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Foreword | *This paper investigates the frequency of intravenous drug use in a cohort of people who inject drugs, and the decline in use over time. It provides an important indication of the effectiveness of current interventions at reducing the consumption of illicit drugs. Comparisons are made between the injection frequency of participants on or off Opioids Substitution Therapy (OST), and according to the settings in which drugs are most frequently purchased and used (eg street, house).*

This research found an overall movement away from street based drug purchasing and drug use, towards more activity in private settings. This has important implications for the harms experienced by people who inject drugs. Intravenous drug use was persistent, with only slow declines observed in the frequency of the cohort's overall use. Lower injection frequency was associated with use in private rather than public locations as well as the uptake of OST.

Additional work is needed to understand how this change in setting is affected by and also affects current interventions, and whether it can be used to help further reduce injecting drug use.

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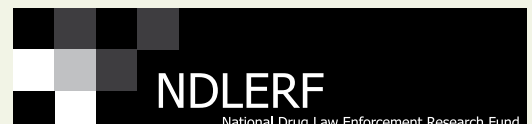
How patterns of injecting drug use evolve in a cohort of people who inject drugs

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People who inject drugs (PWID) typically do so over considerable periods, in some cases up to 20 or 30 years, before stopping for a sustained period (Oppenheimer et al. 1994, Henderson et al. 2002). One aim of drug law enforcement and harm reduction interventions is to reduce the negative health and social consequences experienced by PWID and society during the period in which an individual injects drugs, which is sometimes called their 'injecting career' (Ministerial Council on Drug Strategy 2011). The term 'maturing-out' has long been applied to people who use drugs but then outgrow their habits (Winick 1962), whether with the aid of services or of their own accord. Little is known about whether PWID in Australia mature out of drug use in the longer term, and how this is achieved. Prospective cohort studies such as the Melbourne Injecting Drug User Cohort Study (MIX) (Horyniak et al. 2013) offer an insight into these patterns. This paper considers some of the changes that have been observed in the MIX cohort of PWID over time.

This study also focuses on how the frequency of injecting drug use has changed over time within the MIX cohort. The frequency of a cohort's drug use reflects the group's market demand, and is likely to indicate the risks to which cohort members are exposed (eg blood-borne viruses, police involvement). Without major drug market or policy changes, shifts in the frequency of injecting drug use indicate how use persists over time, making it possible to assess the extent to which PWID mature-out.

Data collected since 2008 on the frequency of drug use of MIX participants indicate that most consider heroin as their drug of choice. Between 2008 and 2014, the price, purity and availability of heroin remained fairly stable (Cogger et al. 2014, Scott et al. 2015b). There were also few policy changes of any major impact during this period. Buprenorphine-based Opioid Substitution Therapy (OST) underwent a program shift from the use of Subutex to Suboxone (NPS RADAR 2011, Australian Institute of Health and Welfare 2014), however



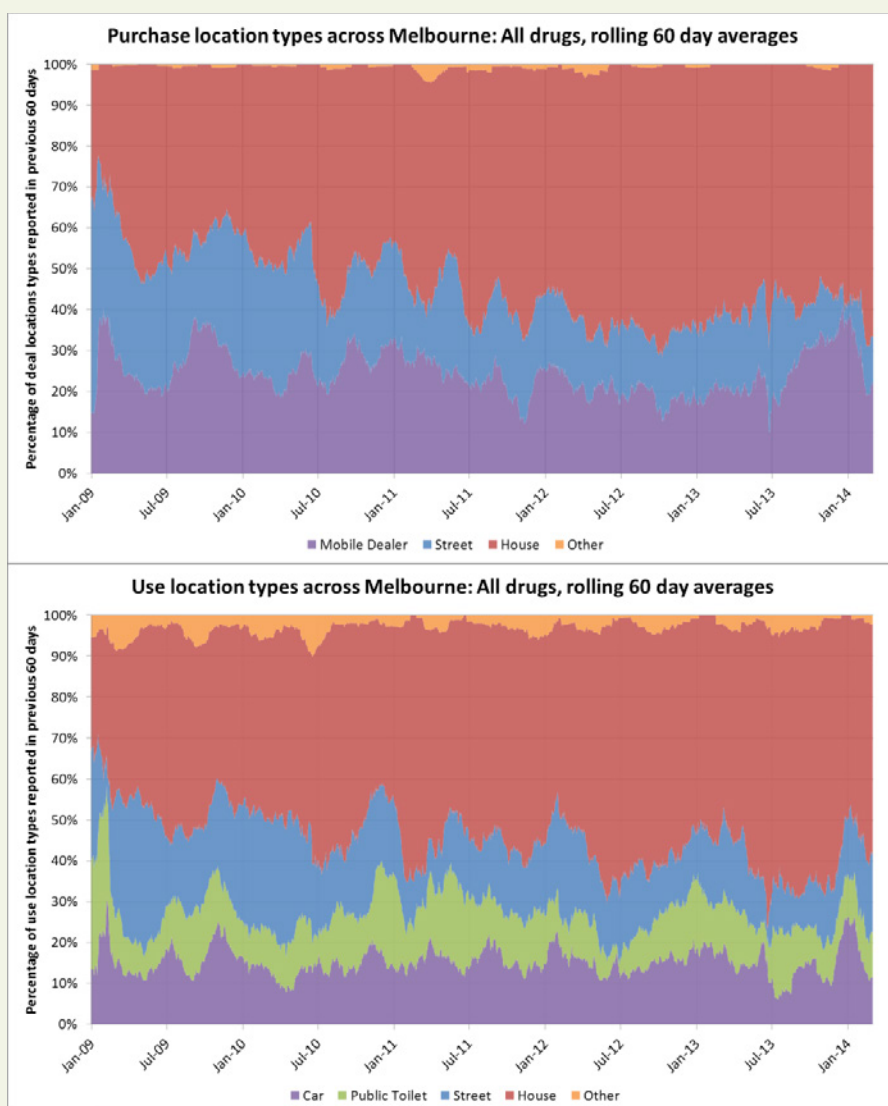
the effect of this on OST uptake is unknown and total OST use in Victoria has been largely stable since 2008 (Cogger et al. 2014). The relative stability of the heroin market and related drug policies provides an opportunity to assess how patterns of drug use evolve under current policy interventions. Treatment programs such as OST are designed to reduce use and harms (Ward, Hall et al. 1999). In Australia OST is provided in two forms, either with methadone or buprenorphine, both being demonstrably effective (Mattick et al. 2003,

Mattick et al. 2014). This study examined correlations between OST enrolment and frequency of drug use in the cohort over time. PWID are known to cycle through periods of increased and lower use before long term cessation (Kimber et al. 2010). The recruitment mechanisms of cohort studies can target individuals currently at the high end of their cycle. Regression to the mean is a phenomenon that occurs when initial observations are systematically biased, and later ones are not (Barnett et al. 2005). This may cause apparent changes in

characteristics that are simply convergence towards their unbiased values, and the potential of this is featured in the data.

The settings of drug deals (eg street, house) and those in which drugs are most likely to be used are reported in MIX, enabling them to be analysed to understand their evolution and the interplay between purchase and use location type, frequency of drug use, and the maturing-out phenomenon. This information can inform when and where interventions may be best pursued (Decker 2005).

Figure 1 Purchase location types and use location types across Melbourne



Methods

Data source

This study used data on drug purchases and drug use obtained from MIX. MIX is a prospective cohort study of 688 PWID who were recruited into the study between April 2008 and January 2010. Another 69 participants, members of a different cohort known as Networks II, were rolled into the study in 2011. MIX participants are young compared with those in most studies of injecting drug use in Australia. Individuals were eligible for the study if they were between 18 and 30 years old and had injected either heroin or methamphetamine at least six times over the previous six months. Experienced fieldworkers interview participants face-to-face every 12 months or so, and obtain detailed information on up to three recent purchases of heroin, methamphetamine, benzodiazepines and other opioids, as well as on the frequency of injecting a range of drugs. Median dates for baseline and the first three follow-up interview waves undertaken to date are July 2009 (interquartile range or IQR, March 2009–November 2009), August 2010 (IQR April 2010–April 2011), September 2011 (IQR April 2011–February 2012) and August 2012 (IQR March 2012–December 2012). Further details on MIX can be found elsewhere (Horyniak et al. 2013, Scott et al. 2015a).

Relevant interview questions relating to each purchase are: the type of location where the drug was purchased, categorised as house (including shared accommodation and public housing), street, mobile dealer or other (Scott et al. 2015a); and the location type where the drug was used, categorised as house, street, public toilet, car or other. For each interview a participant was considered to use more often in private if most of their purchases (maximum of 12, 3 for each of heroin, methamphetamine, benzodiazepine and other opioids) were used in houses. They were considered to use more often in public if most of their purchases were used in public locations (streets, public toilets or cars). Less than

five percent of interviews reported equal locations of use and so were excluded from this classification. A new variable ‘total injections in the last week’ was created by adding the number of injections in the last week reported for each of the drugs: heroin, methadone, buprenorphine, Suboxone, morphine, oxycodone, other opiates, powder methamphetamine, base methamphetamine, crystal methamphetamine, prescription stimulants, cocaine, hallucinogens, ecstasy, benzodiazepines, antipsychotics, antidepressants and other drugs. Most injections were of either heroin or methamphetamine, which together constituted 77 percent of reported injections over all interviews.

Participants reported if they were currently on OST or not. At baseline interviews, 38 percent of MIX participants (n=285) were enrolled in OST. Compared with participants not on the therapy, those on OST were more likely to be slightly older (median age 29 vs 27), female (44% of females vs 34% of males were enrolled, $\chi^2(1)=6.45, p<0.05$), have had a longer injecting career (mean 11.7, 95%CI 11.1–12.3 years vs 9.4, 95%CI 8.9–9.8 years) and have been to prison (42% of participants who had been to prison were enrolled in OST vs 31% of those who had not, $\chi^2(1)=9.57, p<0.01$). Participants on, and not on, OST were similar in terms of current living circumstances, employment status, income, country of birth and language spoken.

Purchase and use location types

All purchases of heroin, methamphetamine, benzodiazepines and other pharmaceutical opioids were pooled across individuals for interviews occurring on each day between 1 January 2009 and 1 March 2014. A rolling 60-day period was used to determine the percentage of drugs bought and used in each location type. So, for the data point plotted for 30 June averages are based on all individuals interviewed between 1 May and 30 June inclusive.

The percentage of purchases and use occurring in each setting was calculated

for each of the first four interview waves by OST status, using all available data from April 2008 to March 2014.

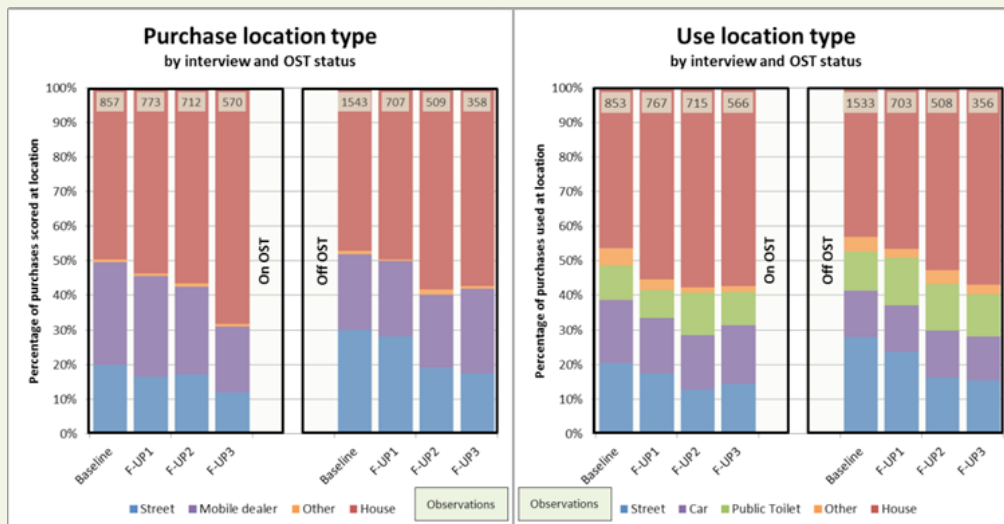
For each interview wave, distributions of total injections in the last week were generated. Among participants reporting recently injecting, the mean injection frequency was calculated for each interview wave and used to estimate the annual decline in average frequency of use, based on median interview dates. Due to a tail of high-frequency injectors these distributions were highly right-skewed, meaning that trends among high frequency injectors may have disproportional or misleading effects on overall changes, particularly if they were greatly different from trends among low frequency injectors. To measure the extent of the skew at each interview wave, the contribution of the most frequently injecting 20% of participants was analysed. The percentage of the cohorts’ total injections attributable to this high use group was calculated.

To measure changes to the overall frequency of participants’ drug use, interviews between January 2009 and December 2013 were pooled into six month periods, and for each period the mean ‘total injections in the last week’ was calculated and plotted over time.

The total number of injections reported in the last week was categorised as either zero, 1–2 times, 3–7 times, 8–14 times or 15 or more times. For each interview wave, the percentage of participants who reported injecting at each categorised frequency was calculated. Separate column charts were generated showing these percentages after stratifying by OST status and by whether a participant used most in private or public locations.

To explore the effects of participants lost to follow-up on the difference in OST status, a comparison was made between the frequency of injecting and percentage enrolment in OST of participants with fewer than four interviews (measured at their final interview) and those of participants with four or more interviews (measured at their fourth interview).

Figure 2 Purchase location types and use location types by interview OST status



Results

Purchase and use location types

Most drugs were bought in houses.

The percentage of purchases in houses increased over time, while that of street purchases fell. House, street and mobile dealer categories made up 46 percent, 28 percent and 25 percent of purchase location types reported in 2009 respectively. By contrast, house, street and mobile dealer categories made up 59 percent, 15 percent and 26 percent of purchase location types reported in 2013 respectively. This difference between years was statistically significant ($\chi^2(2)=62.4, p<0.001$).

The most reported drug use also occurred in houses. The percentage of use sessions occurring in houses increased over time, while that of street use fell. House, street, public toilet and car categories made up 43, 27, 10 and 15 percent of use location types reported in 2009 respectively. By contrast, house, street, public toilet and car categories made up 58, 13, 11 and 15 percent of use location types reported in 2013 respectively, and this difference between years was statistically significant ($\chi^2(3)=77.5, p<0.001$).

Purchase and use location types by OST status

Participants on OST purchased and used in different types of locations than those

who were not on OST. Participants on OST reported fewer street purchases and more purchases in houses. Those on OST reported 17 percent and 56 percent of purchases on the street or in houses over the first four interviews respectively, while participants not on OST reported 26 percent and 51 percent of purchases on the street or in houses respectively. This difference was statistically significant ($\chi^2(2)=84.6, p<0.001$). Participants on OST also reported that fewer purchases were used on the street. Participants on OST reported that 17 percent and 54 percent of purchases were used on the street or in houses over the first four interviews respectively, while participants not on OST reported that 24 percent and 47 percent of purchases were used on the street or in houses respectively. This difference was statistically significant ($\chi^2(2)=71.2, p<0.001$). Mobile dealer purchases, and use in cars or public toilets did not vary with OST status.

Distributions of injection frequency

The distributions of total injections per week were right-skewed, and shifted towards less use with each interview wave (Figure 3, left). Participants who reported recent use had mean weekly injection frequencies of 10.3 (95%CI 9.3–11.1), 8.5 (7.5–9.5), 8.3 (7.1–9.4) and 8.0 (6.8–9.3) at baseline and the first three follow-up interview waves respectively. The top 20 percent of most frequent injectors accounted for 39, 30, 30

and 26 percent of all reported injections in the baseline and first three follow-up interview waves respectively. This indicates that distributions of use became less skewed over time, most notably between baseline and the first follow-up interview waves.

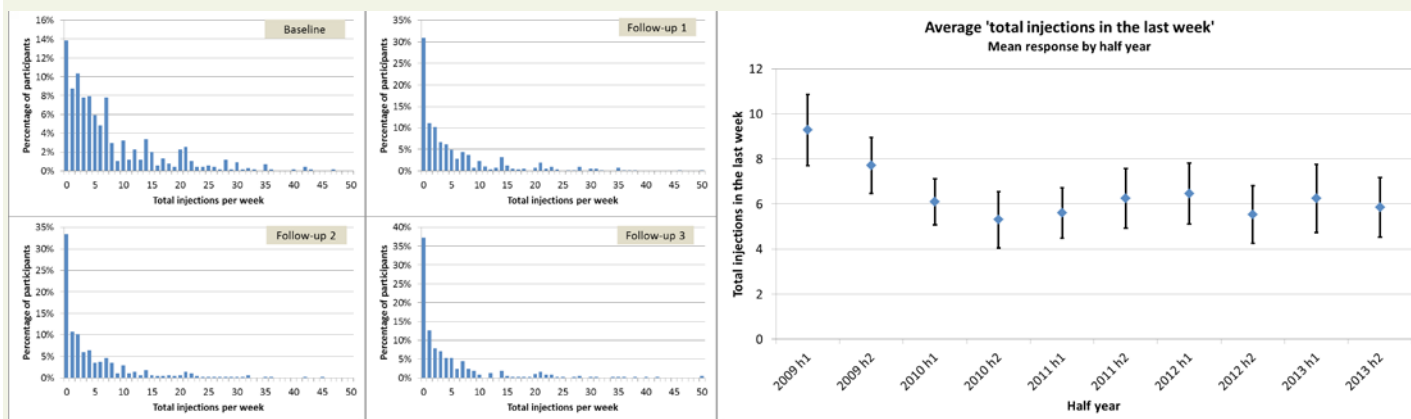
The cohort's overall frequency of use (including those not injecting) declined between 2009 and mid-2010 before experiencing small variations (Figure 3, right). This is consistent with the changes observed in average injection frequency between interview waves.

If the initial decline between the baseline and follow-up interviews is removed (due to the likely effects of regression to the mean), then these results imply that those who reported use reduced their frequency of injecting by 5.9 percent between the follow up one and three interviews. This is about three percent a year, based on median interview dates. This decline was not statistically significant.

Categorised injection frequency, by OST status and use location

Overall, participants on OST injected around 35 percent less frequently than those not on OST. Among participants who reported injecting, the mean weekly frequency was 11.0 (95%CI 10.2–11.8) for those who were not on OST, compared with 7.2 (6.6–7.9) for those who were.

Figure 3 Average 'total injections in the last week'



When categorised, injection frequencies differed by OST status and most common use location (Figure 4). Participants on OST were less likely to be high-frequency injectors and more likely to either abstain from injecting or inject once or twice a week ($2(4)=76.6, p<0.001$). This was also true for participants who used most of their drugs in private, rather than public locations ($2(4)=13.6, p<0.01$). Injection frequency declined across interviews for participants both on and off OST, and for participants who used the most in either public or private locations.

The differences apparent in Figure 4 may also be an underestimate, as participants not included in all four interview wave data were more likely to be high-frequency injectors and not on OST. Participants with fewer than four interviews had an average injection frequency of 8.7 (95%CI 7.2–10.1) and a 40 percent enrolment in OST in their last interview, while participants with four or more interviews had an average injection frequency of 5.1 (95%CI 4.2–6.2) and a 60 percent enrolment in OST ($2(2)=26.2, p<0.001$) in their fourth interview.

Discussion

The study shows a very slow decline in the frequency of injecting drug use among PWID. In particular, after an initial decrease

up to mid-2010, Figure 3 (right) does not show any further significant changes in mean injection frequency. Although distributions of use frequency (Figure 3, left and Figure 4) continued to shift towards less frequent use after follow-up one (approximately corresponding with mid-2010), the additional declines were small. After removing these initial effects, it is estimated that PWID reduce their injecting at a rate of about three percent a year. The fact that frequency of use declines so slowly indicates that injecting drug use requires sustained long-term interventions. Once recruited into use, the decline among PWID to eventual maturing-out is long, and the current levels and types of interventions appear inadequate at curbing the demand from existing PWID.

The mean injection frequency of participants on OST was 35 percent lower than for those not on OST, indicating that access to OST was associated with a reduction in demand for illicit drugs. The reduction in injecting frequency when enrolled in OST is consistent with the findings of numerous previous studies (eg Gowing et al. 2011). Further, as participants lost to follow-up were more likely to be high-frequency injectors and not on OST, the 35 percent reduction observed is likely to be an underestimate and the injection frequency among those not on OST may be understated.

These data show an overall movement away from street-based drug purchasing and drug use towards more activity in private settings. This trend was observed almost equally among participants on and off OST. Since participants on OST were using more in private settings than participants off OST to begin with, increasing coverage of OST within the cohort (38%, 53%, 59% and 60% of participants were on OST for the first four interview waves respectively) may have enhanced this trend when considered for the combined cohort; that is, made the overall shift appear greater than the individual shifts within OST and off OST subgroups.

The reduction in street-based market activity may represent a positive outcome for the MIX cohort, as use in private locations was associated with a lower injection frequency. This may also be a positive outcome for social amenity, which has been seen to improve when injecting drug use declines more generally (Day et al. 2004). However, without knowing the injecting habits of those new to injecting drug use, this study is limited in determining broader levels of social amenity. Despite this change in setting, risks to individuals still exist, such as overdosing that goes with use in more private locations (Darke & Zador 1996). Innovative education and outreach strategies are needed to minimise these risks.

These shifts in purchase and use settings have further implications for drug policy, as purchases occurring in private settings represent the largest and growing market component. This is true both for percentage of deals and their size, as it has been observed that purchases in houses in Melbourne are larger (in dollar value) than purchases made in public locations (Scott et al. 2015a). In general, a better understanding and increased focus on these types of transactions is needed.

Estimating the decay rate of use in this study had two limitations. First, PWID are known to cycle through periods of increased and lower use. It is plausible that the MIX recruitment requirement of 'injecting either heroin or methamphetamine at least six times over the previous six months' or, more generally, a lack of desire to join during a period of cessation, may have biased recruitment towards participants in high use periods of their injecting cycles. If baseline interviews were biased towards higher use,

regression to the mean would explain why changes between baseline and follow-up one interviews were greater than changes observed between other interviews. In particular, the initial decrease in use shown in Figure 3 (right) appears consistent with this phenomenon. If this effect lasted beyond follow-up one, frequency of use may decline even more slowly than observed. Cyclic frequency of use patterns among PWID may also have affected the OST findings. It is plausible that self-initiated enrolment in OST was biased towards PWID who had already reduced their use. Causal links cannot be drawn between OST enrolment and reduced injection frequency.

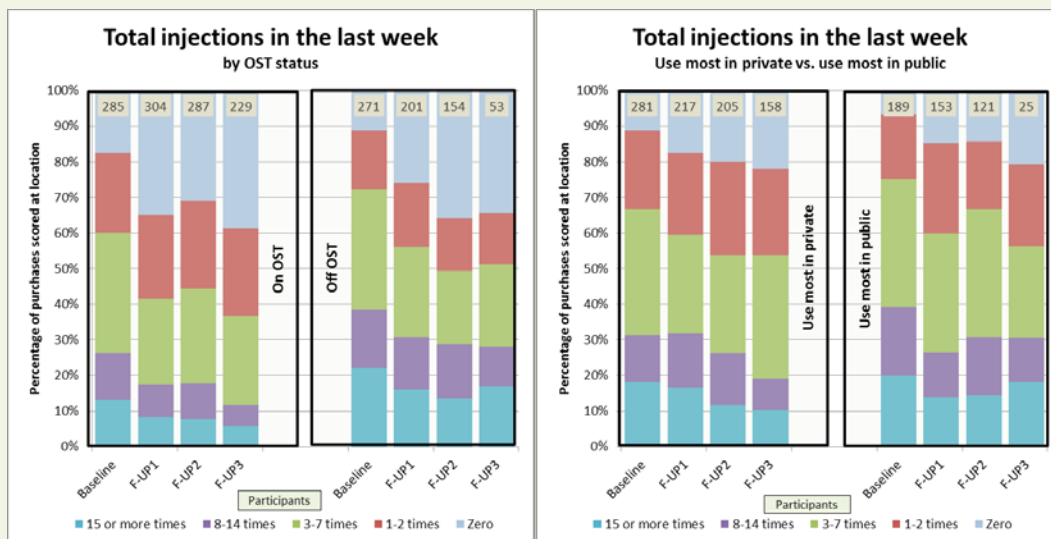
Second, while the heroin market remained fairly stable during this period, methamphetamine dramatically declined in purity-adjusted price and became increasingly available (Scott et al. 2015b). However, as 64 percent of the cohort reported heroin as their drug of choice, against only 12 percent

reporting methamphetamine, changes to the methamphetamine market are only expected to have affected a minority of participants (Scott et al. 2015c).

Conclusion

This study examines some of the ways in which injecting drug use evolves over time in a cohort of PWID. It shows shifts in the settings in which cohort members reported buying and using their drugs. These shifts have important implications for the harms experienced by PWID, and the wider community. Overall, declines in use were slow. However, use in private rather than public locations and the uptake of OST were both associated with lower reported injection frequencies. Further work is needed to understand how this change in setting affects current interventions, and whether it can be used to help further reduce harms related to injecting drug use.

Figure 4 Total injections in the last week by OST status and use most in private and most in public



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