Title: Epidemiology of injection drug use: New trends and prominent issues

Élise Roy, MD, MSc\textsuperscript{1,2} (Corresponding author)
Nelson Arruda, MSc\textsuperscript{1}
Julie Bruneau\textsuperscript{3,4}
Didier Jutras-Aswad, MD, MSc\textsuperscript{3,5}

\textsuperscript{1}Faculty of Medicine and Health Sciences, Université de Sherbrooke, Longueuil, Québec, Canada
\textsuperscript{2}Institut national de santé publique du Québec, Montréal, Québec, Canada
\textsuperscript{3}Research Centre, Centre Hospitalier de l’Université de Montréal (CRCHUM), Montréal, Québec, Canada
\textsuperscript{4}Department of Family Medicine, Université de Montréal, Montréal, Québec, Canada
\textsuperscript{5}Department of Psychiatry, Université de Montréal, Montréal, Québec, Canada

Conflict of interest declaration:

There are no conflicts of interest to declare

Address correspondence to: Élise Roy, Faculté de médecine et des sciences de la santé, Université de Sherbrooke, Campus de Longueuil, 150 Place Charles-Lemoyne, room 200. Longueuil, Québec, Canada. J4K 0A8. E.mail: Elise.Roy@USherbrooke.ca
Abstract

After more than 30 years of research, numerous studies have shown that injection drug use is associated with a wide range of adverse health outcomes, such as drug overdoses, drug-related suicidal behaviours, comorbid psychiatric disorders, bloodborne pathogens and other infectious diseases, and traumas. In this review, new trends and prominent issues associated with injection drug use are explored. The dynamic nature of injection drug use is underlined by examining its recent trends and changing patterns in Canada and other “high-income countries”. Three research topics that could further contribute to the development of comprehensive prevention and intervention strategies aimed at people who inject drugs are also discussed: risk behaviours associated with the injection of prescription opioids, binge injection drug use, and mental health problems as determinants of injection risk behaviours.

Keywords: Injection drug use, drug use patterns, drug trends, injection risk behaviours.

Abbreviations:

APD: Antisocial personality disorder
HCV: Hepatitis C virus
NMUPO: Non-medical use of prescription opioid
PO: Prescription opioid
PWID: People who inject drugs
PWUD: People who use drugs
Introduction

Drug overdoses, drug-related suicidal behaviours, comorbid psychiatric disorders, HIV and hepatitis C virus (HCV) infections, other infectious diseases and traumas are among the most serious health consequences of substance misuse. Substance misuse causes significant morbidity and mortality and, in Canada, the single most important direct cost associated with substance abuse is health care. It has been shown that routes of drug administration influence the experience of users and the risks of negative health consequences. As such, drug injection that produces rapid and intense effects increases the risks of developing addiction and of progressing to patterns of use associated with a more severe clinical course. This includes polysubstance use which is frequent among people who inject drugs (PWID). Thus injection drug use is not only associated with serious health outcomes but also with a more complex clinical presentation, which poses a significant challenge for the clinician.

Drug injection: epidemiological trends in Canada and abroad

Injection drug use is a dynamic phenomenon that is conditioned by both individual and social-environmental factors. This particular pattern of substance misuse can emerge and/or oscillate through time. While following temporal trends in injection drug use presents methodological and analytical challenges, recent publications suggest that injection drug use has been declining in the last two decades or so in Western countries. Building on previous work carried out in the U.S., Tempalsky and colleagues used multiple data sources to calculate the number of current PWID in the United States.
annually from 1992–2007. They found that despite some local variations, drug injection had generally declined at the national level between 1992 and 2002, and remained stable thereafter. There seemed, however, to be some exceptions, one of them being the increase in young PWID prevalence (15–29 years old), with mean rates going from 90 to 100 per 10 000 youth in 1992–1996 to more than 120 per 10 000 youth in 2006–2007. This increase is worrisome as it could mean that a new generation of PWID has emerged in the U.S. Overseas, statistics based on drug treatment admissions in 30 European countries (28 EU member states, plus Norway and Turkey) indicate that current injection drug use is decreasing. For instance, the rate of drug injectors admitted to drug treatment was 21.05/100 000 of the population aged 15 and over in 2000, 13.73/100 000 in 2005, and 10.14/100 000 in 2011. Among first treatment admissions, the prevalence rate was 2.74/100 000 inhabitants in 2011 compared with 4.03/100 000 inhabitants in 2005.

As for Canada, available data for injection drug use prevalence estimates or trends are relatively scarce. Archibald and colleagues attempted to estimate the number of individuals who were injecting drugs in Toronto, Vancouver and Montreal in 1996. They compared four different methods (surveys, a modified Delphi technique, capture-recapture and an indirect method), except for Montreal for which the data required for the indirect method were not available. The point estimates varied depending on the method, ranging from 12 300 to 17 700 for Toronto and from 6400 to 17 500 for Vancouver. Based on the capture-recapture method, analyses yielded an estimate of 11 700 for Montreal, 13 360 for Toronto and 11 670 for Vancouver. A few years later, in
2001, Health Canada published a report stating that “Based on provincial and city estimates, [...] approximately 100 000 people inject illicit drugs in Canada”\textsuperscript{19}. This figure is similar to the estimate of 112 900 current drug injectors reported in 2011 by the Public Health Agency of Canada\textsuperscript{20}. While no conclusions about injection drug use trends in the country can be drawn from these studies, recent analyses from Montreal and Vancouver shed new light on the evolution of drug injection in these cities.

A recent report prepared by the Urban Health Research Initiative of the British Columbia Centre for Excellence in HIV/AIDS presented the scope and extent of Vancouver’s drug problem over a 15-year period (1996–2011)\textsuperscript{21}. Available data indicate that both daily cocaine injection and daily heroin injection have decreased substantially among people who use drugs (PWUD), from 38.1% to 6.9% and from 27.7% to 14%, respectively. It is unclear whether these trends correspond to an actual decline in drug injection among PWUD or to a change or diversification in the types of drugs injected. In fact, the prevalence of injected crystal methamphetamine use increased substantially between 2001 and 2007 to stay relatively high at 13% in 2011, while injection of prescription opioids (POs) increased steadily from 2002 to 2007, with a high of 30.9% in 2007. Unfortunately, it is difficult to comment on temporal trends in the number of PWID in Vancouver based solely on these analyses.

In Montreal, a recent study estimated the size of the population of PWID for the 2009–2010 period\textsuperscript{22}. Based on the capture-recapture method, the study reported an estimate of 3910 PWID representing 2.8 PWID per 1000 residents aged 14–65 years for the
period comprised between July 1, 2009 and June 30, 2010. This is a third of the estimated 11,700 PWID obtained in 1996. In regard to injection frequency among PWID, data from the SurvUDI surveillance network indicate that the proportion of respondents reporting daily injection (of any drug) remained stable between 1995 and 2010 in Montreal.

Despite the uncertainty surrounding the reported figures, among others in Canada, some sources point towards a relatively large decline in drug injection in many countries. Although the exact reasons for this decline are unknown, some hypotheses have been put forward. One of the most plausible is that of generational differences in terms of drug use patterns. As noted by Golub and colleagues, drug use variations over time are anchored in preferences across birth cohorts. According to these authors, “drug epidemics” (or eras as they prefer to call them) pass through four phases: incubation, expansion, plateau and decline. This can result in cycles that occur when a new generation of PWUD forget the adverse consequences associated with a specific drug use pattern. Such a phenomenon seems to have occurred in the U.S. where several distinct heroin epidemics have taken place since the late 1940s. Thus in the case of injection, a generational effect is possible where the observed decline in injection drug use could be attributed to the emergence of a new generation of PWUD choosing other modes of consumption and/or other drugs after witnessing the adverse consequences associated with injection drug use. Montreal may represent a good example of a generational effect. Among the 3,910 estimated PWID for 2009–2010, 18% were 30 years or younger compared with 35.5% of PWID aged less than 30 years.
reported in 1996. Also, the proportion of street youth reporting having ever injected drugs was 24% in a survey conducted in 2011–2012 compared with 47% at entry in a cohort study conducted from 1995–2000. In British Columbia, the aging of the PWID population coupled with fewer younger people initiating injection was put forward as a potential hypothesis to explain the decrease in HIV infections among PWID, but available data did not allow a definitive conclusion.

From a public health perspective, a decline in injection drug use is without doubt good news. However, the cyclical nature of drug use epidemics calls for caution about the future of injection drug use. This is all the more true since several studies, mostly from the U.S., indicate new drug use patterns that might promote initiation to injection drug use among an up-and-coming generation of PWUD. Indeed, an increase in heroin use has been observed recently in the general population in the U.S. Past-year heroin use among individuals aged 12 or older was 404,000 in 2002 and 681,000 in 2013 and the annual average rates of past-year heroin use increased from 1.6 per 1000 persons aged 12 or older in 2002–2004 to 2.6 per 1000 in 2011–2013. One hypothesis to explain such a phenomenon is the possible link between heroin use and the frequent non-medical use of prescription opioids (NMUPO), which rose significantly between 2002–2003 and 2009–2010. Using data from the National Survey on Drug Use and Health (NSDUH), Jones found that past-year heroin use increased from 17.8 per 1000 to 33.9 per 1000 between 2002–2004 and 2008–2010 among people reporting past-year NMUPO. The highest rate (94.7 per 1000) was among frequent NMUPO users (100 days or more) who were also at increased risk for ever injecting heroin or opioids.
Furthermore, in 2002–2004, 64% of the frequent PO users reported having used POs before their first heroin use compared with 83% in 2008–2010.

Other U.S. researchers have further examined the relationship between NMUPO and heroin / injection drug use. Qualitative studies carried out in both opioid users in treatment and in the community found that many users perceived that their PO misuse had been a gateway to their heroin / injection drug use\(^\text{37-39}\). Also, in a study of heroin injectors, younger participants reported that they had transitioned to heroin injection after starting their opiate use career with POs, whereas older users transitioned to heroin injection from non-opiate drugs such as cannabis or cocaine\(^\text{40}\). Similarly, according to surveys carried out among heroin users, pathways leading to heroin use / heroin injection changed over time\(^\text{41-43}\). For instance, a survey carried out among heroin users in treatment showed that, while 75% of heroin users who began their opioid abuse in the 2000s reported that their first regular opioid was a prescription drug, 80% of those who began using opioids in the 1960s said that they initiated their use with heroin\(^\text{43}\). Therefore, these studies shed light on a possible impact of PO misuse on heroin use trends in the U.S. population. Furthermore, studies carried out among PWID living in rural or semi-urban areas show that PO injection is a consumption pattern in itself\(^\text{44,45}\) and that POs can be a first-time injection drug\(^\text{44}\).

Similarly NMUPO seems increasingly common in Canada\(^\text{46,47}\), although its level is probably lower. Yet, it is possible that NMUPO is also fuelling or maintaining injection drug use rates among PWUD. While no studies indicating an association between
NMUPO and initiation to injection drug use or heroin use seem to be available for Canada, there is strong evidence that PO injection among street-based drug users has grown in popularity in the last years across the country. Data from I-Track, a multisite surveillance system that monitors HIV and hepatitis C virus infection rates and associated risk behaviours among Canadian PWID, showed that hydromorphone, non-prescribed morphine and oxycodone ranked second, third and fourth, respectively, as the most commonly reported injected drugs. Only cocaine surpassed them as the most commonly reported injected drug.

While studies show that NMUPO increases the risks of heroin and/or injection initiation, they also suggest that the relationship between NMUPO and heroin / injection drug use is not unidirectional. For instance, in Montreal, our ethnographic work has shown that PO injection was very popular among long-term injectors, mostly using both cocaine and opiates, although POs had only been available for a few years. In this study carried out between 2007 and 2009, we concluded that in this population, POs had perhaps become an alternative to heroin which, unlike in the U.S., was more expensive than POs sold on the streets. As such, NMUPO may contribute to continued drug injection in the PWID population.

Injection of psychostimulant drugs is highly prevalent among Canadian PWID and cocaine has long been the most commonly injected drug in the country. Similar to the way in which the rise of PO availability has changed the patterns of opiate injection, the diversification of available stimulant drugs also seems to have had an impact on
patterns of drug use. As observed in other parts of the world\textsuperscript{54-56}, the emergence of (ready-to-smoke) crack cocaine in Canada during the 2000s has contributed to the reduction of cocaine injection in many cities in the country\textsuperscript{21,53,57}. However, the long-term impact of the recent changes in the stimulant drug market on drug injection trends remains to be understood. As mentioned previously, crystal methamphetamine injection has been increasing in Vancouver in the last 15 years\textsuperscript{21,58}. Furthermore, studies among Canadian street-involved youth have shown that non-injection stimulant use, including crystal methamphetamine use and crack smoking, increased the risk of initiation into drug injection\textsuperscript{59-61}. Finally, the rapid growth of “designer drugs” on the drug market is also a matter of concern. According to studies mainly conducted in Europe, some PWID report injecting drugs such as mephedrone or bath salts\textsuperscript{62,63}. Obviously, the literature shows both that the face of injection drug use in Canada might be changing currently and that its future is uncertain. This phenomenon calls for systematic, flexible and innovative strategies to monitor injection drug use and identify emerging trends in PWID.

**Injection risk behaviours – emerging topics and unresolved questions**

After more than 30 years of public health research, there is an extensive body of literature on risk behaviours among PWID, especially concerning the transmission of bloodborne viruses such as HIV and HCV. While these studies have been crucial in guiding harm reduction policies, we have identified three emerging fields of investigation that could further contribute to the development of comprehensive
prevention and intervention strategies: risk behaviours associated with PO injection, binge injection drug use and mental health disorders as determinants of injection risk behaviours.

Despite the growing importance of NMUPO, and to some degree the injection of POs, little is known about injection practices and the health risks they pose to users. In our cohort study of PWID in Montreal, data at baseline showed that, when compared with non-PO injectors, PO injectors had more high-risk behaviours, notably syringe sharing, higher frequency of injections and injecting in public places. In addition, in an analysis controlling for injection risk behaviours, PO injectors who did not inject heroin were more likely to become infected with HCV, whereas no association was found for participants using both drugs. In the Vancouver cohort of street-involved youth, bivariate analyses showed a significant association between PO injection and HCV seroconversion, but the association was no longer significant after adjustment for confounders. These conflicting results are difficult to explain and a detailed discussion of the possible hypotheses goes beyond the scope of this paper.

While the nature of the association between PO injection and the transmission of bloodborne viruses is still a matter of debate, even less is understood about the underlying mechanisms. In this regard, our ethnographic work carried out in Montreal may have identified a potential cause for this association. Indeed, since most POs used by PWID are designed to be administered per os, dissolving them into an injectable solution requires more steps and water than powder cocaine or heroin. The larger
amounts of water used to dissolve certain tablets or capsules often require PWID to inject more than once during a single injection episode. When the same syringe is used for these multiple injections, the cotton and/or the cooker become contaminated with blood. In fact, compared with powder cocaine and heroin, the preparation of certain POs leaves a significant amount of residue in the cotton and/or cooker. These residues, which PWID call “washes”, are often kept for ulterior use or shared with other injectors. Given that sharing cottons and cookers has previously been associated with HCV infection\textsuperscript{66-71}, sharing PO-contaminated “washes” may represent a specific high-risk behaviour that contributes to the transmission of HCV.

Binge injection drug use is another topic that merits further consideration. Although there is no standardized definition of binge drug use, and by extension binge injection drug use, it is often operationalized as episodes of higher than normal, intensive and compulsive drug use\textsuperscript{72} or as using as much of a drug as possible until a user reaches physical exhaustion or runs out of a drug supply\textsuperscript{73-76}. This intense drug use pattern can last from several hours to numerous days. People engaging in binge drug use are said to exhibit erratic behaviours and have impaired judgment\textsuperscript{74}. While it can involve a variety of substances, it is often associated with the use of psychostimulants, notably methamphetamine and cocaine\textsuperscript{75,77,78}, where binge episodes appear to be triggered by periods of cravings\textsuperscript{74}. In the few Canadian studies on binge injection drug use, it has been associated with HIV incidence and prevalence\textsuperscript{72,79,80}. Miller and colleagues sought to examine the risk behaviours associated with binge drug use among injection drug users (without mentioning the types of drug)\textsuperscript{72}. They found that syringe sharing, sex
trade work and frequent cocaine and heroin injection were independently associated with the outcome. It should also be noted that almost half of the sample reported binge injection drug use throughout follow-up which shows that it is a frequent behaviour.

Mental health problems have been examined as potential determinants of high-risk injection behaviours. However little is known about the differential effects of various markers of mental health, including symptoms, specific diagnoses or general psychological distress. The literature addressing the relationship between depression and injection risk behaviours, for example, mostly relies on cross-sectional studies and symptom assessments. Results generally indicate a significant but weak association with depression. In Montreal, our group found that severe psychological distress increased the risk of needle sharing but not sharing of other injection paraphernalia among cocaine users. We hypothesised that psychological distress preferentially affects behaviours that are more stigmatized and carry higher infection risks and, therefore, are more systematically avoided.

The few studies using diagnostic tools to assess psychiatric diagnoses show inconsistent results. In the U.S., a study conducted among PWID in the community revealed that depression severity was associated with receptive needle sharing among those diagnosed with a primary or substance-induced mood disorder. In contrast, a diagnosis of primary major depression was not found to be associated with injection risk behaviours in another study carried out among young PWID. We are aware of one Canadian study addressing the relationship between depression and injection risk...
behaviours. This study showed that street-based opioid users suffering from depression were more likely to share injection equipment than those without depression.

Inconsistent evidence also exists regarding the relationship between anxiety and injection risk behaviours. In the United States, needle sharing was found to be positively associated with symptoms of anxiety and measures of anxiety or tension. A positive association was also found between severity of anxiety symptoms and several sharing behaviours, including sharing needles, backloading, sharing filters/cookers and sharing rinse water. Conversely, one recent study showed a negative association between anxiety symptoms and needle sharing among PWID in India. Furthermore, among young PWID, although anxiety disorders were more prevalent among those who shared syringes, the association was not statistically significant. In Canada, our group recently carried out a study to estimate the prevalence of mood and anxiety disorders and their relationship with high-risk injection behaviours in a sample of community-based cocaine users who were concomitantly injecting drugs. Final analyses showed that primary anxiety disorders but not mood disorders increased injection risk behaviours among cocaine users injecting drugs.

Few studies have accounted for Axis I and Axis II comorbidity in assessing sharing behaviours among PWID. In Baltimore, PWID newly registered at a syringe exchange program were administered the Structured Clinical Interview for the DSM-IV for Axis I and Axis II disorders. Participants with both antisocial personality disorder (APD) and
an Axis I psychiatric disorder (non–substance related) had the highest levels of risk, but additional regression analyses showed that only APD accounted for a significant portion of variance. The association between APD and syringe sharing has been found in other populations such as cocaine users\textsuperscript{93}. In a study conducted among heroin users in Australia, syringe sharing was associated with APD but only with the co-occurrence of a borderline personality disorder\textsuperscript{94}, suggesting that the presence of APD alone may not be sufficient to explain why PWID engage in risk behaviours that expose them to HCV/HIV. None of these studies accounted for potential confounders.

**Future developments in the study of injection drug use: setting priorities and identifying areas of research**

In Canada, available data seem to indicate that the once cocaine- and heroin-dominated injection drug use patterns are currently changing. In this context, it is of paramount importance to develop and implement monitoring tools to better follow injection drug use trends as well as both the health consequences and the factors involved. In this regard, changes in the drug market, including the growing availability of POs, are worrisome. The link between NMUPO and initiation to heroin and injection drug use is still poorly documented. Surveillance systems and prospective studies are needed in Canada to document the extent of the risk and the characteristics of PO users most likely to make these transitions. These data are the cornerstone on which the planning and implementation of a strong national strategy on drugs can be built.
While Canada may be seeing a decline in injection drug use, a reduction of resources dedicated to harm reduction programs may prove to be costly in the short and long term. In addition to consolidating and constantly improving the services already in place, evidence-based interventions aimed at preventing initiation of injection drug use should be further developed and studied. As Werb and colleagues observed, very few interventions to prevent injection drug use initiation have been evaluated. Efforts to tailor and evaluate such prevention strategies, including social marketing campaigns, peer-based behavioural programs and addiction treatment access, must be maintained despite a decline in injection drug use in order to limit the cyclical nature of drug patterns and, at the same time, limit the negative health outcomes associated with injection drug use.

The health risks associated with PO injection clearly merit further investigation. Initial findings suggest that additional studies examining its association with HIV and HCV should be conducted. Also, our work in Montreal suggests that studies examining the specific processes and contexts associated with PO injection are needed in order to develop flexible, adapted harm reduction strategies. For example, our ethnographic observations have shown that the practical, concrete process of preparing a PO injection differs from that of more traditional drugs such as cocaine and heroin. This suggests that while injection drug use patterns are evolving, the sterile injection material distributed may no longer be suitable for PO injection. In response to this new practice, public health authorities in Quebec have recently conducted evaluation studies of new sterile
injection materials (syringes, filters and containers) that could produce less residue and limit the multiple injections associated with specific POs\textsuperscript{101}.

While bingeing appears to be frequent among stimulant users, little is known about this specific drug use pattern, leaving many questions unanswered about both its causes and consequences. One critical question pertains to the nature of binge injection drug use (or drug bingeing), as no studies have determined whether it is a unique pattern of use or simply a way of using intensively. In other words, are all PWID at risk of bingeing or is it a pattern of use that can be maintained as a primary pattern? Also, is bingeing more likely with particular drugs, for instance stimulants? As for binge injection drug use specifically, more studies are needed to identify the particular reasons underlying the association between bingeing and HIV seroconversion. Furthermore, studies exploring the social and psychopathological aspects of binge injection drug use should be conducted. The link between craving and binge drug use is of particular interest and could be further examined using mixed-method studies combining neuroimaging and quantitative and qualitative approaches. Such studies will provide valuable information that might help tailor self-control strategies for individuals who tend to binge inject.

Finally, more efforts are needed to distinguish the effects of induced mental health symptoms from those of primary symptoms and to identify specific mental health aspects involved in injection risk behaviours. There is a wide variety of validated tools to assess mental health disorders in surveys in the general population, but their performance among drug users is not well documented. Beyond these issues, research
on the mechanisms explaining risk taking is of paramount importance in order to guide therapeutic approaches. We need to know the relative influence of a given diagnosis and of recurrent bouts of psychological distress on sharing and HCV/HIV transmission. Is it better, in terms of prevention, to develop interventions to help PWID cope with impulsivity, to test anti-craving medication, or to increase access to specialized mental health evaluation and treatment even when the symptomatology does not meet the criteria for a specific psychiatric disorder? This is the kind of question we need to answer to truly have an impact on mental health problems that may themselves lead to risky behaviours in PWID.
References


