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The rising prevalence of prescription opioid injection and its association with hepatitis C incidence among street-drug users

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ABSTRACT

Aims To examine trends in prescription opioid (PO) injection and to assess its association with hepatitis C virus (HCV) seroconversion among injection drug users (IDUs). **Design** Prospective cohort study. **Setting** Montreal, Canada. **Participants** HCV-negative IDUs at baseline, reporting injection in the past month. **Measurements** Semi-annual visits included HCV antibody testing and an interview-administered questionnaire assessing risk behaviours. HCV incidence rate was calculated using the person–time method. Time-updated Cox regression models were conducted to examine predictors of HCV incidence. **Findings** The proportion of IDUs reporting PO injection increased from 21% to 75% between 2004 and 2009 ($P < 0.001$). Of the 246 participants (81.6% male; mean age 34.5 years; mean follow-up time 23 months), 83 seroconverted to HCV [incidence rate: 17.9 per 100 person-years; 95% confidence interval (CI) 14.3, 22.1]. Compared to non-PO injectors, PO injectors were more likely to become infected [adjusted hazard ratio (AHR): 1.87; 95%CI:1.16, 3.03]. An effect modification was also found: PO injectors who did not inject heroin were more likely to become infected (AHR: 2.88; 95%CI: 1.52, 5.45) whereas no association was found for participants using both drugs (AHR: 1.19; 95% CI: 0.61, 2.30). Other independent predictors of HCV incidence were: cocaine injection, recent incarceration and >30 injections per month. **Conclusions** Prescription opioid injectors who do not inject heroin are at greater risk for HCV seroconversion than are those injecting both heroin and prescription opioids. Important differences in age, behaviour and social context suggest a need for targeted outreach strategies to this population.

Keywords Cohort study, HCV incidence, illicit opioid misuse, injection drug use, injection risk behaviour, prescription opioid.

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INTRODUCTION

For nearly 20 years, consumption of opioid analgesics has increased in several parts of the world, with the highest frequencies being reported in North America, Europe and Oceania [1]. The growing availability of these analgesics has been accompanied by an increase in prescription opioid (PO) misuse. Not surprisingly, the percentage of patients admitted to detoxification units for abuse of opioids other than heroin in the United States has quintupled, from 1% in 1997 to 5% in 2007 [2]. Moreover, younger enrolees within opiate treatment programmes were at greater odds of using either POs only or both POs and heroin relative to heroin only [3]. In Ontario, Canada, the proportion of new admissions for substance abuse-related PO injection increased from 10.6% in 2004–05 to 17.4% in 2009–10 [4].

This upward trend was also observed among North American street-based drug users. In New York, the prevalence of PO recreational use was observed among 32% of 586 street-based users [5]. In Miami, Florida, 12% of 588 drug-involved, street-based sex workers surveyed reported having used POs without a legitimate prescription [6]. A Canadian multi-site cohort study conducted among regular opioid users between 2001 and 2005 revealed that in five of seven cities in the

country, POs, not heroin, was the major form of opioid drug in use [7]. Participants recruited in Montreal consisted primarily of heroin and cocaine injection drug users, whereas 33% reported PO use in the previous month [7,8].

Studies conducted in diverse settings have also examined the use of POs by injection. In Australia, 46% of injection drug users (IDUs) reported having used morphine in the previous 6 months, with significant variations across states, and up to a prevalence of 85% in the Northern Territories [9]. In a study conducted in rural Kentucky among non-medical PO users, 35.3% reported having injected POs in their life-time [10]. In Quebec, Canada the prevalence of PO injection, specifically hydromorphone tablets, increased from 27.4% to 41.8% among street drug users recruited between 2003 and 2007 through SurvIDU (a provincial epidemiological surveillance network targeting active injectors recruited mainly through syringe access programmes) [11]. In Montreal, PO injection was reported by 46.4% of street-based regular cocaine users [12].

The recent increase in the use of illicit POs and the growing evidence of intravenous administration by a significant number of users is worrisome. IDUs are the population most at risk for hepatitis C virus (HCV) transmission in the developed world [13–17]. Although cocaine injection is the main risk factor for HCV infection among Canadian IDUs [18–21], an independent association between HCV prevalence and injection opiate use, or in combination with stimulants, was reported in two Canadian studies [22,23].

The intermediate steps required in the process of drug preparation and apportioning [24], which may include communal use or sharing of injection paraphernalia (cookers, filters and water), are known to increase the risk for HCV infection [25–27]. There is some evidence indicating that PO injection might further increase the risk of HCV transmission. As opposed to the available form of powder heroin and cocaine in Montreal, which is dissolved easily in water, POs have to be crushed, dissolved and filtered before being injected, leaving significant amounts of residue in the filter [28]. As the residue, known as a 'wash', may contain enough opioid substance to produce a minimal effect, used filters with residue are usually kept for ulterior use. They can also be shared among street drug users, yielding opportunities for HCV transmission between injection partners [28]. Moreover, POs require repeated injections for one single dose, heightening the risk for contamination of filters with infected blood.

The present study was conducted in a population of active drug users recruited and followed longitudinally between 2004 and 2009 in Montreal, Canada. The objectives of the study were twofold: (i) to examine trends in the types of drugs used at the time of recruitment, with a specific focus on POs, and (ii) to assess the association between PO injection use and HCV seroconversion among IDUs.

MATERIALS AND METHODS

Study population

The study population was drawn from the St Luc cohort, an open cohort of IDUs established in Montreal in 1988 to study determinants of human immunodeficiency virus (HIV) transmission [29]. To be eligible, participants had to be current IDUs (i.e. having injected drugs within the previous 6 months) and be 18 years of age or older.

In November, 2004, the cohort's objectives were expanded and a new cohort was assembled to examine individual and contextual factors associated with HCV and HIV infections among current IDUs. Eligible HCV-negative IDUs already enrolled in the former cohort were invited to participate in the new HCV incidence studies ($n = 101$). New participants ($n = 210$) were recruited from street-level and community-based organizations, in a manner consistent with previous strategies and using the same eligibility criteria. A detailed description of the recruitment and follow-up procedures has been published previously [20]. The sample population included HCV-negative participants recruited from the former cohort (32%), as well as new participants recruited through street-level strategies such as word-of-mouth (34%) or through community programme referrals (34%). All participants signed an informed consent in compliance with institutional review board regulations of the Centre Hospitalier de l'Université de Montréal. Cohort visits were scheduled at 6-month intervals and consisted of behavioural questionnaires administered by trained interviewers as well as venous blood samples drawn for HIV and HCV antibody testing. Participants were asked to return for their serostatus test results 2 weeks after their visits, at which time post-test counselling and referrals were provided. All participants received a CAD$15.00 stipend at each visit to compensate them for their time.

Of the overall sample ($n = 311$), 246 participants (79%), HCV-seronegative at enrolment, were followed-up at least once between November 2004 and December 2009, and were included in the incidence analysis. All seroconverters had a documented negative HCV antibody test at the time of enrolment and a subsequent positive HCV antibody test during a follow-up visit.

Measures

The main outcome variable was HCV infection detected by the presence of HCV antibodies. A positive

HCV antibody test was determined by enzyme immunoassay assay (EIA; Abbott Laboratories, Abbott Park, IL, USA) and confirmed by reverse transcription–polymerase chain reaction (RT–PCR; Roche Diagnostic Systems, Indianapolis, IA, USA). Specimens with indeterminate results were sent for confirmatory tests by dual EIA and/or recombinant immunoblot assay (RIBA). Sociodemographic characteristics (age, gender, education, housing arrangements), drug use patterns and injection behaviours were examined according to PO injection use and as potential determinants of HCV seroconversion. Higher education was defined as having completed a college degree. Consistent with previous studies, the idiom 'unstable housing arrangement' was defined as living on the street, in shelters or in apartment-hotels rented on a monthly basis (indicating a rapid turnover compared to typical 12-month rent–lease accommodation standards in Montreal) [30]. Drug-use patterns and injection behaviours were assessed by questioning participants on the type of drugs used, modes of administration and sharing practices regarding syringes or other injection paraphernalia in the past 6 months. For example, participants were asked whether they used illicit POs, heroin, cocaine or crack through snorting, smoking or injecting. An exhaustive list of known commercial and street denominations was proposed to the participants to help them identify prescription opioids among substances in circulation, including opioids such as hydrocodone (dilaudid, dilos) oxycodone (percs, oxycontin, oxys), etc. No detailed information on specific PO-related substances was collected. The terms 'injection paraphernalia' were said to encompass the drug preparation container, water or dilution liquid and filter or cotton.

Statistical analyses

Cochrane–Armitage trend tests were conducted to compare baseline proportions of IDUs reporting injecting POs, cocaine or heroin and smoking crack, by year of enrolment, during the 5-year study period. Descriptive analyses were used to compare IDU characteristics according to PO injection use. The Kaplan–Meier technique was used to estimate the survival function [31]. The date of seroconversion was considered to be the midpoint between the dates of the participants' visits corresponding to the last negative and the first positive HCV test. Cox's proportional hazards regression was used to estimate crude and adjusted hazard ratios (HR), and corresponding 95% confidence interval (CI) to examine the relations between PO injection use and incidence of HCV. Following the purposeful selection procedure [32], significant variables at the 5% level as well as those that showed a confounding effect on significant covariates (that is, those that changed a significant variable's coefficient by more than 20%) were retained in the final multivariate models. In addition, age and gender were retained in the final model as important a priori covariates of the risk of HCV transmission [33–35].

Individual exposure measures, except gender and age, were modelled as time-dependent covariates. A covariate 'recruitment scheme' was included in analyses to account for the differential cohort participation duration and the potential influence of serial HCV counselling and testing on behaviours and transmission between participants recruited from the former cohort membership and those recruited from street-level and community-based strategies. As a subanalysis to investigate whether the effects of particular risk factors on the hazard of HCV seroconversion varied according to PO injection use, Cox's regression analyses tested two-way interactions with relevant risk factors. In the case of a significant interaction, we estimated separate hazard ratios for the associations between a corresponding factor and HCV incidence in each of the two PO injection groups.

For all hypothesis testing, $P < 0.05$ for the two-tailed Wald test was used as the criterion for statistical significance. All analyses were conducted using SAS® version 9.2.

RESULTS

Of the 1042 cohort participants recruited (HIV and/or HCV-negative active IDUs) between November 2004 and December 2009, 731 (70%) had HCV antibodies. Of the 311 HCV-negative cohort members eligible for this investigation, 246 (79%) were followed-up at least once and were included in the incidence analyses. The majority was male (81.6%), with a mean age of 34.5 years [standard deviation (SD) = 9.2]. The average duration of injection drug use was 9.9 years (SD = 8.4). We found no difference between participants included in analyses and those lost to follow-up for most variables, except for cocaine and crack use: participants lost to follow-up were less likely to report cocaine injection (55% versus 69%; $P = 0.04$) and crack use (49% versus 66%; $P = 0.01$).

Figure 1 shows increasing trends for POs and heroin injection use reported at baseline. The proportion of IDUs reporting PO injection more than tripled between 2005 and 2009, from 21% to 75% ($P < 0.001$). When including only the 210 participants who were recruited from street-level and community-based strategies, PO injection use increased significantly, i.e. from 42.4% in 2004–05 to 75% in 2009 (P-value for trend test = 0.002), while cocaine injection, heroin injection and crack use remained stable (data not shown).

Table 1 compares baseline characteristics of the 246 participants included in incidence analyses according to PO injection use. Compared to non-users, PO injection

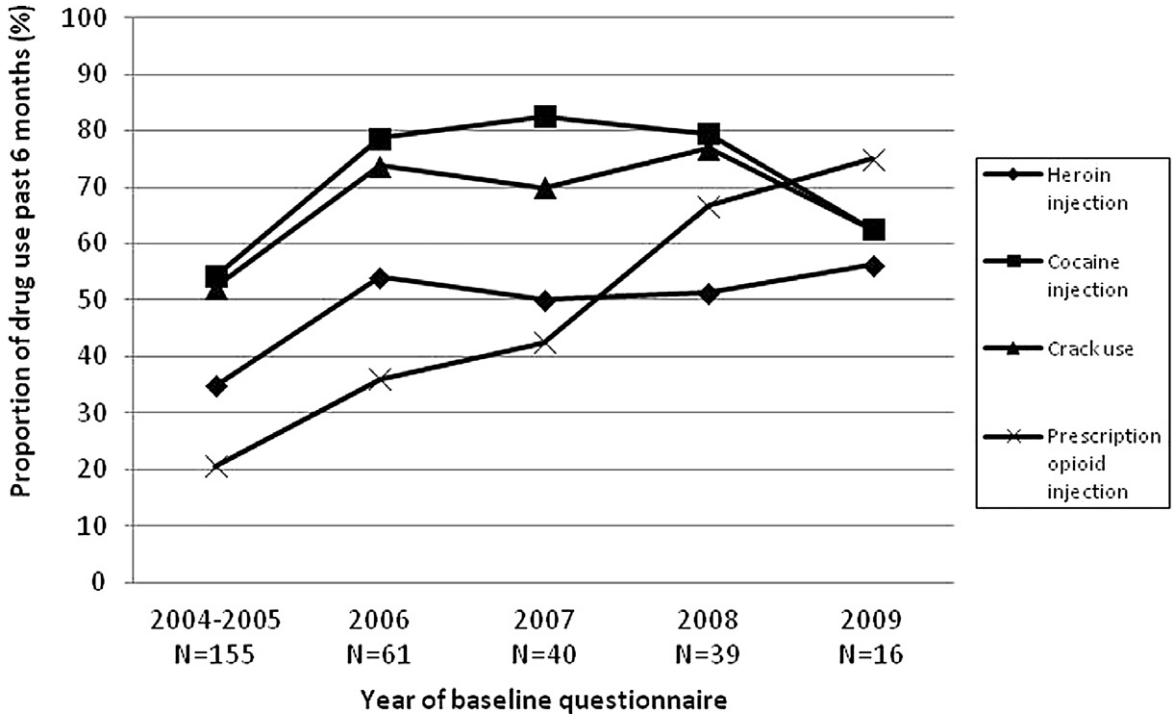

Figure 1 Trends in the baseline proportion of hepatitis C virus (HCV)-negative injection drug users reporting the use or injection of various drugs by year of enrolment, between November 2004 and December 2009 in Montreal, Quebec, Canada. *P*-values by Cochrane–Armitage trend tests: prescription opioid injection: <0.001; cocaine injection = 0.001; heroin injection = 0.01; crack use = 0.005

Table 1 Baseline characteristics of 246 hepatitis C virus (HCV) initially antibody-negative injection drug users, according to their prescription opioid injection use, recruited between November 2004 and December 2009 in the St Luc cohort, Montreal, Quebec, Canada.

	Total *n = 246*	*Prescription Opioid injection*	*No prescription Opioid injection*	
		n = 80	*n = 166*	
Variable	*% (SD)*	*% (SD)*	*% (SD)*	*P-value**
Less than 30 YOA	38.6 (3.1)	53.7 (5.6)	31.3 (3.6)	<0.001
Male gender	81.6 (2.5)	81.2 (4.4)	81.8 (3.0)	0.914
College education or higher	13.4 (2.2)	13.7 (3.9)	13.2 (2.6)	0.915
Unstable housing arrangements past 6 months	36.6 (3.1)	42.5 (5.5)	33.7 (3.7)	0.181
>30 injections past month	52.9 (3.2)	80.0 (4.5)	39.8 (3.8)	<0.001
Heroin injection past 6 months	43.5 (3.2)	57.5 (5.5)	36.7 (3.7)	0.002
Cocaine injection past 6 months	69.1 (3.0)	75.0 (4.8)	66.3 (3.7)	0.165
Crack use past 6 months	65.8 (3.0)	68.7 (5.2)	64.5 (3.7)	0.506
Sharing syringe past 6 months	28.5 (2.9)	42.5 (5.5)	21.7 (3.2)	<0.001
Sharing injection paraphernalia past 6 months	39.4 (3.1)	47.5 (5.6)	35.5 (3.7)	0.072
Incarcerated past 6 months	23.2 (2.7)	33.7 (5.3)	18.1 (3.0)	0.006
Injecting in public places past 6 months	48.4 (3.2)	72.5 (5.0)	36.7 (3.7)	<0.001
Recruited through street-level and community-based strategies (versus former cohort)	67.5 (3.0)	93.7 (2.7)	54.8 (3.9)	<0.001

**P*-values by χ^2 test. SD: standard deviation; YOA: years of age.

users were younger, more likely to report heroin injection and to have been recruited from street-level and community-based strategies. They were also more likely to report high-risk injection behaviours (including sharing syringes, frequent injections and injection in public places) and to have been recently incarcerated.

Prior to seroconversion, participants contributed a total of 463 person-years of observation. The mean

Table 2 Unadjusted estimated relative hazard of hepatitis C virus (HCV) seroconversion according to socio-demographic and behavioural factors for 246 initially HCV-negative injection drug users participating in a prospective cohort in Montreal, Canada, between November 2004 and December 2009.

Variable	*n Seroconversions*	*Person-time*	*Incidence rate*	*95% Confidence interval*	*Hazard ratio*	*95% Confidence interval*
Less than 30 YOA						
No	47	281.07	16.72	12.44, 22.03	1	
Yes	36	156.49	23.00	16.38, 31.48	1.32	0.86, 2.05
Female gender						
No	71	346.45	20.49	16.13, 25.69	1	
Yes	12	89.22	13.45	7.29, 22.86	0.70	0.38, 1.29
College education or higher						
No	77	370.31	20.79	16.53, 25.84	1	
Yes	6	67.25	8.92	3.62, 18.56	0.46	0.20, 1.05
Unstable housing arrangements past 6 months						
No	50	330.97	15.11	11.34, 19.75	1	
Yes	32	105.88	30.22	21.06, 42.11	1.62	1.03, 2.55
>30 injections past month						
No	22	286.55	7.68	4.95, 11.41	1	
Yes	61	150.58	40.51	31.28, 51.66	4.59	2.80, 7.53
Prescription opioid injection past 6 months						
No	44	358.23	12.28	9.04, 16.33	1	
Yes	39	79.33	49.16	35.49, 66.48	3.20	2.06, 4.99
Heroin injection past 6 months						
No	44	277.95	15.83	11.65, 21.05	1	
Yes	39	159.61	24.43	17.64, 33.04	1.40	0.90, 2.16
Cocaine injection past 6 months						
No	9	168.31	5.35	2.61, 9.81	1	
Yes	74	269.25	27.48	21.74, 34.30	4.63	2.31, 9.27
Crack use past 6 months						
No	36	221.94	16.22	11.55, 22.20	1	
Yes	47	215.61	21.80	16.21, 28.72	1.07	0.69, 1.67
Sharing syringe past 6 months						
No	51	337.00	15.13	11.40, 19.73	1	
Yes	32	100.56	31.82	22.17, 44.34	1.87	1.20, 2.92
Sharing injection paraphernalia past 6 months						
No	47	309.01	15.21	11.31, 20.04	1	
Yes	36	127.54	28.23	20.09, 38.62	1.55	1.00, 2.42
Incarceration past 6 months						
No	53	361.19	14.67	11.11, 19.04	1	
Yes	30	76.36	39.29	27.04, 55.32	2.45	1.57, 3.85
Injection in public places past 6 months						
No	29	272.87	10.63	7.27, 15.05	1	
Yes	54	164.69	32.79	24.89, 42.44	2.67	1.69, 4.23
Recruited through street-level and community-based strategies (versus former cohort)						
No	16	213.41	7.50	4.44, 11.92	1	1.92
Yes	67	224.15	29.89	23.36, 37.71	3.34	1.92

YOA: years of age.

follow-up time was 23 months (SD = 16.7) and the median time between consecutive visits was 5.9 months. A total of 83 individuals (33.7%) seroconverted to HCV, for an incidence rate (IR) of 17.9 per 100 person-years (95% CI: 14.3, 22.1).

Table 2 provides crude associations between socio-demographic and behavioural characteristics and the risk of HCV seroconversion. Injecting POs was associated with a 3.2-fold increased risk of HCV acquisition, whereas the association with heroin injection did not reach statistical significance. Injecting cocaine was associated with an increased risk of HCV seroconversion. In addition, several injection-related practices were associated with an increased risk of HCV infection; for example,

Table 3 Covariate-adjusted associations between hepatitis C virus (HCV) seroconversion and prescription opioid injection among 246 initially HCV-negative injection drug users participating in a prospective cohort in Montreal, Canada, between November 2004 and December 2009.

	Model 1		*Model 2*	
			With interaction between injection prescription opioid and heroin use	
Variable	*Adjusted hazard ratio*	*95% Confidence interval*	*Adjusted hazard ratio*	*95% Confidence interval*
Less than 30 years of age				
No	1		1	
Yes	0.86	0.49, 1.50	0.90	0.52, 1.56
Female gender				
No	1		1	
Yes	0.94	0.49, 1.81	0.90	0.46, 1.74
i.v. Opioid use past 6 months				
No	1			
Yes	1.87	1.16, 3.03		
No i.v. opioid use past 6 months			1	
Prescription opioid injection past 6 months *and* heroin injection past 6 months			1.19	0.61, 2.30
Prescription opioid injection past 6 months *and* no heroin injection i.v. past 6 months			2.88	1.52, 5.45
Cocaine injection past 6 months				
No	1		1	
Yes	3.10	1.49, 6.47	3.00	1.44, 6.24
Sharing syringe past 6 months				
No	1		1	
Yes	1.29	0.80, 2.07	1.29	0.81, 2.07
Incarceration past 6 months				
No	1		1	
Yes	2.32	1.45, 3.74	2.41	1.50, 3.89
Recruited through street-level and community-based strategies (versus former cohort)				
No	1		1	
Yes	1.73	0.93, 3.21	1.71	0.92, 3.18
>30 injections past month				
No	1		1	
Yes	2.85	1.65, 4.92	2.72	1.58, 4.70

the sharing of syringes or other paraphernalia, injection frequency and injection in public places. IDUs reporting unstable housing arrangements or recent incarceration were also more likely to seroconvert to HCV, as were IDUs recruited through street-level and community-based strategies, compared to those recruited among members of the former cohort.

Results from two Cox's multivariable models are presented in Table 3. In model 1, injecting POs remains associated significantly with HCV acquisition after adjustment for potential confounders (HR: 1.87; 95% CI: 1.16, 3.03). Other variables associated independently with an increased risk of HCV acquisition included injection cocaine use, frequency of injection and recent incarceration. In the multivariate model, the effect of sharing syringes or paraphernalia and of the recruitment scheme were deemed non-significant.

In model 2, testing for interactions, we found only one marginally statistically significant interaction between PO injection use and heroin injection use. PO injectors were three times more likely to become infected if they did not use intravenous (i.v.) heroin (HR: 2.88; 95% CI: 1. 52, 5.45), whereas the association was not statistically significant for participants who reported using both drugs (HR: 1.19; 95% CI: 0.61, 2.30; *P*-value for interaction term: 0.05). Figure 2 shows the cumulative probability of HCV seroconversion during follow-up according to various combination of opioid use at baseline. The difference between the three curves is highly significant ($P < 0.0001$, log-rank test).

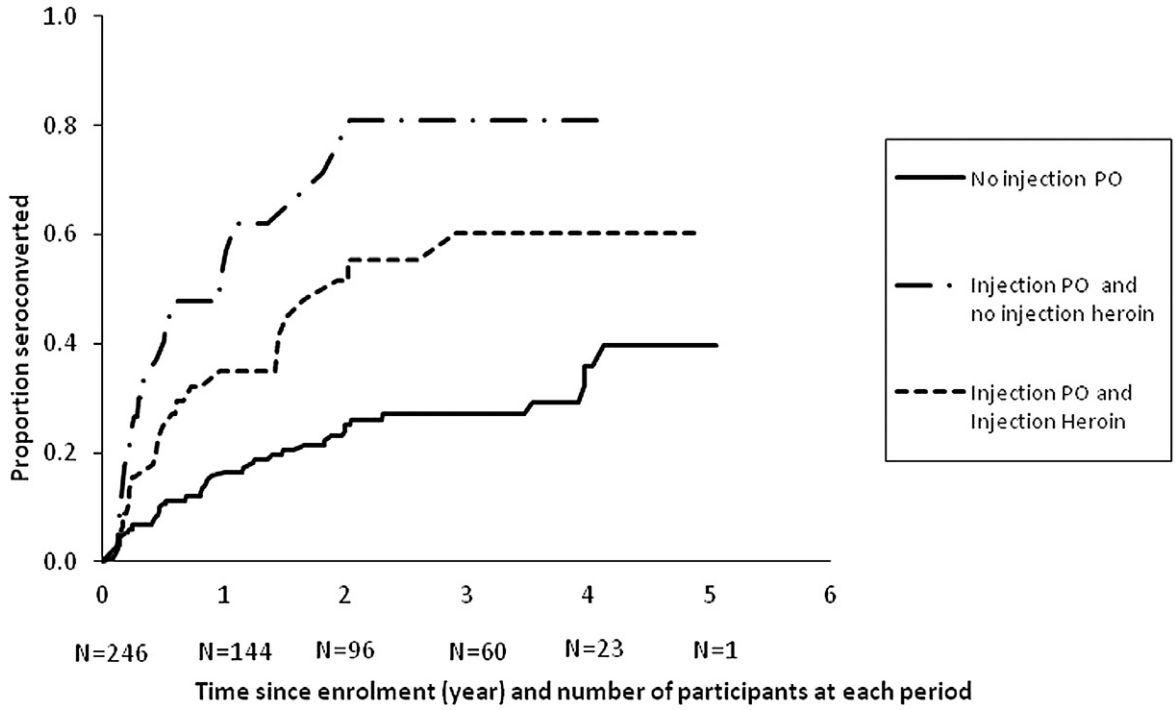

Figure 2 Cumulative hepatitis C virus (HCV) seroincidence among injection drug users according to their prescription opioid (PO) injection use, recruited between November 2004 and December 2009 in the St Luc cohort, Montreal, Quebec, Canada

DISCUSSION

Our results indicate a significant increase in the prevalence of PO injection among HCV-negative IDUs in Montreal between 2005 and 2009. Similar trends have been observed in the last decade in other regions of the world, including Australia, Estonia and Canada [36–39]. Recent ethnographic data from our group have shown that easy access, through independent operators and without the need for personal contacts, as well as low prices, are probably at the root of this emerging illicit market [28]. In line with this finding is the observation that younger IDUs were more likely to report PO injection than their older counterparts. This suggests the emergence of a new drug use pattern at an early stage of injectors' drug use trajectory, whereby illicit PO use serve as the gateway for opiate dependence.

Of concern, we observed that HCV-negative PO injectors were more likely to report high-risk injection practices associated with HCV seroconversion in previous studies, such as high injection frequency [19,34], sharing of used syringes [40,41] and injection in public places [42] when compared to non-PO injectors. In multivariate analyses, PO injectors were 1.9 times more likely to seroconvert compared to non-PO users. The practical aspects of the PO injection preparation process, coupled with indigent social practices, may partly explain the increased risk of HCV acquisition among PO injectors, relative to non-PO injectors. As mentioned, PO preparation requires many steps to dissolve and filter the drug before injection, leading to the availability of potentially contaminated opioid residue contained in filters, known as 'washes' [40]. Conversely, powder cocaine and powder heroin (beige or white), the main forms found on the streets of Montreal, does not produce significant amounts of residue. These are easily dissolvable and filters are not always deemed necessary. However, PO 'washes' have an economic value and are one of the goods that are exchanged or given among street-based users. They play an important role in the moral economy of 'gift-giving' among street-based users [43,44]. Moreover, ethnographic observation suggests that 'washes' are regarded as an independent drug capable of producing a high or countering withdrawal symptoms, rather than as an injection paraphernalia, a factor which may have contributed to increased risk and/or underestimation of sharing injection equipment.

In addition, our data suggest that opioid users who injected POs but not heroin were at greater risk of HCV acquisition compared to those injecting both heroin and POs, controlling for other drugs and risk factors. A recent qualitative investigation conducted in New York and Los Angeles showed that a majority of young IDUs initiated PO injection before heroin injection [3]. Consistent with our results, their sources of opioid at initiation were typically through opioid prescription obtained by a family

member, a friend, the user himself or a street contact. This finding may indicate different social contexts and dynamics relevant to PO and heroin use HCV risk. Our data suggest that PO injectors in Montreal who do not use heroin are less experienced, potentially less informed and therefore at higher risk of HCV infection, relative to IDUs belonging to more 'traditional' networks of heroin users. Major changes in the behaviours and injection culture of heroin users have been observed over time as a result of effective outreach and prevention strategies, including enhanced access to opiate substitution treatment and sterile syringes. PO injectors may be more difficult to reach by these strategies due to their younger age, mode of drug acquisition, separation from older heroin user's culture and the lack of specific strategies to reach them. This finding warrants further investigation.

Consistent with previous study findings in Canada and in Australia [19,21,34,37], cocaine injection was an independent risk factor for HCV transmission. Injection cocaine use was not associated with PO use, and did not explain the relation between HCV seroconversion and PO use. Imprisonment in the past 6 months was associated independently with higher HCV incidence. It has been demonstrated that having injected while in prison predicts HIV and HCV infections [45]. Of the 57 participants who reported a recent imprisonment during the study period, only three reported having injected drugs while in prison. One of these individuals seroconverted to HCV, an event which occurred more than 18 months after being released. As well as the documented risk associated with injection drug use while in prison, heightened vulnerability may play an important role in increasing high-risk injection behaviours and HCV acquisition after release [46].

Contrary to our primary hypothesis, the sharing of syringes or other injection paraphernalia did not predict HCV transmission, after accounting for other covariates. While several studies have reported associations between HCV seroconversion and syringe sharing, many associations were relatively weak after controlling for other factors; other studies failed to find any association [47–50]. Sharing is correlated highly with behaviours driven by specific drug use patterns. Unmeasured drug use patterns, combined with the possible under-reporting of syringe or paraphernalia sharing while intoxicated, have been offered as an explanation for the preponderance of cocaine as an independent predictor of HIV infection over sharing behaviours [18,51,52]. Possibly, the independent association between PO injection and HCV seroconversion observed in our study proceeds from an analogous paradigm, whereby 'washes' injection may have been under-reported.

Our study presents a number of limitations. Participants were not selected randomly; hence, our sample cannot be considered an adequate representation of the Montreal IDU population as a whole. The sample is over-represented in terms of males and chronic cocaine IDUs, compared to Quebec provincial data on IDUs [53]. However, the study was conducted in a large cosmopolitan North American city, facing a rising PO injection use epidemic. As such, it may serve as a valid representation of PO injection misuse relevant to IDUs elsewhere.

Even though our follow-up rates were high for a drug-using population, and that no difference was found between participants retained and those lost except for cocaine and crack use, our data may have been influenced by losses to follow-up. Because of the risk of 'socially desirable' responses, the study of illicit drug use and related behaviours is problematic, especially as the study progresses and bonds evolve between participants and staff. Although there is some published evidence to suggest that drug users provide reliable and valid responses, the risk of bias, if it exists, is more likely to go unreported [54]. In addition, we did not include the 'wash' as a specific item in our definition of injection paraphernalia, allowing only for indirect evidence of its potential role as a driver of HCV transmission among PO users. As for other cohort studies, a lead-time bias exists wherein potentially important risk-behaviour events, which may have occurred prior to participants joining the cohort, could not be measured or accounted for; hence, residual confounding of our results is a possibility.

This study illustrates clearly the rising prevalence of PO injection use among Montreal IDUs. While many have hypothesized that PO injection use is involved with numerous risky behaviours related to blood-borne pathogen transmission, we have shown for the first time that PO injection is actually an independent predictor of HCV transmission. Aside from well-documented individual risk behaviours, our results may indicate that risks related to PO injections may be conditioned by specific drug practices and contexts prevailing outside the traditional networks of heroin IDUs. To act on such a complex phenomenon will thus require innovative strategies. Current approaches, such as increasing the coverage of syringe through comprehensive exchange and distribution services, and providing drug treatment, may be only part of the solution. These results underscore the need for a better understanding of the processes and contexts associated with PO injection use that could lead to more comprehensive prevention and intervention strategies.

Declarations of interest

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