfection techniques using bleach, and the best methods for educating IDUs on these techniques.
- The effectiveness of alternative disinfectants in field settings, particularly in countries where bleach is not available or acceptable.
- Identifying effective strategies for preventing HCV among IDUs.
- The costs and contributions of individual elements of multi-component programs that include needle and syringe exchange on HIV-related risk behavior and HIV incidence.

Recommendations Regarding Taking Action (Chapter 4)

Recommendation 4-1: Because a variety of interventions have been shown to be effective, high-risk countries should act now to prevent the growing problem of HIV among IDUs, their partners, and children.

Recommendation 4-2: To increase their acceptability and likelihood of success, HIV prevention interventions for IDUs should be:
- Tailored to local circumstances and implemented in a culturally appropriate manner;
- Coupled with cost-effectiveness evaluations improve resource-allocation decisions;
- Scaled-up to provide adequate coverage of the interventions to the target populations in order for programs to have a public health impact;
- Integrated with strategies to combat stigma and discrimination among drug users and HIV-infected people;
- Coordinated among national, regional and local public health, criminal justice, and community
leaders to develop a framework for interventions that balance their respective missions;
- Complementary to broader interventions in drug use and HIV, including primary prevention;
- Built upon plans for fiscal and infrastructure sustainability;
- Coupled with monitoring and evaluation.
REFERENCES


PREVENTING HIV INFECTION AMONG IDUs


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SUMMARY


Preventing HIV Infection among Injecting Drug Users in High Risk Countries

An Assessment of the Evidence

Committee on the Prevention of HIV Infection among Injecting Drug Users in High Risk Countries

Board on Global Health
“Knowing is not enough; we must apply. Willing is not enough; we must do.”

—Goethe
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This report has been reviewed in draft form by individuals chosen for their diverse perspectives and technical expertise, in accordance with procedures approved by the NRC's Report Review Committee. The purpose of this independent review is to provide candid and critical comments that will assist the institution in making its published report as sound as possible, and to ensure that the report meets institutional standards for objectivity, evidence, and responsiveness to the study charge. The review comments and draft manuscript remain confidential to protect the integrity of the deliberative process. We wish to thank the following individuals for their review of this report:

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Although the reviewers listed above have provided many constructive comments and suggestions, they were not asked to endorse the conclusions or recommendations, nor did they see the final draft of the report before its release. The review of this report was overseen by Arthur L. Reingold, Professor and Head, Division of Epidemiology, University of California, Berkeley, California; and Floyd Bloom, Chairman and Professor, Department of Neuropharmacology, The Scripps Research Institute, La Jolla, California. Appointed by the National Research Council and Institute of Medicine, they were responsible for making certain that an independent examination of this report was carried out in accordance with institutional procedures, and that all review comments were carefully considered. Responsibility for the final content of this report rests entirely with the authoring Committee and the institution.
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