

CORE

Public Health Functions for BC

Evidence Review:
Communicable Disease
(Harm Reduction)

Population and Public Health
BC Ministry of Healthy Living and Sport

This paper is a review of the scientific evidence for this core program. Core program evidence reviews may draw from a number of sources, including scientific studies circulated in the academic literature, and observational or anecdotal reports recorded in community-based publications. By bringing together multiple forms of evidence, these reviews aim to provide a proven context through which public health workers can focus their local and provincial objectives. This document should be seen as a guide to understanding the scientific and community-based research, rather than as a formula for achieving success. The evidence presented for a core program will inform the health authorities in developing their priorities, but these priorities will be tailored by local context.

This Evidence Review should be read in conjunction with the accompanying Model Core Program Paper.

Evidence Review prepared by:

Thomas Kerr and Evan Wood, BC Centre for Disease Control

Evidence Review accepted by:

Population and Public Health, Ministry of Healthy Living and Sport (July 2008)
Core Functions Steering Committee (January 2009)

TABLE OF CONTENTS

Executive Summary	i
1.0 Overview/Setting the Context.....	1
1.1 An Introduction to This Paper.....	1
1.2 Health Costs of Illicit Drug Use.....	2
1.3 Harm Reduction	3
2.0 Grading of Evidence	5
3.0 Service Thresholds.....	6
4.0 Harm Reduction Interventions.....	8
4.1 Needle Exchange	8
4.2 Prison-based Needle Exchange.....	9
4.3 Safer Crack Kit Distribution	10
4.4 Supervised Injection Facilities.....	10
4.5 Supervised Smoking Facilities.....	12
5.0 Replacement Therapy for Opiate Addiction	14
5.1 Methadone Maintenance Therapy.....	14
5.2 Prison-based Methadone.....	15
5.3 Heroin Prescription	15
6.0 Educational Approaches	18
6.2 Outreach Interventions.....	19
7.0 Factors Affecting the Efficacy of Harm Reduction Programs.....	20
7.1 Early Intervention	20
7.2 Responsiveness	20
7.3 Coverage	21
7.4 Comprehensiveness, Location and Design	21
7.5 Involvement of Current/Former Drug Users.....	21
8.0 Summary	23
References	24

EXECUTIVE SUMMARY

Background

The primary strategies to address the illicit drug problem have historically included: (a) primary prevention of illicit drug use through educational interventions and other means; (b) supply reduction activities that seek to reduce availability of illicit drugs and provide criminal sanctions against those caught using illicit drugs; and (c) drug treatment for those individuals with a clinical diagnosis of addiction.

During the last decade, policy-makers have become increasingly interested in the concept of harm reduction as an illicit drug strategy. Unfortunately, the concept of harm reduction is widely misunderstood both by policy-makers and the public at large. In general, with respect to illicit drugs, the concept of harm reduction requires an acknowledgement of the limits of supply reduction. Harm reduction strategies are based on the pragmatic goal of reducing the associated harms of illicit drug use (e.g., infectious disease spread, overdose deaths, etc.) without aiming for the elimination of substance use or imposing the precondition of abstinence on drug users. Thus, harm reduction has been defined as a policy or program directed towards decreasing the adverse health, social, and economic consequences of drug use without requiring abstinence from drug use.

Harm Reduction Interventions

Most harm reduction programs can be broadly dichotomized into structural interventions and substitution therapies. Structural interventions seek to alter the risk environment, which refers to the context in which illicit drug use takes place (e.g., settings where clean syringes may be scarce). In general, structural interventions involve the provision of sterile syringes, safer crack kits, and/or supervised settings for illicit drug use. However, they also include educational approaches and outreach-based interventions that seek to educate individuals and groups and to modify behaviour.

1. Needle Exchange

Since a primary risk factor for blood-borne infections, including HIV and hepatitis C (HCV) is the sharing of used syringes, a cornerstone of harm reduction for injection drug users (IDU) involves making sterile syringes available through needle exchange programs (NEP) and other means. The specific biologic action of NEP is a form of vector control that acts by reducing the time that needles spend in circulation and by providing ready access to unused syringes.

Evidence: Overall, the evidence regarding the efficacy of NEP for communicable disease control was found to be Class A, given consistent findings from a large body of 2++ studies for efficacy, with strong evidence of corroboration.

2. Prison-based Needle Exchange

An increasing number of penal institutions have established and evaluated needle exchange or distribution programs as a means to control the spread of infectious diseases among inmates who inject drugs.

Evidence: Evaluations of prison-based needle exchange programs have primarily focused on process dimensions, although declines in behaviours that result in infectious disease spread (e.g., syringe sharing) have been noted. Given the favourable results pertaining to implementation of prison-based needle exchange programs, there is no evidence to suggest that the benefits of this approach observed in the community are not replicated in prisons. In fact, given the nature of prison environments, programs such as needle exchange may be particularly beneficial in this setting. Overall, the evidence for prison-based needle exchange programs is Class A.

Further, it should be noted that the “principle of equivalence” is applicable to even the most controversial HIV prevention programs, including needle exchange. Although there have been successes with prison-based needle exchange in a number of countries, including those with limited resources, prison-based needle exchange remains unimplemented in Canadian prisons.

3. Safer Crack Kit Distribution

It has been suggested that a potential source of blood-borne disease transmission lies in the sharing of non-injection drug use equipment: pipes, straws and spoons. The potential risk originates from the fact that the equipment comes into contact with blood or other bodily fluids in the nose and mouth, and thus, when the equipment is shared, it provides a route of transmission for HCV and other pathogens, including tuberculosis.

Evidence: Safer crack kit distribution programs were graded as Class D evidence for communicable disease control. This grade, however, was based on lack of evidence, and evaluation of this approach is warranted given the increasing harms of crack cocaine and the few tools available to address these growing concerns.

4. Supervised Injection Facilities

In response to ongoing drug-related harms among IDU, several countries have added supervised injection facilities (SIF) to the array of health programs and services that are offered. Unlike illegal “shooting galleries” run by drug dealers, SIF are controlled health care settings where drug users inject pre-obtained illicit drugs under staff supervision and receive sterile injecting equipment, primary health care, counselling, and referral to health and social services.

Evidence: Despite the evidence that SIF reduce syringe sharing and injection drug use in risky environments (e.g., shooting galleries, alleys, etc.), to date there have been no studies of the impact of SIF on the incidence of HIV or other blood-borne diseases. In the absence of available studies, SIF were graded as Class B for the evidence of their effectiveness in controlling communicable disease.

5. Supervised Smoking Facilities

Because of the success of SIF in several European nations, Australia, and most recently Vancouver, interest in supervised smoking facilities (SSF) has grown. The primary objectives of SSF are similar to those established for SIF.

Evidence: SSF were graded as Class D evidence for communicable disease control. This grade, however, was based on lack of evidence, and evaluation of SSF is warranted given the increasing harms of crack cocaine and methamphetamine and the few tools available to address these

growing concerns. For instance, SSF may be of value for reducing transition into injection drug use, a key communicable disease control strategy.

6. *Replacement Therapy for Opiate Addiction*

In North America, the primary method for the treatment of opiate addiction is the provision of long-acting opiate agonists, primarily methadone hydrochloride, for short- or long-term maintenance therapy.

- **Methadone Maintenance Therapy**

Methadone is a long-acting synthetic opiate agonist that is easily absorbed when taken orally and has a half-life of 24-36 hours, allowing for once-daily administration. Generally, methadone maintenance therapy (MMT) involves providing methadone on a daily basis to the patient.

Evidence: Overall, the provision of methadone is graded as Class A evidence for communicable disease control, based on randomized studies showing the drug's efficacy for the treatment of opiate dependency and reduction of subsequent drug-related harms.

- **Prison-based Methadone**

A small number of evaluations of MMT programs in prisons have indicated positive results.

Evidence: Given the favourable results pertaining to implementation of prison-based methadone programs, there is no evidence to suggest that the benefits of this approach that have been observed in the community are not replicated in prisons. Specifically, there is nothing about the prison environment that suggests the evidence should not be graded as Class A (i.e., same as community-derived evidence). Further, the WHO has recommended that prisoners on methadone maintenance prior to imprisonment should be able to continue this treatment while in prison. This point is particularly relevant in light of findings indicating that people taken off methadone once incarcerated often return to narcotic use, usually within the penal institutions, and often via injection. Also, consistent with the principle of equivalence, it has further been recommended that MMT should be available in prisons in countries where MMT is available in the community.

- **Heroin Prescription**

Although scientific documentation of the efficacy of methadone treatment is well established, the therapy does not represent a cure-all for the problem of opiate addiction. In light of the limitations with MMT, several European countries have initiated programs that provide alternative forms of drug treatment, including injectable opiates such as heroin.

Evidence: Overall, there is Class A evidence that heroin prescription may be more effective than methadone for reducing the harms associated with opiate addiction, including the spread of communicable disease.

7. *Educational Approaches*

Harm reduction messages are frequently disseminated through a variety of educational programs. Typical strategies include use of posters and brochures in settings and services frequented by drug users, web-based materials, videos, and the use of outreach workers and service providers within health care settings to provide education to individuals and groups. While such educational efforts typically cover a range of topics, including overdose prevention, many focus on the reduction of communicable disease transmission.

Evidence: Overall, there is Class C to Class D evidence indicating that educational interventions, on their own, can reduce the harms of illicit drug use by, among other things, promoting communicable disease control through the reduction of risk behaviour directly linked to communicable disease transmission. However, this grading should be interpreted with great caution, as educational approaches vary immensely in their design and delivery, and therefore not all educational interventions can be regarded as class C or D.

8. *Outreach Interventions*

Outreach programs have also been widely implemented in community-based settings, and have been credited as one of three components contributing to low HIV prevalence in several cities. Outreach programs are used to make contact with out-of-treatment IDU who may be at highest risk for HIV infection. Once initial contact is made, education, resources (e.g., sterile syringes, condoms, bleach kits, literature) and counselling support are often provided. Overall, outreach workers serve as an important link between active IDU and institutional testing, prevention and addiction treatment services.

Evidence: Overall, there is Class A evidence supporting the efficacy of outreach interventions in promoting communicable disease control. However, this rating may not apply equally to all outreach-based interventions, which vary considerably in their design and delivery. The evidence to date indicates that those interventions that involve peers (i.e., drug users), involve the dissemination of sterile syringes, and have direct links to infectious disease testing, counselling services and addiction treatment are likely to be most effective in reducing communicable disease transmission.

9. *Factors Affecting the Efficacy of Harm Reduction Programs*

The present review indicates that rigorous research and evaluation have found various harm reduction interventions to be efficacious. However, given the social circumstances and heterogeneity surrounding illicit drug use, a growing body of literature has identified a number of factors that can positively or negatively affect the efficacy of any harm reduction program. These factors are:

- **Early Intervention**

Although there is considerable regional heterogeneity associated with communicable disease transmission among drug users as a result of differences in drug-use patterns and available programs, once established, diseases such as HIV and HCV can spread rapidly within drug-using communities. Therefore, it is critical that interventions be implemented as early as possible.

- Responsiveness

In order to address immediate and emerging risk behaviours, harm reduction interventions should be informed by ongoing data collection and monitoring. Strategies that have been successful in informing harm reduction interventions include participant observation, key informant interviews, inclusion of drug users in service design and rapid assessment methods.

- Coverage

While communicable disease transmission among drug users is often attributed to needle sharing, secondary transmission to sexual partners and offspring is also widespread. Therefore, in order to ensure adequate coverage, HIV prevention and risk reduction programs should target not only drug users but also their intimate partners, and the social networks they participate in. Examples of successful social network interventions have been documented throughout the developed and developing world.

- Comprehensiveness, Location and Design

Given the observed diversity in risk behaviour within and across drug-using communities, an effective harm reduction response requires that a comprehensive range of low and medium threshold interventions be delivered in various locations and at various times.

- Involvement of Current/Former Drug Users

In response to the limitations of traditional provider-client models of service delivery, peer-driven interventions, involving current/former drug users, have been developed throughout the world as one method of promoting the reduction of communicable disease transmission.

Summary

Injection drug use affects all Canadians. The costs of law enforcement, incarceration and health care expenditures result in an enormous financial burden. In addition, there are large social and human costs that stem from the crime, disease and death that arise from illicit drug use. A review of the scientific evidence indicates that various harm reduction programs have been implemented successfully and now serve to complement ongoing enforcement, treatment and prevention initiatives. Given the ongoing drug-related harm throughout British Columbia, efforts to significantly expand and appropriately evaluate harm reduction programs are an urgent priority.

1.0 OVERVIEW/SETTING THE CONTEXT

In 2005, the British Columbia Ministry of Health released a policy framework to support the delivery of effective public health services. The *Framework for Core Functions in Public Health* identifies communicable disease as one of the 21 core programs that a health authority provides in a renewed and comprehensive public health system.

The process for developing performance improvement plans for each core program involves completion of an evidence review used to inform the development of a model core program paper. These resources are then utilized by the health authority in their performance improvement planning processes.

This evidence review was developed to identify the current state of the evidence-based on the research literature and accepted standards that have proven to be effective, especially at the health authority level. In addition, the evidence review identifies best practices and benchmarks where this information is available.

1.1 An Introduction to This Paper

Illicit drug use presents an urgent and growing threat to community and public health. Unfortunately, the majority of resources aimed at addressing the illicit drug problem have gone to interventions with little evidence of benefit or interventions that have been scientifically shown to result in net community harm and/or harm to public health. A 2001 Auditor General's report on Canada's illicit drug strategy concluded: "of particular concern is the almost complete absence of basic management information on spending of resources, on expectations, and on results" (Auditor General of Canada, 2001).¹ As such, there is an urgent need to implement evidence-based systems to control communicable diseases and other harms from illicit drug use.

Among the greatest concerns of illicit drug use is the growing popularity of injection drug use, and conservative estimates suggest that there are now more than 100,000 Canadians who are injection drug users (IDU).² Injection drug use is associated with an array of adverse outcomes, including overdose, infectious disease, loss of social and economic functioning and engagement in criminal activity.³ British Columbia has been the epicentre of one of North America's worst and most long-standing illicit drug use epidemics. In 1997, an explosive HIV epidemic was documented among Vancouver's IDU, with an HIV incidence peaking at 18 per 100 persons and persistently elevated HIV rates continuing up to the end of 2005.⁴ The high HIV and hepatitis C (HCV) rates have resulted in an estimated 35 per cent of the city's estimated 15,000 injection drug users becoming HIV-infected and greater than 85 per cent becoming HCV-infected; in recent years, the epidemic has changed from one of asymptomatic infection to one of increasing HIV- and HCV-related morbidity and mortality among infected IDU.^{5,6} In addition to the spread of infectious diseases, vast numbers of citizens have died of drug overdoses in the last decade, with up to one death per day being documented in the province in recent years.⁷

More recently, the use of crack cocaine and methamphetamine has also grown astronomically in western Canada, with Vancouver as the epicentre of this drug use epidemic. These concerns have led to Vancouver developing one of North America's worst property crime rates, and violence

related to the use of methamphetamine has become a growing concern. Finally, as in other settings, addiction to illicit drugs in Vancouver has been intimately linked to a burgeoning survival sex-trade industry.⁸ This problem has received international attention because of the disappearance of more than 60 women from the city's Downtown Eastside.

Throughout most of the world, the primary response to the health and social impacts of illicit drug use has been to intensify the enforcement of drug laws in an effort to limit the supply and use of illicit drugs.⁹ The consequences of this policy approach include an unprecedented growth in prison populations and increasing concerns regarding drug-related harms within prisons.^{10,11} However, political promises to enact tougher sentences for illicit drug users remain politically popular due to the mistaken belief among the public that this activity will reduce the growing drug problem.¹² In reality, no country in the world has ever reduced its drug problem by enacting tougher penalties and subsequently increasing incarceration rates; in reality, this approach actually worsens the overall problem in several ways.¹² For instance, it has long been recognized that the incarceration of IDU also has major consequences for public health, because of the potential for infectious disease transmission among drug-using inmates. This may be of particular concern for HIV transmission, which has been previously documented among inmates in a Scottish prison¹³ and is suspected in several other settings as a result of syringe sharing between incarcerated IDU.^{14,15}

Similar concerns exist in British Columbia. A recent study suggested that the number of known HIV cases in Canadian prisons has risen by 35 percent in the last five years, and it is suspected that HIV may be spreading rapidly in this setting.^{16,17} A recent study of community-recruited IDU from Vancouver demonstrated that having been incarcerated in the last six months was independently associated with a greater than 2.5-fold risk of HIV seroconversion.¹⁸ An external evaluation of these data suggested that 21 per cent of all HIV infections among Vancouver IDU may have been acquired in prison.¹⁹ Subsequent studies have shown disturbing rates of syringe sharing among drug users incarcerated in Canadian prisons.^{15,20-22}

Within prisons, HIV-infected populations are often kept in close proximity to high-risk populations, and these social network characteristics undoubtedly contribute to HIV risk behaviour within these environments.²⁰ Unfortunately, this problem is typically exacerbated by the fact that proven prevention methods that exist in the community are often not available in prison settings. This occurs despite the fact that many international instruments convey a general consensus that the standard of health care provided to prisoners must be comparable to that available in the general community. For example, as adopted by the United Nations General Assembly in 1990, the *Basic Principles for the Treatment of Prisoners* states: "Prisoners shall have access to the health services available in the country without discrimination on the grounds of their legal situation."²³ Given ongoing observations of high-risk behaviour and infectious disease transmission among incarcerated drug users, there is now growing agreement that efforts to control the spread of infectious diseases among this population must also focus on the prison context.

1.2 Health Costs of Illicit Drug Use

In addition to the social costs described earlier (e.g., loss of productivity, crime, legal costs, prison costs), there are the substantial related costs to the medical system. A recent "cost of

illness” analysis based on data from a cohort of untreated opiate addicts in Toronto yielded an estimate of more than \$45,000 in societal costs per addict per year.²⁴ In addition, there are the medical costs of the HIV and HCV epidemics. For instance, it is known that the average lifetime medical cost of each case of HIV infection is approximately \$150,000. Based on current HIV prevalence estimates, the estimated costs to the health care system stemming from the HIV epidemic in Vancouver’s Downtown Eastside will be greater than \$215,000,000.²⁵ However, this same study estimated that approximately \$130,000,000 could be saved through effective interventions aimed at curbing HIV rates.²⁵ Because the prevalence of HCV is much higher than that of HIV among IDU, the medical costs for addressing HCV infection among IDU are expected to substantially exceed those for HIV.³ In addition to HIV and HCV, bacterial infections acquired through non-sterile injection techniques often result in lengthy and expensive acute hospitalizations among IDU.³

1.3 Harm Reduction

The primary strategies to address the illicit drug problem have historically included: (a) primary prevention of illicit drug use through educational interventions and other means; (b) supply reduction activities which seek to reduce availability of illicit drugs and provide criminal sanctions against those caught using illicit drugs; and (c) drug treatment for those individuals with a clinical diagnosis of addiction. While there is a large body of scientific evidence to support addiction treatment, the evidence in support of supply reduction and primary prevention strategies is lacking. On the contrary, educational interventions and supply reduction activities have largely been shown to be ineffective in reducing levels of illicit drug use and overall drug-related harm. However, during the last decade, policy-makers have become increasingly interested in the concept of *harm reduction* as an illicit drug strategy.

In general, with respect to illicit drugs, the concept of harm reduction requires an acknowledgement that illicit drug use will remain extremely difficult if not impossible for governments to control. One pertinent example of this challenge is in prisons: while prisons are some of the most tightly controlled environments in the world, illicit drug markets have continued to flourish despite the application of extreme supply reduction efforts that could never be replicated in the community.¹⁵ In recognition of the limits of supply reduction, harm reduction strategies are based on the pragmatic goal of reducing the associated harms of illicit drug use (e.g., infectious disease spread, overdose deaths, etc.) without aiming for the elimination of substance use or imposing the precondition of abstinence on drug users. This is an important concept, and there are major avenues available to reduce the harms of illicit drugs, since many of these harms stem from the context in which drugs are used (e.g., shooting galleries where syringe sharing is common) rather than the effects of the drugs themselves. In recognition of the above, harm reduction has been defined as a “policy or program directed towards decreasing the adverse health, social, and economic consequences of drug use without requiring abstinence from drug use.”²⁶

Unfortunately, the concept of harm reduction is widely misunderstood by policy-makers and the public at large. This misunderstanding is highly problematic, since harm reduction principles are responsible for several of public health’s most notable recent achievements. For instance, in the 1980s, greater recognition emerged of the harms attributable to teenage drinking and driving. When it became obvious that efforts to eliminate teenage drinking through a “Don’t Drink”

campaign were unlikely to be successful, a more pragmatic campaign emerged under the slogan, “If you drink, don’t drive.” This strategy embodies the concept of harm reduction, in that it acknowledges that it will be difficult to eliminate teenage drinking through policies, and instead focuses on seeking to reduce one of the main downstream harms of this activity (i.e., drunk driving).

While harm reduction advocates do not preclude abstinence as a worthwhile goal, they question the long-established notion that abstinence is the only acceptable drug policy or program outcome. The concept of harm reduction, first conceived and implemented in Europe in the 1980s, began in response to open drug scenes in Europe’s major urban centres, where the failure of classical drug strategies led policy-makers to seek new methods to shift the focus from drug use to its related harms.²⁷ The Dutch government paved the way by providing youth with a relatively safe, police-supervised atmosphere for soft drug experimentation. With the emergence of the HIV epidemic, this tolerance soon extended to IDU, prompting the opening of Amsterdam’s first needle exchange program in 1984. This program was embraced by many existing clinics, work programs, and shelters. The Netherlands now boasts the lowest rates of drug-related HIV seroconversion in Europe.²⁷

Frankfurt and several Swiss cities have similar success stories. Following 20 years of ineffective police action to eliminate Frankfurt’s open drug scene, a needle exchange program was introduced in 1986. Low threshold methadone maintenance therapy and supervised consumption facilities were added in the early 1990s. As a result, Frankfurt witnessed a significant lowering of drug deaths and HIV infections from 1991 through 1997, with overdose deaths reduced by more than 75 per cent.²⁸ In Switzerland, HIV serconversion and drug-related death rates decreased considerably following the expansion of low threshold services. The Swiss now claim that 65 per cent of drug users are participating in treatment, while the remaining 35 per cent are believed to have regular contact with harm reduction programs.²⁷ More recently, harm reduction has been increasingly embraced in North America and abroad, alongside abstinence-based strategies.

In an effort to dispel several of the misunderstandings surrounding harm reduction strategies and to inform policy-makers regarding the potential impact of harm reduction interventions, this evidence review will outline the evidence and best practice for the employment of harm reduction activities in programs aimed at controlling communicable diseases. Since harm reduction programs focus primarily on illicit drug use, this review will focus on harm reduction strategies employed in this area. Thus, the focus of the review will be on several established harm reduction strategies, including needle exchange programs, safer crack kit distribution programs, supervised injection facilities, supervised smoking facilities, methadone maintenance therapy, heroin prescription, educational approaches and outreach-based interventions. Given the high rates of incarceration among drug users and the role prison contexts play in perpetuating epidemics of infectious diseases, this review will also consider the evidence supporting selected prison-based harm reduction strategies. Lastly, given the large body of evidence addressing factors that frequently compromise the effectiveness of harm reduction programs, this review will consider factors that are key to the success of harm reduction programs, including the importance of early intervention, responsiveness, coverage, comprehensiveness, location, design, and the involvement of current and former drug users in program delivery.

2.0 GRADING OF EVIDENCE

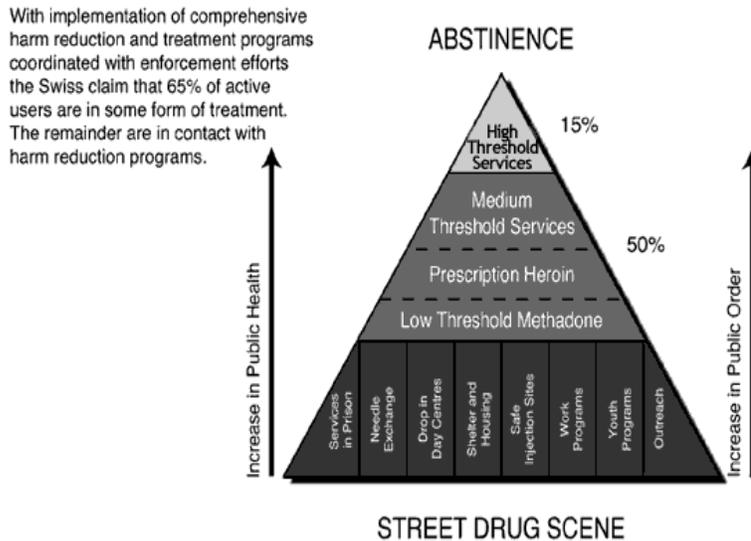
This review employs the grading scheme for public health interventions developed by the Health Development Agency of the National Health Service in the United Kingdom. Specifically, at the end of each relevant section, programs are graded in a range from Class A (strong evidence) to Class D (weak evidence), based on the available literature in this area. However, it is important to note that some interventions were rated as Class D because of a lack of evaluation in this area, rather than evidence showing they were ineffective. It should also be stressed that, with respect to illicit drug use, the context in which drugs are used (e.g., risk environments, syringe sharing, etc.) are key determinants of communicable disease spread. Hence, while this review focused on the control of communicable diseases, harm reduction strategies were evaluated with respect to their ability to control communicable disease incidence as well as their ability to reduce risk behaviours (e.g., syringe sharing) and to modify environments where risk behaviours are elevated (e.g., public drug use).

3.0 SERVICE THRESHOLDS

Before reviewing these harm reduction strategies, it is important to consider the concept of *service threshold*. In general, health services currently offered to illicit drug users can be classified according to level of threshold. Threshold refers to the eligibility criteria for entrance into the service and the state of readiness of individuals to participate and meet the demands of the program. High threshold programs, such as intensive residential treatment, typically demand strict attendance and require that participants abstain completely from drugs and alcohol. Medium threshold programs have less strict requirements and include services such as outpatient treatment and methadone maintenance therapy. Low threshold programs, such as needle exchanges and supervised consumption facilities, aim to reduce drug-related harm while requiring little commitment from participants. Low threshold services typically serve to reduce harm among people who continue to use illicit substances.

As Figure 1 illustrates, evidence from Switzerland indicates that a comprehensive approach that includes a variety of low threshold programs is most effective in ensuring optimal uptake of health services among IDU.²⁷

Figure 1



Most of the health services currently offered to IDU in Canada are high or medium threshold; therefore, they are primarily available to those people who are able to meet strict program demands and requirements (e.g., abstinence from all illicit substances). Research from the United States and Switzerland shows that medium and high threshold services attract only 5 to 20 per cent of all active drug users.^{29,30} Given the high proportion of drug users who have not been reached with existing services, experts have repeatedly called for the expansion of low threshold services in Canada.³¹⁻³³ It is unlikely that expansion of high threshold services will be sufficient to reduce the low proportion of drug users in treatment. For example, in a survey of untreated opiate users who were offered immediate admission to methadone maintenance

Core Public Health Functions for BC: Evidence Review
Communicable Disease (Harm Reduction)

therapy, 48 per cent would have accepted treatment, 33 per cent would have rejected it outright, and 19 per cent were ambivalent.³⁴ Similar findings have been reported elsewhere.^{35,36} Furthermore, high rates of attrition and limited efficacy of abstinence-based treatment indicate that alternative strategies should be explored.³⁷

In addition to limited reach and effectiveness, there are also legal implications of relying on high threshold services. For instance, according to the Canadian HIV/AIDS Legal Network (1999):

from a legal perspective, compelling abstinence as a condition of medical treatment, may constitute a violation of the Canadian Charter of Rights and Freedoms, human rights codes, professional codes of conduct, and international human rights convention. Similarly, it is unethical to insist on cessation of drug use as a condition of medical treatment if this is beyond the capabilities of the drug user.³¹

In order to reach and accommodate individuals who continue to use drugs, an increasing number of countries have begun adding new and innovative harm reduction programs to their existing public health efforts.

4.0 HARM REDUCTION INTERVENTIONS

Most harm reduction programs can be broadly dichotomized into structural interventions and substitution therapies. Structural interventions seek to alter the *risk environment*, which refers to the context in which illicit drug use takes place (e.g., settings where clean syringes may be scarce). In general, structural interventions involve the provision of sterile syringes, safer crack kits, and/or supervised settings for illicit drug use. However, this review will also address other interventions, such as educational approaches and outreach-based interventions, that seek to educate individuals and groups and to modify behaviour.

4.1 Needle Exchange

Since a primary risk factor for blood-borne infections including HIV and HCV is the sharing of used syringes,³⁸⁻⁴¹ a cornerstone of harm reduction for IDU involves making sterile syringes available through needle exchange programs (NEP) and other means. The specific biologic action of NEP is a form of vector control that acts by reducing the time that needles spend in circulation and by providing ready access to unused syringes.⁴² Over a decade of systematic evaluation has indicated that NEP have been effective at reducing HIV risk behaviour^{38,43} and rates of HIV transmission.^{40,44-46} Needle exchange has been shown to afford a crucial opportunity to reach drug users and provide them with additional resources such as HIV testing and counselling, referrals to drug treatment and intensive case management. Because of ethical constraints, NEP have primarily been evaluated through ecological and cohort studies. One study, using data from the US Centers for Disease Control and Prevention, demonstrated that, on average, HIV seroprevalence increased by 5.9 per cent per year in 52 cities without NEP and decreased by 5.8 per cent per year in 29 cities with NEP.⁴⁵ One study of New York's syringe exchange programs suggested that not using the exchanges was associated with a hazard ratio of 3.35 (95% CI 1.29, 8.65) for incident HIV infection compared with using the exchanges.⁴⁰ Studies from Seattle and New Haven have also shown reductions in hepatitis C, hepatitis B and HIV associated with use of needle exchange. Together, the evidence in support of NEP has led to the endorsement of NEP by many large scientific bodies, including the World Health Organization.^{47,48}

There has been some controversy about the fact that Vancouver has experienced an explosive HIV epidemic despite the existence of a large NEP.⁴⁹ This issue has been explored in detail but will be described here briefly.⁵⁰ First, the elevated risks of HIV transmission associated with cocaine injection have been demonstrated in a number of settings, and the prevalence of cocaine injection is higher in Vancouver than in most other North American cities.^{18,51,52} The higher risk of HIV among cocaine injectors, in comparison to heroin injectors, is believed to be due to the short half-life of cocaine and the fact that users can inject up to 20 times per day.¹⁸ Other local variables also explain the elevated HIV rate. Specifically, the population using the Vancouver exchange more frequently was shown to have high rates of homelessness and sex-trade involvement, both of which have been shown to predispose IDU to HIV infection.^{53,54} Among those Vancouver IDU not living on the street or in shelters, most reside in densely packed single room occupancy hotels, where the potential for network formation is exceedingly high.⁵³ As well, a number of programmatic deficiencies related to the delivery of local NEP services contributed to a situation where a substantial number of IDU had persistent difficulty accessing

syringes.⁴³ Specifically, factors such as limited hours of operation and one-for-one syringe exchange policies contributed to the problems of sterile syringe access locally.⁵⁵ Finally, it is also noteworthy that the community has been characterized by limited access to addiction treatment.^{4,56} As such, the fact that Vancouver has experienced an HIV epidemic among IDU despite the existence of a NEP does not detract from the overall evidence that NEP are an effective strategy for infectious disease prevention.

4.1.1 Conclusions

Overall, the evidence regarding the efficacy of NEP for communicable disease control was found to be Class A, given consistent findings from a large body of 2++ studies for efficacy, with strong evidence of corroboration.

4.2 **Prison-based Needle Exchange**

An increasing number of penal institutions have established and evaluated needle exchange or distribution programs as a means to control the spread of infectious diseases among inmates who inject drugs. In Switzerland, prison-based NEP were first implemented in the early 1990s.⁵⁷ Since this time, NEP have been introduced in penal institutions in Germany, Spain, Moldova, Kyrgyzstan and Belarus.⁵⁸ A recent international review suggests that Italy, Portugal and Greece are also considering introducing NEP within prisons.⁵⁷

Evaluations of European prison-based NEP have been highly favourable, indicating positive results for all programs reviewed.^{57,59} These programs distributed syringes in a variety of ways, including doctors, vending machines, drug counselling services, correctional staff or external staff. The evaluations indicated that the prison-based NEP were associated with stable or decreased levels of drug use, declines in syringe sharing, and no new cases of HIV or HCV infection. In addition, the negative consequences of NEP that have been projected by prison officials and staff were not observed in any of the settings. Syringes were not used as weapons against guards or inmates, increases in injection drug use were not observed, and transition into injection drug use among prisoners was not reported. Staff attitudes towards NEP were also said to be generally positive.

4.2.1 Conclusions

Evaluations of prison-based needle exchange programs have primarily focused on process dimensions, although declines in behaviours that result in infectious disease spread (e.g., syringe sharing) have been noted. Given the favourable results pertaining to implementation of prison-based needle exchange programs, there is no evidence to suggest that the benefits of this approach observed in the community are not replicated in prisons. In fact, given the nature of prison environments, programs such as needle exchange may be particularly beneficial in this setting. Overall, the evidence for prison-based NEP is Class A.

Further, it should be noted that the “principle of equivalence” is applicable to even the most controversial HIV prevention programs, including needle exchange. For instance, in 1993, the WHO published its *Guidelines on HIV Infection and AIDS in Prisons*, which states that “in countries where clean syringes and needles are made available to injecting drug users in the

community, consideration should be given to providing clean injecting equipment during detention.²³ Although there have been successes with prison-based needle exchange in a number of countries,⁶⁰ including those with limited resources, prison-based needle exchange remains unimplemented in Canadian prisons.

4.3 Safer Crack Kit Distribution

It has been suggested that a potential source of blood-borne disease transmission lies in the sharing of non-injection drug use equipment: pipes, straws and spoons.⁶¹⁻⁶⁴ The potential risk originates from the fact that the equipment comes into contact with blood or other bodily fluids in the nose and mouth, and thus, when the equipment is shared, it provides a route of transmission for HCV and other pathogens, including tuberculosis.^{63,65,66} This is of particular concern for HCV because of the virus's ability to maintain its infectivity in the environment and the high prevalence of HCV among illicit drug users.⁶⁷ Further, crack smokers have a high prevalence of oral lesions (blisters, sores, cuts) on their lips and in their mouths.^{68,69} These lesions are frequently caused by contact of the mouth and lips with hot smoke, hot glass or metal pipe stems, steel wool used as stem filters, or the sharp edges of glass pipe stems.^{68,69} Alternatively, drug users often manufacture their own crack pipes out of various materials. The metal tubes of these devices may conduct the heat from the flame used to vaporize the crack, and therefore burned and blistered lips are increasingly common in these settings.⁶⁹ There is some evidence that sores caused by crack smoking may facilitate oral transmission of blood-borne infections.⁶⁸ Crack stems are frequently shared, and consequently crack users may have high-risk blood exposure through burned, blistered or cut lips.⁶⁹

In response to the harms associated with crack use, a growing number of cities have implemented crack kit distribution programs.⁷⁰⁻⁷² These kits are typically distributed during the course of outreach work and at times by fixed-site needle exchange operators. The kits most often include a straight shooter for smoking (i.e., glass stem and mouthpiece), metal screens, matches, Vaseline, condoms, lubricant, hand wipes, and alcohol swabs. Some kits also include lip balm, chewing gum, and information materials concerning safer crack use and treatment of oral sores and lesions. Despite the well-known harms associated with crack cocaine smoking and the potential for the reduction of these harms through the distribution of safer crack kits, there have been no formal evaluations of this strategy to date.⁷²

4.3.1 Conclusions

Safer crack kit distribution programs were graded as Class D evidence for communicable disease control. This grade, however, was based on lack of evidence, and evaluation of this approach is warranted given the increasing harms of crack cocaine and the few tools available to address these growing concerns.

4.4 Supervised Injection Facilities

In response to ongoing drug-related harms among IDU, several countries have added supervised injection facilities (SIF) to the array of health programs and services that are offered. Unlike illegal “shooting galleries” run by drug dealers, SIF are controlled health care settings where drug users inject pre-obtained illicit drugs under staff supervision and receive sterile injecting

equipment, primary health care, counselling, and referral to health and social services. SIF have been referred to throughout the world as health rooms, safe injection rooms, lane rooms, fix-rooms, consumption rooms, medically supervised injecting centres, and off-street injecting facilities.⁷³ It should be noted that SIF vary considerably in their design and operation, driven by the specific local concerns, overarching policy considerations, and the unique needs of the populations they serve.⁷⁴ At one end of a continuum are facilities that offer a safe and hygienic environment in which IDU can consume their pre-obtained drugs using sterile equipment provided on-site, while being overseen by personnel trained in basic first aid and cardio-pulmonary resuscitation. At the other end are comprehensive SIF that, in addition to the above, offer a much larger array of health and social services for IDU.⁷³

The goals associated with the establishment of SIF are to reduce blood-borne disease transmission, fatal and non-fatal overdose, and public nuisance associated with injection drug use; to improve the general health of clients; and to increase client uptake of health and social services.⁷⁵ Typically, SIF achieve these goals by: (a) supervising injections in a controlled setting to ensure safety and quick response to overdose; (b) providing sterile injecting equipment and condoms and collecting used syringes; (c) providing information on safer sex and injecting practices; (d) providing counselling and primary medical care; and (e) maintaining and improving contact with marginalized clients and facilitating reintegration through referral to drug treatment, detox, and other medical and health services.⁷⁶ There are approximately 50 SIF in operation around the world, including 16 in the Netherlands, 17 in Switzerland, 13 in Germany, and at least one in each of Spain, Luxembourg and Austria.^{77,78} An 18-month trial of a SIF has recently been completed in Sydney, Australia.⁷⁹

Supervised injection facilities appear to serve a unique and important function, particularly in terms of providing immediate response to overdoses, increasing uptake of health and social services, and reducing the problems associated with public injection. While outreach services and needle exchanges are able to provide sterile injecting equipment, and in some cases referral, there are no indications that these services reduce the amount of injection drug use occurring in public spaces.⁷⁴ Within SIF, staff engage with IDU in a secure setting where they can inject, and therefore staff are more favourably positioned to engage IDU in a help-seeking relationship, to discuss health concerns, and to provide them with immediate medical care, counselling or referrals.⁷⁴

On September 22, 2003, Vancouver, Canada opened North America's first government-sanctioned SIF.⁷ Federal approval for the three-year project was granted on the condition that the health and social impacts of the SIF be rigorously evaluated. As such, the evaluation has provided some of the most rigorous data on the impacts of SIF. To date, the Vancouver SIF has been shown to attract a population of extremely high-risk IDU, to improve public order by reducing public drug use and public disposal of used syringes, and to improve uptake of addiction treatment. These strategies have immediate implications for the prevention of communicable diseases, since activities such as public drug use are positively associated with syringe sharing and infectious disease incidence (e.g., HIV and HCV), whereas provision of detoxification services and addiction treatment may protect against the acquisition of infectious diseases by helping to reduce or eliminate injection drug use.

Although there is currently no definitive evidence demonstrating that SIF reduce the incidence of HIV and HCV, the provision of sterile injecting equipment, condoms and education within SIF has likely reduced the risk of blood-borne disease transmission. Support for such effects is indicated by reports of increased safe injecting and reduced needle sharing among SIF clients.⁷⁷ Again, the most compelling evidence to date comes from the Vancouver SIF evaluation. In one study, use of the SIF was independently associated with reduced syringe sharing in comparison to non-SIF users.⁸⁰ Although these results could have been due to differences between SIF users and non-users, SIF users actually have several characteristics that have previously been shown to be associated with higher rates of syringe sharing. A subsequent study showed that SIF use was associated with less syringe borrowing by HIV-negative IDU and less syringe lending by HIV-infected IDU.⁸¹

4.4.1 Conclusions

Despite the evidence that SIF reduce syringe sharing and injection drug use in risky environments (e.g., shooting galleries, alleys, etc.), to date there have been no studies of the impact of SIF on the incidence of HIV or other blood-borne diseases. In the absence of available studies, SIF were graded as Class B for the evidence of their effectiveness in controlling communicable disease.

4.5 Supervised Smoking Facilities

Because of the success of SIF in several European nations, Australia, and most recently Vancouver, interest in supervised smoking facilities (SSF) has grown. The primary objectives of SSF are similar to those established for SIF. They generally include reducing public drug use and the sharing of non-injection drug use paraphernalia; improving contact between a highly marginalized, “at-risk” population and the health care system; enhancing recruitment into addiction treatment; increasing access to general social services, such as housing and welfare; and reducing drug overdoses.⁸² Within SSF, non-injecting drug users are generally provided with sterile drug use equipment (e.g., crack pipes), a clean and safe environment in which to use pre-obtained illicit drugs, and education as to the possible risks associated with smoking illicit drugs. Safer smoking sites would be expected to provide medical attention in the event of an overdose, and access or referral to primary health care and other services, including drug treatment.

A recent review of the potential impacts of SSF concluded that implementation of a SSF evaluation could be based on a sound public health rationale related to the goals of improved public order, prevention of infectious disease, prevention of transition to injection drug use, and improved access to medical care and addiction treatment services.⁸³ Two subsequent feasibility studies have implied that SSF would be successful at attracting the target population, including individuals who frequently share crack pipes.^{82,84} Although there are limited data on the impact of SSF from Switzerland, there are very limited data on the impacts of these programs and no data on communicable disease control.⁸³

4.5.1 Conclusions

Supervised smoking facilities were graded as Class D evidence for communicable disease control. This grade, however, was based on lack of evidence, and evaluation of SSF is warranted given the increasing harms of crack cocaine and methamphetamine and the few tools available to address these growing concerns. For instance, SSF may prove of value for reducing transition into injection drug use, a key communicable disease control strategy.⁸⁵

5.0 REPLACEMENT THERAPY FOR OPIATE ADDICTION

In North America, the primary method for the treatment of opiate addiction is the provision of long-acting opiate agonists, primarily methadone hydrochloride, for short- or long-term maintenance therapy.^{86,87} An alternative oral opiate substitution therapy, levo-alpha acetylmethadyl (LAAM), was approved for use in 1993.⁸⁸ In addition, buprenorphine is an opiate substitute used for addiction maintenance that has recently been approved for use in Canada.^{89,90} Although it was not statistically significant, one meta-analysis suggests that there is a small treatment preference for methadone over LAAM.⁹⁰ A recent randomized trial, published in the *New England Journal of Medicine*, demonstrated that retention rates at 17 weeks with high-dose methadone were comparable with, if not higher than, buprenorphine or LAAM (73 per cent vs. 58 per cent vs. 53 per cent).⁹¹ Because of the similar retention rates found among patients on methadone, buprenorphine and LAAM in clinical trials, and the fact that methadone is the current standard of care in Canada, this review will focus on methadone over LAAM and buprenorphine in assessing the value of currently available substitution therapies. Since heroin prescription is currently being evaluated as an additional potential intervention, the evidence in this area will also be assessed.

5.1 Methadone Maintenance Therapy

Methadone is a long-acting synthetic opiate agonist that is easily absorbed when taken orally and has a half-life of 24-36 hours, allowing for once-daily administration.⁹² Generally, methadone maintenance therapy (MMT) involves providing methadone on a daily basis to the patient.^{93,94} Previous studies have demonstrated that MMT is successful in blocking the effects of opiate withdrawal symptoms and the euphoria produced by opioids such as heroin, and may correct and stabilize a lesion or defect in the endogenous opioid system.⁹⁵⁻⁹⁷ As a result, MMT is the most cost-effective strategy for reducing major risks, harms and costs associated with untreated opiate addiction among patients attracted to and successfully retained in MMT.⁹⁸⁻¹⁰⁰ MMT has been shown to lead to reductions in, and even the elimination of, the use of opiates,¹⁰¹⁻¹⁰⁶ as well as reductions in criminal activity, unemployment and mortality rates.^{96,101,102,107-111} MMT is also associated with reduced HIV and viral hepatitis transmission rates.^{108,112-115} Several studies have also shown reductions in risk behaviours such as needle sharing, having numerous sexual partners, engaging in sex without condom use, and exchange of sex for drugs or money.^{104,116-119}

Optimal treatment outcomes have generally been correlated with a number of programmatic factors, including sufficient methadone dosing, high level and quality of psychosocial care services, duration of treatment retention, and patient identification with the rules of the methadone program and staff of treatment centres.^{35,36,120-122} Participation in methadone maintenance treatment may also play a crucial role in the management of HIV disease among HIV-infected opioid-dependent patients.¹²³

5.1.1 Conclusions

Overall, the provision of methadone is graded as Class A evidence for communicable disease control, based on randomized studies showing the drug's efficacy for the treatment of opiate dependency and reduction of subsequent drug-related harms.

5.2 Prison-based Methadone

A small number of evaluations of MMT programs in prisons have indicated positive results.^{124,125} For example, results from a randomized controlled trial of the MMT program in prisons in New South Wales, Australia indicated lower rates of heroin, injection drug use, and syringe sharing among those enrolled in MMT compared to controls.¹²⁵ In Canada, the federal prison system expanded access to MMT after evaluations demonstrated that MMT has a positive impact on release outcome and on institutional behaviour.¹²⁶

5.2.1 Conclusions

Given the favourable results pertaining to implementation of prison-based methadone programs, there is no evidence to suggest that the benefits of this approach that have been observed in the community are not replicated in prisons. Specifically, there is nothing about the prison environment that suggests the evidence should not be graded as Class A (i.e., same as community-derived evidence). Further, the World Health Organization *Guidelines on HIV Infection and AIDS in Prisons* has recommend: “Prisoners on methadone maintenance prior to imprisonment should be able to continue this treatment while in prison”.¹²⁷ This point is particularly relevant in light of findings indicating that people taken off methadone once incarcerated often return to narcotic use, usually within the penal institutions, and often via injection.¹²⁸ Also, consistent with the principle of equivalence, it has further been recommended that MMT should also be available in prisons in countries where methadone maintenance is available in the community.¹²⁷

5.3 Heroin Prescription

Although scientific documentation of the efficacy of methadone treatment is well established, the therapy does not represent a cure-all for the problem of opiate addiction. One limitation to the overall effectiveness of MMT is its restricted success in retaining patients in treatment. Studies suggest that MMT programs lose one-third of their original treatment population within the first 12 months and another third within the following 24 months.¹²⁹⁻¹³¹ Although methadone has proven effective as a first-line therapy for opiate-addicted individuals, additional treatment strategies have been required for opiate-addicted individuals who fail MMT. In light of the limitations of MMT, several European countries have initiated programs that provide alternative forms of drug treatment, including injectable opiates such as heroin. For instance, England has provided injectable heroin and methadone for the treatment of opiate addiction for several decades.¹³²⁻¹³⁵

Among the most detailed scientific information on the health and social impacts of heroin prescription comes from a three-year, multi-centre study in Switzerland conducted from 1994 to 1997.^{31,136} The entry criteria of the Swiss study required that participants demonstrate a long-term drug abuse history and multiple failed treatment attempts. Overall, the study provided heroin-substituted opiate addiction treatment to over 1,000 opiate addicts,¹³⁷ and almost 2,000 opiate addicts have received heroin-substituted treatment as part of this ongoing program since 1997.^{31,136} The Swiss study showed that prescription heroin could have a dramatic impact as a treatment for drug users. For instance, overall, the heroin prescription program was able to retained 69 percent of its original sample of highly addicted and treatment-resistant drug users

for the first 18-month study period. These findings are in contrast to the studies of MMT, LAAM and buprenorphine reported earlier in this document, which found that these approaches typically lose one-third of their original treatment population within the first 12 months and another third within the following 24 months.^{129,131}

Of those who dropped out of heroin-assisted treatment in the Swiss study, more than half switched to other treatments, such as methadone, or became abstinent. No deaths occurred in the treatment program as a direct consequence of any of the opiates prescribed, including heroin. Analysis of 12-month retention rates showed that among the heroin maintenance group, the retention rate was double that of methadone maintenance and double residential drug-free treatment samples from other studies in Switzerland. Self-reported drug use decreased dramatically during the course of the study. Of those who remained in treatment for 18 months, 81 per cent reported illicit heroin use at entry, whereas by 6 months, 61 per cent reported no illicit heroin use, and by 18 months, 74 per cent reported no illicit heroin use.¹³⁷⁻¹³⁹

An additional benefit of heroin prescription was a reduction in cocaine use from 31 per cent to 7 per cent. This may be of particular importance in Canada, where poly-drug (heroin and cocaine) and cocaine injectors have been shown to be at the highest risk of blood-borne disease infection and HIV risk behaviour.

With regard to health and social outcomes, substantial improvements were also documented across several measured domains.¹³⁷⁻¹³⁹ First, the proportion of participants with unstable housing fell during the 18 months (43 per cent on admission to 21 per cent at 18 months). Similarly, the rate of employment doubled from 14 per cent to 32 per cent. Decreases in criminal activity were also observed, with a decrease in illegal sources of income of 69 per cent to 10 per cent. There was also a greater than 50 per cent reduction in criminal offences registered by the police among participants in the study during the first 18 months. A subsequent cost-benefit analysis of the study suggested that the outcomes were cost-effective at a ratio factor of almost 2 to 1. As a result of the program's success, the Swiss public has voted in recent referenda in favour of continuing the trial as a long-standing program. Much has been made about the validity of the Swiss findings because the Swiss study was not conducted as part of a randomized controlled trial, which is the regular standard for approval of pharmaceutical agents. In response to criticisms, the results of the Swiss study have been evaluated by an independent panel hired by the World Health Organization (WHO). The WHO panel supported the Swiss findings and issued a call for continued exploration into the effectiveness of heroin therapy, including randomized studies.¹³⁹

As a result of the apparent successes observed in Switzerland, the Dutch government commissioned the implementation of two multi-site controlled, randomized trials that involved prescribing injectable heroin to highly addicted individuals. These trials began in July 1998. In the early results of these trials, the investigators concluded that:

The results of both [Dutch] trials showed that the supervised co-prescription of heroin to chronic, treatment-resistant methadone patients led to improvements in all health outcome domains: physical health, mental status and social functioning.¹⁴⁰

The report's first recommendation states:

The consistency of the results both within the Dutch trials and between the Dutch trials and the studies in Switzerland constitutes a sufficient basis for the development of a last-resort pharmaco-therapeutic option of medically prescribed heroin to chronic, treatment-resistant heroin dependent and methadone treated patients.¹⁴⁰

The results of the Dutch heroin prescription trials have subsequently been published and have concluded that "Supervised co-prescription of heroin is feasible, more effective, and probably as safe as methadone alone in reducing the many physical, mental, and social problems of treatment resistant heroin addicts."¹⁴¹

5.3.1 Conclusions

Overall, there is Class A evidence that heroin prescription may be more effective than methadone for reducing the harms associated with opiate addiction, including the spread of communicable disease.

6.0 EDUCATIONAL APPROACHES

Harm reduction messages are frequently disseminated through a variety of educational programs. Typical strategies include use of posters and brochures in settings and services frequented by drug users, web-based materials, videos, and the use of outreach workers and service providers within health care settings to provide education to individuals and groups. While such educational efforts typically cover a range of topics, including overdose prevention, many focus on the reduction of communicable disease transmission.

The evaluation of educational approaches is challenging, most often because it is difficult to isolate the effects of such approaches, given that they are typically offered as one component of a larger harm reduction program (e.g., one that includes provision of sterile syringes). However, a few evaluations have demonstrated that these approaches are well accepted by drug users, and a few studies have demonstrated some effects of educational efforts on knowledge change and risk behaviour. For example, in a study involving drug users in Kathmandu, Nepal, indicators of unsafe injecting related to communicable disease transmission fell as knowledge of HIV rose, more so among those who had been in touch for a longer period with a program delivering harm reduction education and sterile syringes than among those who had had less exposure to the program.¹⁴² In another study involving IDU in Baltimore, providing education to “peer leaders” resulted in a significant increase in condom use and in cleaning used syringes with bleach.¹⁴³ The peer leaders’ social network members, compared with controls, were also significantly more likely to report greater rates of syringe cleaning, and the acquisition of syringe cleaning education was traced to the peer leaders. Another study also involving the use of peers to provide outreach-based education found that a peer-driven intervention model produced substantial increases in HIV prevention knowledge and decreases in HIV risk behaviour.¹⁴⁴ This approach involving the use of peers also outperformed a traditional outreach program and was considerably more cost-effective.¹⁴⁵ However, given the heterogeneity of educational interventions and the methods used to evaluate them, it is not surprising that evaluations of these approaches have produced equivocal results.^{146,147}

6.1.1 Conclusions

Overall, there is Class C to Class D evidence indicating that educational interventions, on their own, can reduce the harms of illicit drug use by, among other things, promoting communicable disease control through the reduction of risk behaviour directly linked to communicable disease transmission. However, this grading should be interpreted with great caution, as educational approaches vary immensely in their design and delivery, and therefore not all educational interventions can be regarded as Class C or D. Further, the more efficacious educational interventions typically are undertaken by outreach workers and therefore should not be regarded as simple educational interventions (see Section 6.2 on outreach interventions). It should be noted, however, that the World Health Organization recommends that educational interventions be included as an essential part of HIV prevention strategies.¹⁴⁸

6.2 Outreach Interventions

Outreach programs have also been widely implemented in community-based settings, and have been credited as one of three components contributing to low HIV prevalence in several cities.⁴⁴ Outreach programs are used to make contact with out-of-treatment IDU who may be at highest risk for HIV infection.¹⁴⁵ Once initial contact is made, education, resources (e.g., sterile syringes, condoms, bleach kits, literature) and counselling support are often provided. Overall, outreach workers serve as an important link between active IDU and institutional testing, prevention and addiction treatment services.¹⁴³

Numerous evaluations of outreach-based interventions have been undertaken. These evaluations have considered a range of outreach approaches and employed a range of evaluation methods. One of the more comprehensive evaluations of outreach interventions was undertaken by Coyle, Needle and Normand in 1998.¹⁴⁹ These authors reviewed 36 published studies of HIV-focused outreach interventions. According to the authors,

because most of the evaluations were based on pretest and posttest measures of behavior rather than on controlled studies, results were examined with respect to accepted criteria for attributing intervention causality, that is, the plausibility of cause and effect, correct temporal sequence, consistency of findings across reports, strength of associations observed, specifically of associations, and dose-response relationships between interventions and observed outcomes.

The majority of studies in this review showed that IDU in various contexts reduced risk behaviours related to communicable disease transmission following participation in outreach interventions; there were reductions in drug injections,¹⁵⁰⁻¹⁶⁶ crack use,^{156,166-168} sex-related risks,^{150,152,154,157,158,162,169,170} and the sharing and/or reuse of syringes and other injection equipment.^{151-154,157,160,162-167,171-173} The outreach interventions were also shown to have promoted entry into drug treatment^{152,156,162,170} and to have increased the rates of syringe disinfection.^{151-153,163,166,171,174} One quasi-experimental study also found a reduction in HIV seroincidence.¹⁷⁵ The authors of this review concluded that the accumulated evidence strongly indicated that “outreach-based interventions have been effective in reaching out-of-treatment IDUs, providing the means for behavior changes and inducing behavior change in the desired direction.” They further concluded that there is evidence that participation in outreach-based HIV prevention interventions can lead to lower rates of HIV incidence.

6.2.1 Conclusions

Overall, there is Class A evidence supporting the efficacy of outreach interventions in promoting communicable disease control. However, this rating may not apply equally to all outreach-based interventions, which vary considerably in their design and delivery. The evidence to date indicates that those interventions that involve peers (i.e., drug users), involve the dissemination of sterile syringes, and have direct links to infectious disease testing, counselling services and addiction treatment are likely to be most effective in reducing communicable disease transmission. Outreach-based interventions incorporating these components are generally regarded as an essential part of a comprehensive harm reduction strategy to reduce communicable disease transmission among illicit drug users.

7.0 FACTORS AFFECTING THE EFFICACY OF HARM REDUCTION PROGRAMS

The present review indicates that rigorous research and evaluation have found various harm reduction interventions to be efficacious. However, given the social circumstances and heterogeneity surrounding illicit drug use, a growing body of literature has identified a number of factors that can positively or negatively affect the efficacy of any harm reduction program. These factors are early intervention; responsiveness; coverage; comprehensiveness, location and design; and involvement of current/former drug users. These factors are described in more detail in the sections that follow.

7.1 Early Intervention

Although there is considerable regional heterogeneity associated with communicable disease transmission among drug users as a result of differences in drug use patterns and available programs, once established, diseases such as HIV and HCV can spread rapidly within drug-using communities.⁴ Therefore, it is critical that interventions be implemented as early as possible. As Strathdee et al. (1998) note, “[t]he delicate balance between an epidemic that is averted and one that is merely delayed argues against complacency in the realm of prevention”⁹⁰. However, harm reduction interventions, in particular NEP, have also been credited with reversing epidemics in high prevalence settings, and should not be overlooked in these instances.^{90,176}

7.2 Responsiveness

It has been well documented that risks for HIV and HCV infection among drug users can vary considerably within and across settings.¹⁷⁷ As well, risk behaviour is known to change over time as a result of changes in patterns of drug use, prevention initiatives and evolving social networks.¹⁷⁸ Consequently, it is critical that methods be employed that identify existing and emerging risk behaviours and environments. For instance, needle-sharing behaviours are known to vary across settings and have been attributed to various factors, including public injection, attendance at shooting galleries, and contact with “professional injector dealers” who inject several consumers with one syringe.¹⁷⁹⁻¹⁸² In other settings, HIV risk has been attributed primarily to the sharing of syringes within the context of intimate relationships.¹⁸³ Furthermore, immediate HIV risk behaviour is known to change rapidly in the face of evolving drug supply and specific local consumption practices, such as the widespread use of cocaine injection and the use of crack cocaine.^{18,43,184}

In order to address immediate and emerging risk behaviours, harm reduction interventions should be informed by ongoing data collection and monitoring. Strategies that have been successful in informing harm reduction interventions include participant observation, key informant interviews, inclusion of drug users in service design and rapid assessment methods.^{179,185}

7.3 Coverage

While communicable disease transmission among drug users is often attributed to needle sharing, secondary transmission to sexual partners and offspring is also widespread.⁹⁰ Therefore, in order to ensure adequate coverage, HIV prevention and risk reduction programs should target not only drug users but also their intimate partners, who may or may not be drug users themselves. As well, because risk practices are often established within the context of drug-using social networks, it is important that programs identify and target not only individual IDU but also the social networks they participate in.¹⁸⁶ Examples of successful social network interventions have been documented throughout the developed and developing world.^{185,186}

7.4 Comprehensiveness, Location and Design

Given the observed diversity in risk behaviour within and across drug-using communities, an effective harm reduction response requires that a comprehensive range of low and medium threshold interventions be delivered in various locations and at various times. Relying on any one service as an isolated intervention is unlikely to be sufficient to avert communicable disease epidemics. For instance, despite its widely noted benefits with regards to HIV prevention, offering syringe exchange as an isolated intervention in Vancouver, Canada was inadequate in preventing the city's HIV epidemic,⁴ with recent analyses indicating that a lack of addiction treatment⁵⁶ and programmatic deficiencies in the NEP contributed to the epidemic.^{43,187} Conversely, in other settings such as Australia, where syringe exchange has been complemented by the addition of outreach and educational programs, peer-driven organizations and drug treatment, the comprehensiveness of the programs offered have been credited with sustaining low HIV prevalence among IDU.⁴⁴

However, the location and design of specific programs must be tailored to meet the needs of the local population. Experience suggests that programs are most effective when placed in close proximity to drug-using networks and when programs are offered at all hours when drug consumption and other related risk behaviours are occurring (e.g., at night).¹⁶ Finally, because it is known that drug users often avoid institutional care and are driven to hidden locations as a result of police activities, harm reduction programming should also incorporate outreach as a means of expanding the coverage of prevention and risk reduction programs.¹⁴⁴

7.5 Involvement of Current/Former Drug Users

The majority of these services and programs designed to reduce the harms associated with illicit drug use operate under the “provider-client” model, in which service providers strive to meet the needs of drug users. The limitations of this model are becoming increasingly recognized, and include the difficulty that service providers have in reaching drug users on their own turf, difficult communication between providers and clients, and fear among drug users that use of services may alert police to their activities.^{144,145,188,189}

In response to the limitations of traditional provider-client models of service delivery, peer-driven interventions, involving current/former drug users, have been developed throughout the world as one method of promoting the reduction of communicable disease transmission.^{186,190} These programs are often implemented to address gaps in conventional service delivery, and

have been found to expand the reach and effectiveness of various harm reduction programs, including syringe exchange, education and outreach programs.^{145,186,189,190} These programs have also been found to be more cost-effective than traditional service-provider models.¹⁴⁴ Many peer-driven interventions focus on specific drug-using social networks and the risk-specific practices (e.g., syringe sharing) occurring within these networks.¹⁴³ These interventions often involve peer or “indigenous leaders” within networks for the purpose of disseminating educational messages and modifying established risk practices within distinct social networks,¹⁴³ while other interventions have focused on creating systems of reinforcement for safer behaviour among peers.^{144,145} Given the well-noted benefits of involving drug users, harm reduction programs should involve “peers” in order to ensure maximum effectiveness.

8.0 SUMMARY

Injection drug use affects all Canadians. The costs of law enforcement, incarceration and health care expenditures result in an enormous financial burden. In addition, there are large social and human costs that stem from the crime, disease and death that arise from illicit drug use.

However, growing evidence suggests that a great deal of this human and financial cost can be reduced by harm reduction programs. Unfortunately, in Canada, the majority of resources have been directed to those interventions whose effectiveness is most in doubt. For instance, the majority of resources have been directed to supply reduction strategies, as well as high and medium threshold health services. This approach has been a well-documented failure,¹⁹¹⁻¹⁹⁴ and the rates of overdose and blood-borne infectious diseases in Canada are among the highest in the developed world.¹⁹¹ A review of the scientific evidence indicates that various harm reduction programs have been implemented successfully and now serve to complement ongoing enforcement, treatment and prevention initiatives. Given the ongoing drug-related harm throughout British Columbia, efforts to significantly expand and appropriately evaluate harm reduction programs are an urgent priority.

REFERENCES

1. Auditor General of Canada. Chapter 11—Illicit drugs: The Federal Government's role. 2001 December report of the Auditor General of Canada. Ottawa (ON): Author; 2001 [cited 2002 Jan]. Available from: <http://www.oag-bvg.gc.ca/internet/docs/0111ce.pdf> .
2. Federal/Provincial/Territorial Advisory Committee on Population Health. Reducing the harm associated with injection drug use in Canada. Ottawa (ON): Minister of Public Works and Government Services Canada; 2001.
3. Wood E, Kerr T, Spittal PM, Tyndall MW, O'Shaughnessy MV, Schechter MT. The health care and fiscal costs of the illicit drug use epidemic: The impact of conventional drug control strategies. *BCMJ* 2003;45(3):128–134.
4. Strathdee SA, Patrick DM, Currie SL, Cornelisse PG, Rekart ML, Montaner JS, et al. Needle exchange is not enough: Lessons from the Vancouver injecting drug use study. *AIDS* 1997;11(8):F59–65.
5. Miller CL, Johnston C, Spittal PM, Li K, Laliberté N, Montaner JS, et al. Opportunities for prevention: Hepatitis C prevalence and incidence in a cohort of young injection drug users. *Hepatology* 2002;36(3):737–742.
6. Wood E, Montaner JS, Tyndall MW, Schechter MT, O'Shaughnessy MV, Hogg RS. Prevalence and correlates of untreated human immunodeficiency virus type 1 infection among persons who have died in the era of modern antiretroviral therapy. *J Infect Dis* 2003;188(8):1164–1170.
7. Wood E, Kerr T, Montaner JS, Strathdee SA, Wodak A, Hankins CA, et al. Rationale for evaluating North America's first medically supervised safer injecting facility. *Lancet Infect Dis* 2004;4(5):301–306.
8. Kuyper LM, Lampinen TM, Li K, Spittal PM, Hogg RS, Schechter MT, et al. Factors associated with sex trade involvement among male participants in a prospective study of injection drug users. *Sex Transm Infect* 2004;80(6):531–535.
9. Wodak A. Can we prevent HIV transmission among IDU's? [Abstract No. 17] Annual Conference / Australasian Society for HIV Medicine 1996;8:43.
10. Drucker E. Drug prohibition and public health: 25 years of evidence. *Public Health Rep* 1999;114(1):14–29.
11. Dolan K, Wodak A, Penny R. AIDS behind bars: Preventing HIV spread among incarcerated drug injectors. *AIDS* 1995;9(8):825–832.
12. Drucker E. Drug prohibition and public health: 25 years of evidence. *Public Health Rep* 1999;114(1):14–29.
13. Taylor A, Goldberg D, Emslie J, Wrench J, Gruer L, Cameron S, et al. Outbreak of HIV infection in a Scottish prison. *BMJ* 1995;310(6975):289–292.
14. Small W, Kain S, Laliberte N, Schechter MT, O'Shaughnessy MV, Spittal PM. Incarceration, addiction, and harm reduction: Inmates' experience injecting drugs in prison. *Subst Use Misuse* 2003;40(6):831–843.

15. Wood E, Li K, Small W, Montaner JS, Schechter MT, Kerr T. Recent incarceration independently associated with syringe sharing by injection drug users. *Public Health Rep* 2005;120(2):150–156.
16. Wood E, Tyndall MW, Spittal P, Li K, Hogg RS, O'Shaughnessy MV, et al. Needle exchange and difficulty with needle access during an ongoing HIV epidemic. *Int J Drug Policy* 2002;13(2):95–102.
17. Wood E, Hogg RS, Yip B, Harrigan PR, O'Shaughnessy MV, Montaner JS. Effect of medication adherence on survival of HIV-infected adults who start highly active antiretroviral therapy when the CD4 cell count is 0.200 to 0.350 109 cells/L. *Ann Intern Med* 2003;139(10):810–816.
18. Tyndall MW, Currie S, Spittal P, Li K, Wood E, O'Shaughnessy MV, et al. Intensive injection cocaine use as the primary risk factor in the Vancouver HIV-1 epidemic. *AIDS* 2003;17(6):887–893.
19. Hagan H. The relevance of attributable risk measures to HIV prevention planning. *AIDS* 2003; 17(6):911–913.
20. Small W, Kain S, Laliberte N, Schechter MT, O'Shaughnessy MV, Spittal PM. Incarceration, addiction, and harm reduction: Inmates' experience injecting drugs in prison. *Subst Use Misuse* 2003;40(6):831–843.
21. Hankins C. Confronting HIV infection in prisons. *CMAJ* 1994;151(6):743–745.
22. Hankins CA, Gendron S, Handley MA, Richard C, Tung MT, O'Shaughnessy M. HIV infection among women in prison: An assessment of risk factors using a nonnominal methodology. *Am J Public Health* 1994;84(10):1637–1640.
23. Office of the High Commissioner for Human Rights. Basic principles for the treatment of prisoners. Geneva: United Nations; 1990.
24. Wall R, Rehm J, Fischer B, Brands B, Gliksman L, Stewart J, et al. Social costs of untreated opioid dependence. *J Urban Health* 2000;77(4):688–722.
25. Kuyper LM, Hogg RS, Montaner JS, Schechter MT, Wood E. The cost of inaction on HIV transmission among injection drug users and the potential for effective interventions. *J Urban Health* 2004;81(4):655–660.
26. Des Jarlais DC. Harm reduction—a framework for incorporating science into drug policy [editorial]. *Am J Public Health* 1995;85(1):10–12.
27. Fischer B, Rehm J, Blitz-Miller T. Injection drug use and preventive measures: a comparison of Canadian and western European jurisdictions over time. *CMAJ* 2000;162(12):1709–1713.
28. de Jong W, Wever U. The professional acceptance of drug use: A closer look at drug consumption rooms in the Netherlands, Germany, and Switzerland. *Int J Drug Policy* 1999;10(2): 99–108.
29. Wood E, Tyndall M, Schechter M. Drug supply and drug abuse. *CMAJ* 2003;168(9):1113.
30. Woodfall B, Hogg RS, Strathdee SA, Le R, Schechter MT, Montaner JS, et al. Predictors of hospitalization in persons with HIV-disease [Abstract No. PD0396]. *Int Conf AIDS* 1994;10(1):447.

31. Rehm J, Gschwend P, Steffen T, Gutzwiller F, Dobler-Mikola A, Uchtenhagen A. Feasibility, safety, and efficacy of injectable heroin prescription for refractory opioid addicts: A follow-up study. *Lancet* 2001;358(9291):1417–1423.
32. Reid RJ. A benefit-cost analysis of syringe exchange programs. *J Health Soc Policy* 2000;11(4): 41–57.
33. Yip B, Hogg RS, Frank O, Ostrow M, Strathdee SA, Montaner JS, et al. Comparative demographic analysis of patterns of HIV/AIDS mortality in industrialised nations [Abstract No. Mo.C.1544]. *Int Conf AIDS* 1996;11(1):148.
34. Veugelers PJ, Strathdee SA, Kaldor JM, Page-Shafer KA, Schechter MT, Coutinho RA, et al. Incidence and prognostic significance of symptomatic primary HIV-1 infection in homosexual men [Abstract no. Mo.C.324]. *Int Conf AIDS* 1996; 11(1):35.
35. Villelabeitia I. Columbia steps up anti-drug fight with U.S. help. *Reuters Top Stories* 2000 May 8.
36. Zule WA, Desmond DP. Attitudes toward methadone maintenance: implications for HIV prevention. *J Psychoactive Drugs* 1998;30(1):89–97.
37. Sergeev B, Karpets A, Sarang A, Tikhonov M. Prevalence and circumstances of opiate overdose among injection drug users in the Russian Federation. *J Urban Health* 2003;80(2):212–219.
38. Bluthenthal RN, Kral AH, Gee L, Erringer EA, Edlin BR. The effect of syringe exchange use on high-risk injection drug users: A cohort study. *AIDS* 2000;14(5):605–611.
39. McGeary KA, French MT. Illicit drug use and emergency room utilization. *Health Serv Res* 2000;35(1 Pt 1):153–169.
40. Des Jarlais DC, Marmor M, Paone D, Titus S, Shi Q, Perlis T, et al. HIV incidence among injecting drug users in New York City syringe-exchange programmes. *Lancet* 1996;348(9033):987–991.
41. Hagan H, Jarlais DC, Friedman SR, Purchase D, Alter MJ. Reduced risk of hepatitis B and hepatitis C among injection drug users in the Tacoma syringe exchange program. *Am J Public Health* 1995;85(11):1531–1537.
42. Drucker E, Lurie P, Wodak A, Alcabes P. Measuring harm reduction: The effects of needle and syringe exchange programs and methadone maintenance on the ecology of HIV. *AIDS* 1998;12(Suppl A):S217–230.
43. Wood E, Tyndall MW, Spittal PM, Li K, Hogg RS, Montaner JS, et al. Factors associated with persistent high-risk syringe sharing in the presence of an established needle exchange programme. *AIDS* 2002;16(6):941–943.
44. Des Jarlais DC, Hagan H, Friedman SR, Friedmann P, Goldberg D, Frischer M, et al. (1995). Maintaining low HIV seroprevalence in populations of injecting drug users. *JAMA* 1995;274(15):1226–1231.
45. Hurley SF, Jolley DJ, Kaldor JM. Effectiveness of needle-exchange programmes for prevention of HIV infection. *Lancet* 1997;349(9068):1797–1800.
46. Heimer, R, Kaplan, EH, Khoshnood, K, Jariwala, B, Cadman, EC. Needle exchange decreases the prevalence of HIV-1 proviral DNA in returned syringes in New Haven, Connecticut. *Am J Med* 1993;95(2):214–220.

47. Vlahov, D, Des Jarlais, DC, Goosby, E, Hollinger, PC, Lurie, PG, Shriver, MD, et al. (2001). Needle exchange programs for the prevention of human immunodeficiency virus infection: Epidemiology and policy. *Am J Epidemiol* 2001;154(Suppl 12):S70–77.
48. Normand, J, Vlahov, D, Moses, LE. Preventing HIV transmission: The role of sterile needles and bleach. Washington (DC): National Academy Press; 1995.
49. Schechter, MT, Strathdee, SA, Cornelisse, PG, Currie, S, Patrick, DM, Rekart, ML, et al. Do needle exchange programmes increase the spread of HIV among injection drug users? An investigation of the Vancouver outbreak. *AIDS* 1999;13(6):F45–51.
50. Wood, E, Lloyd-Smith, E, Li, K, Strathdee, SA, Small, W, Tyndall, MW, et al. Frequent needle exchange use and HIV incidence in Vancouver, Canada. *Am J Med* 2007;120(2):172–179.
51. Chaisson, RE, Bacchetti, P, Osmond, D, Brodie, B, Sande, MA, Moss, AR. Cocaine use and HIV infection in intravenous drug users in San Francisco. *JAMA* 1989;261(4):561–565.
52. Schoenbaum, EE, Hartel, D, Selwyn, PA, Klein, RS, Davenny, K, Rogers, M, et al. Risk factors for human immunodeficiency virus infection in intravenous drug users. *N Engl J Med* 1989;321(13):874–879.
53. Corneil TA, Kuyper, LM, Shovellor, J, Hogg, RS, Li, K, Spittal, PM, et al. Unstable housing, associated risk behavior, and increased risk for HIV infection among injection drug users. *Health Place* 2006;12(1):79–85.
54. Kuyper, LM, Palepu, A, Kerr, T, Li, K, Miller, CL, Spittal, PM, et al. Factors associated with sex-trade involvement among female injection drug users in a Canadian setting. *Addict Res Theory* 2005;13(2):193–199.
55. Spittal, P, Small, W, Laliberte, N, Johnson, C, Wood, E. How otherwise well meaning exchange agents can contribute to limited sterile syringe availability in Vancouver, Canada. *Int J Drug Policy* 2003;15:36–45.
56. Wood, E, Spittal, PM, Li, K, Kerr, T, Miller, CL, Hogg, RS, et al. Inability to access addiction treatment and risk of HIV-infection among injection drug users. *J Acquir Immune Defic Syndr* 2004;36(2):750–754.
57. Dolan, K, Rutter, S, Wodak, AD. Prison-based syringe exchange programmes: A review of international research and development. *Addiction* 2003;98(2):153–158.
58. Lines, R, Jürgens, R, Stover, H, Laticeschi, D, Nelles, J. Prison needle exchange: A review of the international evidence and experience. Montreal (PQ): Canadian HIV/AIDS Legal Network; 2004.
59. Lines, R, Jürgens, R, Stover, H, Laticeschi, D, Nelles, J. Prison needle exchange: A review of the international evidence and experience. Montreal (PQ): Canadian HIV/AIDS Legal Network; 2004.
60. Dolan, K, Rutter, S, Wodak, AD. Prison-based syringe exchange programmes: A review of international research and development. *Addiction* 2003;98(2):153–158.
61. Tortu, S, Neaigus, A, McMahon, J, Hagen, D. Hepatitis C among noninjecting drug users: A report. *Subst Use Misuse* 2001;36(4):523–534.
62. Tortu, S, McMahon, JM, Pouget, ER, Hamid, R. Sharing of noninjection drug-use implements as a risk factor for hepatitis C. *Subst Use Misuse* 2004;39(2):211–224.

63. McMahon, JM, Tortu, S. A potential hidden source of hepatitis C infection among noninjecting drug users. *J Psychoactive Drugs* 2003;35(4):455–460.
64. Alter, HJ, Conry-Cantilena, C, Melpolder, J, Tan, D, Van Raden, M, Herion, D, et al. Hepatitis C in asymptomatic blood donors. *Hepatology* 1997;26(3 Suppl 1):29S–33S.
65. McElroy, PD, Rothenberg, RB, Varghese, R, Woodruff, R, Minns, GO, Muth, SQ, et al. A network-informed approach to investigating a tuberculosis outbreak: Implications for enhancing contact investigations. *Int J Tuberc Lung Dis* 2003;7(12 Suppl 3):S486–S493.
66. Howard, AA, Klein, RS, Schoenbaum, EE, Gourevitch, MN. Crack cocaine use and other risk factors for tuberculin positivity in drug users. *Clin Infect Dis* 2002;35(10):1183–1190.
67. Centers for Disease Control and Prevention. (2004). Top 11 most frequently asked questions about viral hepatitis. 2004. Available from: http://www.cdc.gov/Ncidod/diseases/hepatitis/common_faqs.htm.
68. Faruque, S, Edlin, BR, McCoy, CB, Word, CO, Larsen, SA, Schmid, DS, et al. Crack cocaine smoking and oral sores in three inner-city neighborhoods. *J Acquir Immune Defic Syndr* 1996;13(1):87–92.
69. Porter, J, Bonilla, L. Crack users' cracked lips: An additional HIV risk factor. *Am J Public Health* 1993;83(10):1490–1491.
70. Garmaise, D. Groups distribute harm-reduction kits to crack users. *HIV AIDS Policy Law Rev* 2004;9(3):30–31.
71. Garmaise, D. Ottawa: City Council approves distribution of crack kits. *HIV AIDS Policy Law Rev* 2005;10(2):16–17.
72. Haydon, E, Fischer, B. Crack use as a public health problem in Canada: Call for an evaluation of 'safer crack use kits'. *Can J Public Health* 2005;96(3):185–188.
73. Jones, R, Gruer, L, Gilchrist, G, Seymour, A, Black, M, Oliver, J. (2002). Recent contact with health and social services by drug misusers in Glasgow who died of a fatal overdose in 1999. *Addiction* 2002;97(12):1517–1522.
74. Wood, E, Hogg, RS, Yip, B, Harrigan, PR, O'Shaughnessy, MV, Montaner, JS. Provider bias in the selection of NNRTI and PI-based HAART and HIV treatment outcomes in observational studies. *AIDS* 2003;17(18):2629–2634.
75. Doherty, MC, Garfein, RS, Monterroso, E, Brown, D, Vlahov, D. Correlates of HIV infection among young adult short-term injection drug users. *AIDS* 2000;14(6):717–726.
76. Kerr, T, Palepu, A. Safe injection facilities in Canada: Is it time? *CMAJ* 2001;165(4): 436–437.
77. Dolan, K, Kimber, J, Fry, C, Fitzgerald, J, McDonald, D, Frautmann, F. Drug Consumption facilities in Europe and the establishment of supervised injecting centres in Australia. *Drug Alcohol Rev* 2000;19:337–346.
78. Des Jarlais, DC, Friedman, SR. Shooting galleries and AIDS: Infection probabilities and 'tough' policies. *Am J Public Health* 1990;80(2):142–144.
79. Kent, H. Australia's Safe "Shooting Gallery" proving popular. *CMAJ* 2001;165(10):1375.

80. Kerr, T, Tyndall, M, Li, K, Montaner, J, Wood, E. Safer injection facility use and syringe sharing in injection drug users. *Lancet* 2005;366(9482):316–318.
81. Wood, E, Tyndall, MW, Stoltz, J, Small, W, Lloyd-Smith, E, Zhang, R, et al. Factors associated with syringe sharing among users of North America's first medically supervised safer injecting facility. *Am J Infect Dis* 2005;1(1):50–54.
82. Collins, CL, Kerr, T, Kuyper, LM, Li, K, Tyndall, MW, Marsh, DC, et al. Potential uptake and correlates of willingness to use a supervised smoking facility for noninjection illicit drug use. *J Urban Health* 2005;82(2):276–284.
83. Collins, CL, Kerr, T, Tyndall, MW, et al. Rationale to evaluate medically supervised safer smoking facilities for non-injection illicit drug users. *Can J Public Health* 2005;96(5):344–347.
84. Shannon, K, Ishida, T, Morgan, R, Bear, A, Oleson, M, Kerr, T, et al. Potential community and public health impacts of medically supervised safer smoking facilities for crack cocaine users. *Harm Reduct J* 2006;3:1.
85. Vlahov, D, Fuller, CM, Ompad, DC, Galea, S, Des Jarlais, DC. Updating the infection risk reduction hierarchy: preventing transition into injection. *J Urban Health* 2004;81(1):14–19.
86. Schmidt, J, Williams, E. When all else fails, try harm reduction. *Am J Nurs* 1999;99(10):67–70.
87. Fischer, B. Prescriptions, power and politics: The turbulent history of methadone maintenance in Canada. *J Public Health Policy* 2000;21(2):187–210.
88. Rosenberg, H, Melville, J, McLean, PC. Acceptability and availability of pharmacological interventions for substance misuse by British NHS treatment services. *Addiction* 2002;97(1):59–65.
89. Henrion, R. Effectiveness of measures taken in France to reduce the risks of heroin addiction via intravenous route. *Bull Acad Natl Med* 1997;181(6):1177–1185; discussion 1186–1189.
90. Strathdee, SA, van Ameijden, EJ, Mesquita, F, Wodak, A, Rana, S, Vlahov, D. Can HIV epidemics among injection drug users be prevented? *AIDS* 1998;12(Suppl A):S71–S79.
91. Selvey, LA, Wignall, J, Buzolic, A, Sullivan, P. Reported prevalence of hepatitis C among clients of needle exchanges in southeast Queensland. *Aust N Z J Public Health* 1996;20(1):61–64.
92. Van Beek, I, Dakin, A, Kimber, J. Drug overdoses in a supervised injecting room setting. Presented at the 14th International Conference on Reduction of Drug Related Harm, Chiang Mai, Thailand; 2003 Apr 6-10.
93. Van Beek, I, Gilmour, S. (2000). Preference to have used a medically supervised injecting centre among injecting drug users in Kings Cross, Sydney. *Aust N Z J Public Health* 2000;24(5):540–542.
94. van Benthem, BH, Veugelers, PJ, Cornelisse, PG, Strathdee, SA, Kaldor, JM, Shafer, KAP, et al. Is AIDS a floating point between HIV seroconversion and death? Insights from the Tricontinental Seroconverter Study. *AIDS* 1998;12(9):1039–1045.

95. Senay, E, Uchtenhagen, A. Methadone in the treatment of opioid dependence: A review of world literature. In: Arif A, Westermeyer J, editors. Methadone maintenance in the management of opioid dependence. New York: Prager; 1990.
96. Dole, VP, Robinson, JW, Orraca, J, Towns, E, Searcy, P, Caine, E. Methadone treatment of randomly selected criminal addicts. *N Engl J Med* 1969;280(25):1372–1375.
97. Goldstein, A. Heroin addiction: Neurobiology, pharmacology, and policy. *J Psychoactive Drugs* 1991;23(2):123–133.
98. Bertschy, G. Methadone maintenance treatment: An update. *Eur Arch Psychiatry Clin Neurosci* 1995;245(2):114–124.
99. Rosenbaum, M, Washburn, A, Knight, K, Kelley, M, Irwin, J. Treatment as harm reduction, defunding as harm maximization: The case of methadone maintenance. *J Psychoactive Drugs* 1996;28(3):241–249.
100. World Health Organization, United Nations Office on Drugs and Crime, United Nations Programme on HIV/AIDS. Substitution maintenance therapy in the management of opioid dependence and HIV/AIDS prevention: Position paper. Geneva: World Health Organization; 2004.
101. Ball, J, Ross, A. The effectiveness of methadone maintenance treatment: Patients, programs, services and outcomes. New York: Springer-Verlag; 1991.
102. Hubbard, RL, Rachal, JV, Craddock, SG. Treatment Outcome Prospective Study (TOPS): Client characteristics before, during, and after treatment. Washington, DC: NIDA; 1984.
103. Strain, EC, Bigelow, GE, Liebson, IA, Stitzer, ML. Moderate- vs high-dose methadone in the treatment of opioid dependence: A randomized trial. *JAMA* 1999;281(11):1000–1005.
104. Sees, KL, Delucchi, KL, Masson, C, Rosen, A, Clark, HW, Robillard, H, et al. Methadone maintenance vs 180-day psychosocially enriched detoxification for treatment of opioid dependence: A randomized controlled trial [see comments]. *JAMA* 2000;283(10):1303–1310.
105. Vanichseni, S, Wongsuwan, B, Choopanya, K, Wongpanich, K. A controlled trial of methadone maintenance in a population of intravenous drug users in Bangkok: Implications for prevention of HIV. *Int J Addict* 1991;26(12):1313–1320.
106. Condelli, WS, Dunteman, GH. Exposure to methadone programs and heroin use. *Am J Drug Alcohol Abuse* 1993;19(1):65–78.
107. Gearing, F, Schweitzer, M. An epidemiologic evaluation of long-term methadone maintenance treatment for heroin addiction. *Am J Epidemiol* 1974;100(2):101–112.
108. Newman, RG, Whitehill, WB. Double-blind comparison of methadone and placebo maintenance treatments of narcotic addicts in Hong Kong. *Lancet* 1979;2(8141):485–488.
109. Newman, RG, Peyser, N. Methadone treatment: Experiment and experience. *J Psychoactive Drugs* 1991;23(2):115–121.
110. Stenbacka, M, Leifman, A, Romelsjo, A. The impact of methadone on consumption of inpatient care and mortality, with special reference to HIV status. *Subst Use Misuse* 1998;33(14):2819–2834.

111. Sheerin, I, Green, T, Sellman, D, Adamson, S, Deering, D. Reduction in crime by drug users on a methadone maintenance therapy programme in New Zealand. *N Z Med J* 2004;117(1190):U795.
112. Novick, D, Joseph, H, Croxson, T. Absence of antibody to human immunodeficiency virus in long-term, socially rehabilitated methadone maintenance patients. *Arch Intern Med* 1990;150(1):97–99.
113. Hartel, DM, Schoenbaum, EE. Methadone treatment protects against HIV infection: Two decades of experience in the Bronx, New York City. *Public Health Rep* 1998;113(Suppl 1):107–115.
114. Metzger, DS, Woody, GE, McLellan, AT, O'Brien, CP, Druley, P, Navaline, H, et al. Human immunodeficiency virus seroconversion among intravenous drug users in- and out-of-treatment: An 18-month prospective follow-up. *J Acquir Immune Defic Syndr* 1993;6(9):1049–1056.
115. Zangerle, R, Fuchs, D, Rossler, H, Reibnegger, G, Riemer, Y, Weiss, SH, et al. Trends in HIV infection among intravenous drug users in Innsbruck, Austria. *J Acquir Immune Defic Syndr* 1992;5(9):865–871.
116. Iguchi, MY. Drug abuse treatment as HIV prevention: Changes in social drug use patterns might also reduce risk. *J Addict Dis* 1998;17(4):9–18.
117. Martin, GS, Serpelloni, G, Galvan, U, Rizzetto, A, Gomma, M, Morgante, S, et al. Behavioural change in injecting drug users: evaluation of an HIV/AIDS education programme. *AIDS Care* 1990;2(3):275–279.
118. Watkins, KE, Metzger, D, Woody, G, McLellan, AT. High-risk sexual behaviors of intravenous drug users in- and out-of-treatment: Implications for the spread of HIV infection. *Am J Drug Alcohol Abuse* 1992;18(4):389–398.
119. Wells, EA, Calsyn, DA, Clark, LL, Saxon, AJ, Jackson, TR. Retention in methadone maintenance is associated with reductions in different HIV risk behaviors for women and men. *Am J Drug Alcohol Abuse* 1996;22(4):509–521.
120. Van Hulst, Y, Broadhead, RS, Heckathorn, DD, Mills, R, Carbone, M. Scoring clean works after a needle exchange is shut down [Abstract No. 33381]. *Int Conf AIDS* 1998;12, 666.
121. Vargas, JA, Torres, A. Crisis in Puerto Rico - Project 325. *SIDAhora: Un Proyecto del Departamento de Publicaciones del PWA Coalition*, NY 1997:34–35.
122. Vidal-Trecan, G, Coste, J, Coeuret, M, Delamare, N, Varescon-Pousson, I, Boissonnas, A. Risk behaviors of intravenous drug users: Are females taking more risks of HIV and HCV transmission? *Rev Epidemiol Sante Publique* 1998;46(3):193–204.
123. Wood, E, Hogg, RS, Kerr, T, Palepu, A, Zhang, R, Montaner, JS. Impact of accessing methadone on the time to initiating HIV treatment among antiretroviral-naïve HIV-infected injection drug users. *AIDS* 2005;19(8):837–839.
124. Dolan, K, Hall, W, Wodak, A. Methadone maintenance reduces injecting in prison. *BMJ* 1996;312(7039):1162.
125. Dolan, KA, Shearer, J, MacDonald, M, Mattick, RP, Hall, W, Wodak, AD. A randomised controlled trial of methadone maintenance treatment versus wait list control in an Australian prison system. *Drug Alcohol Depend* 2003;72(1):59–65.

126. Sibbald, B. Methadone maintenance expands inside federal prisons. *CMAJ* 2002;167(10):1154.
127. World Health Organization. WHO Guidelines on HIV Infection and AIDS in Prisons. Geneva: Author; 1993.
128. Shewan, D, Gemmell, M, Davies, JB. Behavioural change amongst drug injectors in Scottish prisons. *Soc Sci Med* 1994;39(11):1585–1586.
129. Veugelers, PJ, Cornelisse, PG, Craib, KJ, Marion, SA, Hogg, RS, Strathdee, SA, et al. Models of survival in HIV infection and their use in the quantification of treatment benefits. *Am J Epidemiol* 1998;148(5):487–496.
130. Veugelers, PJ, Kaldor, JM, Strathdee, SA, Page-Shafer, KA, Schechter, MT, Coutinho, RA, et al. Incidence and prognostic significance of symptomatic primary human immunodeficiency virus type 1 infection in homosexual men. *J Infect Dis* 1997;176(1):112–117.
131. Mino, A, Page, D, Dumont, P, Broers, B. Treatment failure and methadone dose in a public methadone maintenance treatment programme in Geneva. *Drug Alcohol Depend* 1998;50(3):233–239.
132. Vlahov, D, Junge, B. The role of needle exchange programs in HIV prevention. *Public Health Rep* 1998;113(Suppl 1):75–80.
133. Vlahov, D. The role of epidemiology in needle exchange programs. *Am J Public Health* 2000;90(9):1390–1392.
134. Vogt, RL, Breda, MC, Des Jarlais, DC, Gates, S, Whitticar, P. Hawaii's statewide syringe exchange program. *Am J Public Health* 1998;88(9):1403–1404.
135. McCusker, C, Davies, M. Prescribing drug of choice to illicit heroin users: The experience of a U.K. community drug team. *J Subst Abuse Treat* 1996;13(6):521–531.
136. Perneger, TV, Giner, F, del Rio, M, Mino, A. Randomised trial of heroin maintenance programme for addicts who fail in conventional drug treatments. *BMJ* 1998;317(7150):13–18.
137. Voth, EA. The war on drugs. *N Engl J Med* 1994;331(2):127–128; discussion 128–129.
138. Steffen, T, Christen, S, Blattler, R, Gutzwiller, F. Infectious diseases and public health: risk-taking behavior during participation in the Swiss program for a medical prescription of narcotics (PROVE). *Subst Use Misuse* 2001;36(1–2):71–89.
139. Voth, EA. The war on drugs: Time to relocate the battlefield? *JAMA* 1995;273(6):459–460.
140. Shick, JF, Dorus, W, Hughes, PH. Adolescent drug using groups in Chicago parks. *Drug Alcohol Depend* 1978;3(3):199–210.
141. van den Brink, W, Hendriks, VM, Blanken, P, Koeter, MW, van Zwieten, BJ, van Ree, JM. Medical prescription of heroin to treatment resistant heroin addicts: Two randomised controlled trials. *BMJ* 2003;327(7410):310.
142. Peak, A, Rana, S, Maharjan, SH, Jolley, D, Crofts, N. Declining risk for HIV among injecting drug users in Kathmandu, Nepal: The impact of a harm-reduction programme. *AIDS* 1995;9(9):1067–1070.

143. Latkin, CA. Outreach in natural settings: The use of peer leaders for HIV prevention among injecting drug users' networks. *Public Health Rep* 1998;113(Suppl 1):151–159.
144. Broadhead, RS, Heckathorn, DD, Grund, JC, Stern, LS, Anthony, DL. (1995). Drug users versus outreach workers in combating AIDS: Preliminary results of a peer-driven intervention. *J Drug Issues* 1995;25(3):531–564.
145. Broadhead, RS, Heckathorn, DD, Weakliem, DL, Anthony, DL, Madray, H, Mills, RJ, et al. Harnessing peer networks as an instrument for AIDS prevention: Results from a peer-driven intervention. *Public Health Rep* 1998;113(Suppl 1):42–57.
146. McCusker, J, Stoddard, AM, Hindin, RN, Garfield, FB, Frost, R. Changes in HIV risk behavior following alternative residential programs of drug abuse treatment and AIDS education. *Ann Epidemiol* 1996;6(2):119–125.
147. Sorensen, JL, London, J, Heitzmann, C, Gibson, DR, Morales, ES, Dumontet, R, et al. Psychoeducational group approach: HIV risk reduction in drug users. *AIDS Educ Prev* 1994;6(2):95–112.
148. World Health Organization. Harm reduction approaches to injecting drug use. Geneva: Author; 2006.
149. Coyle, SL, Needle, RH, Normand, J. Outreach-based HIV prevention for injecting drug users: A review of published outcome data. *Public Health Rep* 1998;113(Suppl 1):19–30.
150. Neaigus, A, Sufian, M, Friedman, SR, Goldsmith, DS, Stepherson, B, Mota, P, et al. Effects of outreach intervention on risk reduction among intravenous drug users. *AIDS Educ Prev* 1990;2(4):253–271.
151. Stephens, RC, Feucht, TE, Roman, SW. Effects of an intervention program on AIDS-related drug and needle behavior among intravenous drug users. *Am J Public Health* 1991;81(5):568–571.
152. Sufian, M, Friedman, SR, Curtis, R, Neaigus, A, Stepherson, B. Organizing as a new approach to AIDS risk reduction for intravenous drug users. *J Addict Dis* 1991;10(4):89–98.
153. Colon, HM, Rivera Robles, R, Sahai, H, Matos, T. Changes in HIV risk behaviors among intravenous drug users in San Juan, Puerto Rico. *Br J Addict* 1992;87(4):585–590.
154. Friedman, S, Neaigus, A, Des Jarlais, DC, Sotheran, JL, Woods, J, Sufian, M. (1992). Social interventions against AIDS among injecting drug users. *Br J Addict* 1992;87:393–404.
155. Birkel, RC, Golaszewski, T, Koman, JJ, Singh, BK, Catan, V, Souply, K. Findings from the Horizontes Acquired Immune Deficiency Syndrome Education project: The impact of indigenous outreach workers as change agents for injection drug users. *Health Educ Q* 1993;20(4):523–538.
156. Booth, RE, Crowley, TJ, Zhang, Y. Substance abuse treatment entry, retention and effectiveness: Out-of-treatment opiate injection drug users. *Drug Alcohol Depend* 1996;42(1):11–20.
157. Deren, S, Beardsley, M, Tortu, S, Davis, R, Clatts, M. Behavior change strategies for women at high risk for HIV. *Drugs Soc* 1993;7:119–128.

158. McCoy, C, Rivers, J, Khoury, E. (1993). An emerging public health model for reducing AIDS-related risk behavior among injecting drug users and their sexual partners. *Drugs Soc* 1993;7:143–159.
159. Stephens, R, Simpson, DD, Coyle, SL, McCoy, CB, NADR Consortium, editors. Comparative effectiveness of NADR interventions. Westport (CT): Greenwood Press; 1993.
160. Wechsberg, W, Cavanaugh, ER, Dunteman, GH, Smith, FJ. Changing needle practices in community outreach and methadone treatment. *Eval Program Plann* 1994;17:371–379.
161. Camacho, L, Williams, ML, Vogtsberger, KN, Simpson, DD. Cognitive readiness of drug injectors to reduce AIDS risks. *Am J Addict* 1995;4:49–55.
162. Deren, S, Davis, WR, Beardsley, M, Tortu, S, Clatts, M. Outcomes of a risk-reduction intervention with high-risk populations: The Harlem AIDS project. *AIDS Educ Prev* 1995;7(5):379–390.
163. Siegal, HA, Falck, RS, Carlson, RG, Wang, J. Reducing HIV needle risk behaviors among injection-drug users in the Midwest: An evaluation of the efficacy of standard and enhanced interventions. *AIDS Educ Prev* 1995;7(4):308–319.
164. He, H, Stark, M, Fleming, D, Gould, J, Russell-Alexander, Y, Weir, B. Facilitation into drug treatment or self help among out-of-treatment IDUs in Portland: You can lead a horse to water, but. *J Drug Issues* 1996;26:649–661.
165. Weeks, M, Himmelgreen, DA, Singer, M, Woolley, S, Romero-Daza, N, Grier, M. Community-based AIDS prevention: Preliminary outcomes of a program for African American and Latino injection drug users. *J Drug Issues* 1996;26:561–590.
166. Stevens, S, Estrada, A, Estrada, B. HIV sex and drug risk behavior and behavior change in a national sample of injection drug and crack cocaine using women. *Women Health* 1998;27:25–48.
167. Kotranski, L, Semaan, S, Collier, K, Lauby, J, Halbert, J, Feighan, K. Effectiveness of an HIV risk reduction counseling intervention for out-of-treatment drug users. *AIDS Educ Prev* 1998;10(1):19–33.
168. McCoy, C, Weatherby, NL, Metsch, LR, McCoy, HV, Rivers, JE, Correa, R. Effectiveness of HIV interventions among crack users. *Drugs Soc* 1996;7:137–154.
169. Colon, H, Robles, RR, Freeman, D, Matos, T. Effects of HIV risk reduction education program among injection drug users in Puerto Rico. *Puerto Rico Health Science Journal* 1993;12:27–34.
170. Deren, S, Davis, WR, Tortu, S, Beardsley, M, Ahluwalia, I, the National AIDS Research Consortium. Women at high risk for HIV: Pregnancy and risk behaviors. *J Drug Issues* 1995;25:57–71.
171. Booth, R, Koester, S, Brewster, JT, Weibel, WW, Fritz, RB. Intravenous drug users and AIDS: Risk behaviors. *Am J Drug Alcohol Abuse* 1991;17(3):337–353.
172. Booth, R, Wiebel, WW. Effectiveness of reducing needle-related risks for HIV through indigenous outreach to injection drug users. *Am J Addict* 1992;1:277–287.
173. Camacho, L, Williams, ML, Vogtsberger, KN, Simpson, DD. Cognitive readiness of drug injectors to reduce AIDS risks. *Am J Addict* 1995;4:49–55.

174. Watters, J. A street-based outreach model of AIDS prevention for intravenous drug users: preliminary evaluation. *Contemporary Drug Problems* 1987 Fall:411–423.
175. Wiebel, WW, Jimenez, A, Johnson, W, Ouellet, L, Jovanovic, B, Lampinen, T, et al. Risk behavior and HIV seroincidence among out-of-treatment injection drug users: A four-year prospective study. *J Acquir Immune Defic Syndr* 1996;12(3):282–289.
176. Des Jarlais, DC, Perlis, T, Friedman, SR, Deren, S, Chapman, T, Sotheran, JL, et al. Declining seroprevalence in a very large HIV epidemic: Injecting drug users in New York City, 1991 to 1996. *Am J Public Health* 1998;88(12):1801–1806.
177. Des Jarlais, DC, Friedman, SR, Hagan, H. Maintaining low HIV seroprevalence among injecting drug users. *JAMA* 1996;275(8):597–598.
178. Des Jarlais, DC, Friedman, SR, Sotheran, JL, Wenston, J, Marmor, M, Yancovitz, SR, et al. Continuity and change within an HIV epidemic. Injecting drug users in New York City, 1984 through 1992. *JAMA* 1994;271(2):121–127.
179. Ball, AL, Rana, S, Dehne, KL. HIV prevention among injecting drug users: Responses in developing and transitional countries. *Public Health Rep* 1998;113(Suppl 1):170–181.
180. Wood, E, Spittal, PM, Kerr, T, Small, W, Tyndall, MW, O'Shaughnessy, MV, et al. Requiring help injecting as a risk factor for HIV infection in the Vancouver epidemic: Implications for HIV prevention. *Can J Public Health* 2003;94(5):355–359.
181. Latkin, C, Mandell, W, Vlahov, D, Oziemkowska, M, Knowlton, A, Celentano, D. My place, your place, and no place: Behavior settings as a risk factor for HIV-related injection practices of drug users in Baltimore, Maryland. *Am J Community Psychol* 1994;22(3):415–430.
182. Kral, AH, Bluthenthal, RN, Erringer, EA, Lorvick, J, Edlin, BR. Risk factors among IDUs who give injections to or receive injections from other drug users. *Addiction* 1999;94(5):675–683.
183. Spittal, PM, Craib, KJ, Wood, E, Laliberté, N, Li, K, Tyndall, MW, et al. Risk factors for elevated HIV incidence rates among female injection drug users in Vancouver. *CMAJ* 2002;166(7):894–899.
184. Edlin, BR, Irwin, KL, Faruque, S, McCoy, CB, Word, C, Serrano, Y, et al. Intersecting epidemics--crack cocaine use and HIV infection among inner-city young adults. Multicenter Crack Cocaine and HIV Infection Study Team. *N Engl J Med* 1994;331(21):1422–1427.
185. Kerr, T, Small, W, Peeace, W, Pierre, A, Wood, E. Harm reduction by a 'user-run' organization: A case study of the Vancouver Area Network of Drug Users. *Int J Drug Policy* 2006;17(2):61–69.
186. Broadhead, RS, Heckathorn, DD, Weakliem, DL, Anthony, DL, Madray, H, Mills, RJ, et al. Harnessing peer networks as an instrument for AIDS prevention: Results from a peer-driven intervention. *Public Health Rep* 1998;113(Suppl 1):42–57.
187. Spittal, P, Small, W, Laliberte, N, Johnson, C, Wood, E. How otherwise well meaning exchange agents can contribute to limited sterile syringe availability in Vancouver, Canada. *Int J Drug Policy* 2003;15:36–45.

188. Rich, JD, Towe, CW, Salas, CM, Foise, CK, Strong, L, McKenzie, M. Obstacles to needle exchange participation in Rhode Island. *National HIV Prevention Conference* 1999:613.
189. Grund, JP, Blanken, P, Adriaans, NF, Kaplan, CD, Barendregt, C, Meeuwssen, M. Reaching the unreached: Targeting hidden IDU populations with clean needles via known user groups. *J Psychoactive Drugs* 1992;24(1):41–47.
190. Kerr, T, Oleson, M, Wood, E. Harm-reduction activism: A case study of an unsanctioned user-run safe injection site. *Canadian HIV AIDS Policy Law Rev* 2004;9(2):13–19.
191. Kerr, T, O'Briain, W. Drug policy in Canada - The way forward. *Canadian HIV AIDS Policy Law Rev* 2002;7(1):1–32.
192. Wood, E, Spittal, PM, Small, W, Kerr, T, Li, K, Hogg, RS, Tyndall, MW, Montaner, JS. Displacement of Canada's largest public illicit drug market in response to a police crackdown. *CMAJ* 2004;170:1551–1556.
193. Wood, E, Kerr, T, Spittal, PM, Tyndall, MW, O'Shaughnessy, MV, Schechter, MT. The health care and fiscal costs of the illicit drug use epidemic: The impact of conventional drug control strategies. *BCMJ* 2003;45(3):128–134.
194. Wood, E, Tyndall, MW, Spittal, PM, Li, K, Anis, AH, Hogg, RS, et al. Supply-side policies for control of illicit drugs in the face of the AIDS and overdose epidemics: Investigation of a massive heroin seizure. *CMAJ* 2003;168(2):165–169.