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Research Paper

Emergence of Novel Psychoactive Substance injecting associated with rapid rise in the population prevalence of hepatitis C virus

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ABSTRACT

Background: Novel Psychoactive Substance (NPS) use has increased in recent years and generated significant concern within public health. People who inject drugs (PWID) are at increased risk of blood borne viruses, in particular Hepatitis C virus (HCV). However, little is known about the extent of NPS injecting at a national level and its association with HCV. This study provides one of the first epidemiological analyses of the association between NPS injecting and HCV among a population level sample of PWID.

Methods: Five cross sectional surveys of almost 13,000 PWID attending services providing injecting equipment across Scotland between 2008 and 2016 were analysed. Logistic regression was used to determine associations between NPS injecting and HCV.

Results: The proportion of PWID reporting that they had injected NPS in the previous six months increased from 0.2% in 2008–09 to 11.0% in 2015–16. Those who reported injecting NPS were considerably more likely to be resident in the Lothian NHS Board area at the time of the study (AOR 5.6 (95% CI 4.1–7.5)) and to have had recent experience of homelessness (AOR 1.4 (95% CI 1.0–1.9)). People who injected NPS were also significantly more likely to be HCV positive (AOR 1.7 (95% CI 1.2–2.4)). In Lothian, HCV prevalence rose from around 30% between 2008 and 2012 to 41% and then 48% in 2013–14 and 2015–16 respectively. Increases in prevalent HCV infection in Lothian may be partly attributed to increases in NPS injecting.

Conclusion: In Scotland, people who had injected Novel Psychoactive Substances were at increased risk of hepatitis C virus. Novel Psychoactive Substance injecting poses a threat to HCV elimination strategies.

Introduction

The United Nations define Novel Psychoactive Substances (NPS) as "substances of abuse, either in a pure form or a preparation, that are not controlled by the 1961 Single Convention on Narcotic Drugs or the 1971 Convention on Psychotropic Substances, but which may pose a public health threat" (United Nations Office on Drugs & Crime, 2013). Although no universal categorisation exists, NPS can be generally classified within the following groups: stimulants, cannabinoids, hallucinogens, or depressants (Tracy, Wood, & Baumeister, 2017). In response to growing concern about NPS use and related harms, the UK Psychoactive Substances Act came into force in 2016 which criminalised the production, supply, possession, importation and exportation of "any substance intended for human consumption that is capable of producing a psychoactive effect".

General population surveys internationally estimate past-year prevalence of NPS use between 0.4% and 5.9% (Khaled et al., 2016) but are likely to under-represent groups known to use NPS such as prisoners (Ralphs, Williams, Askew, & Norton, 2017) and those with experience of homelessness (Smith et al., 2017). Moreover, evidence of NPS injecting among other vulnerable populations has emerged in recent years, in particular among current and former opioid users (European Monitoring Centre for Drugs & Drug Addiction, 2017; Oprea, Ceausu, & Ruta, 2013). In these examples, stimulant-type NPS injecting has typically been adopted as a substitute for, or complement to, traditional psychoactive drugs such as heroin.

NPS use by people who inject drugs (PWID) is associated with high frequencies of injecting episodes and sharing of equipment (Karila,

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Megarbane, Cottencin, & Lejoyeux, 2015) thus placing users at considerable risk of physical health harms including blood-borne viruses (BBV) (Tarján et al., 2015). Recent examples include an outbreak of HIV infection among NPS injectors in Dublin (Ireland) associated with frequency of injecting and homelessness (Giese et al., 2015), increases in BBV incidence among NPS injectors in Hungary associated with frequency of injecting, homelessness and low coverage of Injecting Equipment Provision (IEP) sites (Rácz et al., 2016; Tarján et al., 2015), and increased risk of needle/syringe sharing and BBV infection among NPS injectors in England and Wales (Hope et al., 2016).

An outbreak of severe skin and soft tissue infections, bacteraemias and infective endocarditis among PWID was detected in the Lothian NHS Board area (henceforth 'Lothian') of Scotland in 2014 (Griffith, Mackintosh, & Inverarity, 2016; Yeung et al., 2017). Those most likely to be affected by this outbreak were former heroin injectors known to be injecting ethylphenidate, a stimulant-type NPS similar in chemical structure to methylphenidate and known to be associated with a high frequency of injecting (Lafferty, Smith, Coull, & Shanley, 2016). The decision to adopt ethylphenidate as a drug of injection is complex, however it is likely to have been influenced by its availability in 'head shops' (shops traditionally associated with the sale of drug use paraphernalia) which are more prevalent in Lothian than in other parts of Scotland (Lafferty et al., 2016). Notably, Lothian also experienced a significant increase in prevalence of HCV in 2015-16 despite traditionally having one of the lowest rates in Scotland (Health Protection Scotland, University of the West of Scotland, & Glasgow Caledonian University and the West of Scotland Specialist Virology Centre, 2017). We hypothesised that this changing trend in HCV prevalence was associated with increases in NPS injecting in that locality.

Using data from Scotland's national surveillance system of infections and risks among PWID (Health Protection Scotland et al., 2017), this paper aims to: (i) to examine the prevalence of NPS injecting over time in Scotland among PWID and associated sociodemographic factors (ii) to assess the association between HCV and NPS injecting and (iii) examine NPS injecting with respect to HCV incidence.

Materials and methods

Data sources

The Needle Exchange Surveillance Initiative (NESI) is a voluntary, anonymous, cross-sectional survey of PWID, attending services providing injecting equipment, in mainland Scotland to monitor rates of BBV infection and risk behaviours in this population (Health Protection Scotland et al., 2017). During 2008–2016, five NESI surveys have been undertaken, each involving a sample of approximately 2500 PWID. Participants are asked to take part in a short survey and to give a dried blood spot sample to test anonymously for the presence of BBVs. A £5 shopping voucher is provided to individuals who complete the survey as compensation for their time. The interviews are carried out by trained interviewers who obtain informed consent from all participants prior to data collection. Since NESI commenced, all dried blood spot samples have been tested for HCV antibodies. RNA testing has also been undertaken on antibody negative samples since 2008, principally to help identify incident (new) HCV infections. More recently, routine RNA testing (of HCV antibody positives) has been introduced in NESI to monitor the impact of HCV treatment. NESI sampling and laboratory testing methods have been previously described in further detail (Health Protection Scotland et al., 2017). Ethical approval for the NESI survey was granted by the NHS West of Scotland Research Ethics Committee (REC Ref: 08/S0709/46).

Setting

Scotland has approximately 60,000 problem drug users (defined as those with problematic use of opioids and/or benzodiazepines) (NHS National Services Scotland, 2016), around 15,000–20,000 of which are estimated to be PWID (Hay, Gannon, Casey, & McKeganey, 2009; Overstall, King, Bird, Hay, & Hutchinson, 2014). The Lothian area of Scotland includes Edinburgh, the capital city of Scotland, and is estimated to have almost 10,000 problem drug users and around 3000 PWID.

Outcomes

In our first model, the outcome measure – NPS injecting – was derived from responses to NESI questions on drugs injected, specifically those answering *Yes* to whether they injected 'Legal Highs' (a common colloquialism for NPS in the UK) or not. Participants who named specific Legal Highs (e.g. mephedrone) within the 'other' section were also included following review. Prior to 2015–16, NPS injecting was identified in the 'other' field of drugs injected, however in 2015–16 a specific field for 'Legal Highs' was added.

Those who provided a sufficient quality dried blood spot sample to be tested for HCV antibodies were included in our second model of HCV risk among NPS. The third model in our series also focussed on the HCV antibody dried blood spot result, specifically examining changes in the aggregate HCV positive rate over time among the population of PWID recruited in Lothian.

Exposures of interest

We assessed outcomes according to relevant sociodemographic and behavioural factors: age at time of survey; biological sex; NHS board of interview (Lothian, not in Lothian); recent homelessness (in the last six months, not in the last six months); recent history of heroin injecting (in the last six months, not in the last six months); prisoner status (never imprisoned, ever imprisoned); currently prescribed methadone (yes, no); injecting frequency (1–3 times per month, about once a week, 2–6 times per week, once a day, 2–3 times per day, 4 or more times per day); recent needle sharing (in the last six months, not in the last six months) and needle re-use in the last six months (never, once or twice, 3–5 times, 5+ times).

Analysis

In total, 8878 PWID who had injected within the previous six months recruited as part of the 2008–2016 NESI surveys were available for multivariate analysis following the removal of duplicate survey participants using basic identifiers (initials, gender, date of birth) and questionnaires with insufficient or missing demographic data. Where duplicates were identified, the survey with the first positive exposure to the outcome was selected (e.g. first reported NPS injecting or first positive HCV dried blood spot result). For those with no exposure to NPS and / or HCV infection, data from the first survey participation was included. Unadjusted and adjusted logistic regression was then used to identify: (i) factors associated with NPS injecting and (ii) the association between HCV and NPS injecting. In the first model, data from all NESI surveys was pooled for analysis. For our second model, we focussed on data from 2068 individuals participating in the 2015-16 NESI survey given the increase in NPS objecting observed at that time and the change in our survey methods to better identify NPS injecting.

In our third model, we also used logistic regression to specifically examine NPS injecting with respect to HCV prevalence in 2015-16 among the population of PWID in Lothian. Here, the dependent variable was the aggregate HCV positivity rate for each survey and the covariates included were survey year and the percentage of PWID that reported injecting NPS in those years. Therefore, the model gives the average predicted HCV percentage for each NESI year and fits the binary dependent variable based on numbers of HCV positive and negative cases.

Our final analysis explored recent [incident] HCV infection. In the

very early stages of HCV infection, individuals have high levels of HCV virus (RNA) before developing antibodies; recent infections therefore refer to individuals who are HCV antibody negative and HCV RNA positive on dried blood spot testing. An estimate of HCV incidence can then be calculated using the formula:

$$I = \frac{(365/T)n}{(N-n) + (365/T)n}$$

where T is the estimated duration of the window period, n is the number of recently acquired infections and N is the number of susceptibles (i.e. HCV antibody negatives) (Hope, Hickman, Ngui, Jones, & Telfer, 2011). An estimate of the duration of the window period (51 days) was derived from the literature (Page-Shafer et al., 2008).

All analyses were completed using R Statistical Software version 3.4.3.

Results

Participant characteristics

Among the 8878 participants overall, 72% (n = 6432) were male and 52% (n = 4637) were aged under 35 years (Table 1). A quarter (25%; n = 2267) had experienced homelessness in the past six months and just under two-thirds (61%; n = 5412) had ever spent some time in prison. The vast majority (94%; n = 8373) had recently injected heroin and over two thirds were currently prescribed methadone (69%; n = 6150).

People who had injected NPS in the previous six months made up 3% (236/8878) of the sample in total, but the proportion of NPS injectors recruited per survey increased over time from 0.2% (5/2081) in 2008–09 to a high of 11.0% (186/1693) in 2015–16. Exclusive NPS use was rare and accounted for only 0.3% of the total sample (24/8878).

In comparison to those who had not injected NPS, people who inject NPS were significantly more likely to be recruited from the Lothian region (accounting for over half of all NPS injectors) and to have been homeless within the past six months. Injecting risk behaviours were also more prevalent in those who had injected NPS including high frequency of injecting (four or more times per day), needle and syringe sharing and multiple re-use of needles (more than 5 times) in the past 6 months. In contrast, people who injected NPS were significantly less likely than non-NPS injectors to have also injected heroin in the past six months, however rates were still high at over 80%.

Model 1: factors associated with NPS injecting

NPS injecting was most strongly associated with participation in more recent NESI surveys, in particular participation in 2015–16 when almost 80% of all NPS injectors were recruited in NESI (Table 2). In addition, those interviewed within Lothian were significantly more likely to report NPS injecting compared to those interviewed elsewhere. Odds of NPS injecting were also significantly higher for those who had recently experienced homelessness compared to those who had not and those who had ever been in prison compared to those never incarcerated. In contrast, those injecting heroin in the previous six months were significantly less likely to be NPS injectors compared to those who did not. Age was also negatively associated with each year increase in age significantly reducing the likelihood of being an NPS injector.

In sensitivity analysis, we included an interaction effect between age and survey year (Table S1). The interaction coefficients in our model were not significant therefore it is unlikely that the strong association between NESI year and NPS injecting is dependent on age.

Model 2: NPS injecting association with hepatitis C virus in Scotland

In 2015–16, Individuals who reported injecting NPS were significantly more likely to be HCV positive compared to those who did not report NPS injecting (Table 3). This association remained significant in our adjusted model even after accounting for other known HCV risk and protective factors.

In Scotland, HCV prevalence among active PWID (i.e. those who had injected in the previous six months) rose slightly between 2008 and 2016, from 52% to 58% (Fig. 1). In Lothian, where prevalence of NPS injecting (29%) in NESI 2015–16 was highest in Scotland, HCV antibody prevalence rose from around 30% between 2008 and 2012 to 41% and then 48% in 2013–14 and 2015–16 respectively. This is particularly notable among recent onset injectors (i.e. those who commenced injecting in the past three years) where prevalence has almost doubled from 16% in 2008–09 to 30% in 2015–16. The increase in HCV prevalence in Lothian from 2011–12 onwards mirrors the onset of an increase in NPS injecting within the same locality.

Model 3: NPS injecting association with hepatitis C virus in Lothian

In Lothian, unadjusted analysis associates NESI survey year with HCV prevalence (OR 1.14, 95% CI 1.09–1.19) and NPS injecting prevalence with HCV prevalence (OR 1.03, 95% CI 1.02–1.03). However, the effects of NESI survey year and NPS injecting prevalence diminish when taking into account prevalence of NPS in each survey. This suggests that increasing HCV prevalence in Lothian over time may be partly attributed to the parallel increase in NPS injecting, but as NPS injecting also loses statistical significance in the adjusted model, other factors that have not been considered in this model are also likely to be important (Table 4).

Also in Lothian, the incidence of HCV in 2015–16 was 18.4 per 100 person years—on the basis of seven identified cases (antibody negative, PCR positive) of which three reported NPS injecting. Excluding Lothian, incidence of HCV in the rest of Scotland was 9.2 per 100 person years on the basis of 11 identified cases, none of which reported NPS injecting (data not shown).

Increases in HCV prevalence and HCV incidence in Lothian, parallel to increases in reported NPS injecting, occurred at a time where other potential drivers of HCV infection have either remained relatively stable (e.g. shared needles/syringes in the last six months) or shown no similar trends (e.g. shared paraphernalia in the last six months) (Table 5).

Discussion

Infections associated with NPS injecting is an under-researched but important area of public health. This study adds to an emerging evidence base in this field by providing one of the first robust estimates of NPS injecting prevalence among a nationally representative sample of PWID and illuminating factors associated with a group at increased risk of BBV. Further, we also highlight the potential of NPS injecting clusters to reverse progress toward HCV elimination, a key target of the World Health Organization (2016).

Homelessness as a risk factor for NPS injecting reflects findings from studies conducted in both Ireland (Giese et al., 2015) and Hungary (Rácz et al., 2016; Tarján et al., 2015). Homeless populations experience considerable health inequalities (Aldridge et al., 2018) and are amongst the hardest to reach in terms of both prevention and treatment. These challenges are compounded among individuals who are homeless and who also use drugs and prevalence of drug use in this population is known to be high (Fazel, Bains, & Doll, 2006). Homelessness in the UK has been increasing since 2009 (Public Health England, 2018), alongside increases in the availability of NPS over a similar period (European Monitoring Centre for Drugs & Drug Addiction, 2017), and at a time of declining heroin purity in the UK (Ahmad & Richardson, 2016). These factors contribute to a high risk environment (Rhodes, 2009) of considerable public health concern. Efforts to reduce homelessness should be combined with efforts to

Table 1
Characteristics of people who inject drugs (PWID) in Scotland participating in the Needle Exchange Surveillance Initiative, overall and for those who had reported injecting NPS, 2008–2016.

		PWID Excluding NPS users	%	People who inject NPS	%	p[a]
		8642		236		
	People who injected NPS only	0	0.0	24	10.2	
NESI Year	2008–12	2076	24.0	5	2.1	
	2010	2106	24.4	0	0.0	
	2011–12	1434	16.6	1	0.4	
	2013–14	1519	17.6	44	18.6	
	2015–16	1507	17.4	186	78.8	
Region of Scotland	Rest of Scotland	7515	87.0	116	49.2	< 0.001
	Lothian	1127	13.0	120	50.8	< 0.001
Gender	Female	2336	27.0	61	25.8	0.742
	Male	6259	72.4	173	73.3	0.822
	Other/Unknown	47	0.5	2	0.8	0.860
Age Group	< 35 years	4505	52.1	132	55.9	0.277
	35 years +	4126	47.7	102	43.2	0.191
	Unknown/Missing	11	0.1	2	0.8	0.046
Ever Been in Prison	No	3359	38.9	81	34.3	0.178
	Yes	5259	60.9	153	64.8	0.243
	Unknown/Missing	24	0.3	2	0.8	0.323
Homeless in the Last 6 Months	No	6434	74.5	153	64.8	0.001
	Yes	2186	25.3	81	34.3	0.002
	Unknown/Missing	22	0.3	2	0.8	0.273
Currently on Methadone	No	2640	30.5	85	36.0	0.084
	Yes	5999	69.4	151	64.0	0.087
	Unknown/Missing	3	0.0	0	0.0	1.000
Injected Heroin in the Last 6 Months	No	459	5.3	43	18.2	< 0.001
	Yes	8180	94.7	193	81.8	< 0.001
	Unknown/Missing	3	0.0	0	0.0	1.000
Average Injecting Frequency in the Last 6 Months	Less than daily	4039	46.7	78	33.1	< 0.001
	1–3 times a day	3729	43.1	108	45.8	0.464
	4 or more times a day	868	10.0	49	20.8	< 0.001
	Unknown/Missing	6	0.1	1	0.4	0.461
Shared Needles/Syringes in the Last 6 Months	No	7733	89.5	198	83.9	0.008
	Yes	854	9.9	35	14.8	0.017
	Unknown/Missing	55	0.6	3	1.3	0.433
Average Needle Reuse in the Last 6 Months	Never	3897	45.1	79	33.5	< 0.001
	Once or twice	2757	31.9	66	28.0	0.226
	3–5 times	1087	12.6	39	16.5	0.089
	5+ times	847	9.8	50	21.2	< 0.001
	Unknown/Missing	54	0.6	2	0.8	0.992
HCV Antibody Positive	No	3964	45.9	83	35.2	0.001
	Yes	4539	52.5	147	62.3	0.004
	Unknown/Missing	139	1.6	6	2.5	0.392

[a] Chi-square test for association.

prevent NPS use among homeless populations given the health risks studies such as ours and others have shown. For example, harm reduction services should consider how they re-orientate themselves to better accommodate NPS and/or homeless injectors e.g. by adopting more assertive outreach approaches such as street-based needle and syringe provision.

Past prison experience as a risk factor for NPS use was not unexpected given the links established within previous studies (McAuley et al., 2015) and the high prevalence of PWID in prison populations (Blackman & Bradley, 2017). That said, the limited evidence base to date has focussed on synthetic cannabinoid use among prisoners (Blackman & Bradley, 2017; Ralphs et al., 2017), whilst our analysis exclusively focussed on PWID and therefore provides new insight on NPS injecting risk among former prisoners. Few people in our NESI surveys actually report injecting while incarcerated, therefore NPS injecting is likely to occur prior to admission, or following liberation. Despite this, prison should be viewed as an important setting for implementing NPS specific interventions aimed at reducing levels of harm.

The association between NPS injecting and younger age has also been reported in Hungary (Tarján et al., 2015) and the rest of the UK (Hope et al., 2016) and is of particular concern given the progress in reducing prevalence of injecting drug use in Scotland in recent years. Background epidemiology from needle and syringe exchange services (Health Protection Scotland et al., 2017), drug treatment services (NHS National Services Scotland, 2017a), drug-related hospital admissions (NHS National Services Scotland, 2017b) and drug-related deaths (National Records of Scotland, 2018) suggests that PWID in Scotland are an ageing cohort with fewer new injectors joining year on year. The increased risk of morbidity and mortality associated with injecting drug use is well established (Mathers et al., 2013), therefore any new threat to declining trends in injecting should be afforded the highest priority.

Interesting findings regarding the relationship between NPS injecting and heroin injecting also emerged from our model, with heroin injectors less likely to also inject NPS. Despite this negative association, heroin injecting was considerably high amongst NPS injectors in our sample suggesting that exclusive NPS was uncommon. Such evidence reinforces the importance of effective opioid agonist therapy in potentially limiting the risk of drug users substituting one psychoactive

Table 2
Factors associated with NPS injecting among 8767 PWID reporting injecting in the previous six months, Scotland, 2008–2016.

NPS injectors, 228/8767 (2.6%)				
	OR (95% CI)	*p*	AOR (95% CI)	*p*
Age (Per Year Increase)	1.00 (0.98–1.02)	0.847	0.95 (0.93–0.97)	< 0.001
NESI Year				
2008–09, 2010, 2011–12	1.00		1.00	
2013–14	27.11 (11.53–63.74)	< 0.001	26.06 (10.99–61.78)	< 0.001
2015–16	115.52 (51.14–260.96)	< 0.001	120.65 (52.91–275.11)	< 0.001
Gender				
Female	1.00		1.00	
Male	1.06 (0.79–1.42)	0.706	0.92 (0.65–1.29)	0.623
Region of Scotland				
Rest of Scotland	1.00		1.00	
Lothian	6.90 (5.30–8.97)	< 0.001	5.57 (4.14–7.49)	< 0.001
Homeless in the Last 6 Months				
No	1.00		1.00	
Yes	1.56 (1.19–2.05)	0.001	1.42 (1.04–1.94)	0.030
Injected Heroin in the Last 6 Months				
No	1.00		1.00	
Yes	0.25 (0.18–0.36)	< 0.001	0.30 (0.20–0.46)	< 0.001
Ever Been in Prison				
No	1.00		1.00	
Yes	1.21 (0.92–1.58)	0.177	1.60 (1.16–2.22)	0.005

substance for another in response to changes in drug markets.

The significantly elevated risk of HCV among NPS injectors in Scotland mirrors the results from a similar study by Hope et al. (2016). Moreover, our new evidence challenges the advances made in recent years in reducing incidence of this infection through high coverage of harm reduction interventions (Palmateer et al., 2014). Although we were unable to attribute increases in incidence of HCV infection in Scotland specifically to NPS due to a lack of statistical power, it is notable that the area with the highest prevalence of NPS injecting in Scotland, Lothian, observed one of the highest absolute (7%) and relative (17%) increases in HCV prevalence between 2013–14 and 2015–16. This was despite attendances at IEP services in Lothian increasing during the same period (NHS National Services Scotland, 2017c). The rate of new infections in this locality (18.4 per 100 person years) was also markedly higher compared to the rest of Scotland in 2015–16 (9.2 per 100 person years). If NPS injecting is a key factor behind such increases, as it has been in Hungary (Tarján et al., 2015), then it poses a major threat to the call by the World Health Organisation Global Health Sector Strategy on viral hepatitis to reduce newly acquired chronic HCV infections by 30% by 2020 and 90% by 2030 (World Health Organization, 2016). Regular testing is a key component of HCV prevention through identification of new cases, linkage to treatment and care and providing opportunities for awareness raising regarding risk behaviours. Future research should determine the extent to which NPS injectors have been tested and treated for HCV given the highly effective therapies now available in the Direct Acting Antiviral (DAA) era.

As the first multivariate analysis of NPS injecting and related harms among a nationally representative sample of PWID, this study has important implications for policy and practice. Primarily it will be of interest to policymakers focussed on reducing harms associated with drug use and achieving realistic public health goals such as HCV elimination. NPS injecting threatens both these targets. Internationally, robust population level studies such as these are important in highlighting and quantifying the impact of NPS injecting within different countries to allow strategies to be developed prospectively to mitigate similar impacts elsewhere. Lessons from Scotland highlight that high harm reduction coverage is not sufficient on its own to prevent negative impacts associated with NPS injecting. However, given a lack of evidence on the effectiveness of interventions to address NPS-related harm, approaches that are known to reduce injecting related harms (i.e. IEP and BBV testing and treatment) should be modified for NPS users (European Monitoring Centre for Drugs & Drug Addiction, 2016). This includes adapting content of existing interventions, enhancing their delivery in settings where NPS users are likely to be accessible, and ensuring staff (and peers where appropriate) are adequately trained to deliver them. Legislative changes to specific NPS have been effective at reducing harms in the past within an outbreak situation (Yeung et al., 2017). It remains to be seen whether more universal approaches, such as the recent UK Psychoactive Substances Act, will have a similar positive effect. A comparable blanket ban in Ireland, implemented in 2010, has yet to be systematically evaluated (Reuter & Pardo, 2017).

We acknowledge a number of limitations with this study. Firstly, the inclusion of an NPS specific question in the survey in 2015-16 may partly explain the increase in NPS use we observed. However, numerous other sources (Griffith et al., 2016; Lafferty et al., 2016; Pettie et al., 2018; Yeung et al., 2017) have also confirmed a rise in NPS injecting in Lothian at this time therefore we are reassured that the increase we observed in our data is reflective of the actual trend occurring at the time. Similarly, it became clear during the course of the outbreak that heroin available in Lothian had been mixed with ethylphenidate, therefore increasing the possibility that individuals were injecting NPS unknowingly (Yeung et al., 2017). This also may have underestimated rates of NPS use, therefore our model estimates should be viewed as conservative which is perhaps even more concerning in public health terms. Secondly, our primary outcome measure, NPS injecting, is derived from self-reported responses which may be subject to response bias despite our use of independent researchers. The reliability of self-report to describe drug use behaviours has previously been validated (Darke, 1998) and we assume similar validity applied to the responses in this study. The comparability of our findings to the limited number of studies conducted in this area thus far provided reassurance regarding this assumption. Lastly, our sample is biased towards those attending sites providing IEP and therefore under represents PWID who do not regularly engage with such services. Despite this, use of IEP among PWID in Scotland is typically high and the 2015–16 NESI survey covered 118 IEP sites across all of mainland Scotland (relating to approximately 63% of all sites across the country) (NHS National Services Scotland, 2017c) therefore we are confident that the sample is nationally representative.

Conclusion

The phenomenal growth in the availability and use of NPS internationally has presented a key challenge for public health in recent years. The lack of evidence on the drugs themselves, and harms associated with their use, has hindered policymakers and practitioners in their responses. Our study has shown that people who inject NPS in Scotland are at increased risk of HCV, despite high coverage of harm reduction interventions. This increased risk appears to have reversed previously stable trends in HCV prevalence in a locality where NPS injecting took hold quickly and substantially. Prevention efforts should optimise harm reduction approaches, with a particular focus on homeless and ex-prisoner populations who appear particularly vulnerable to NPS injecting and related harms.

Conflicts of interest

None.

Table 3
Factors associated with HCV antibody infection among 2068 PWID reporting injecting in the previous six months, Scotland, 2015–16.

HCV positive, 1201/2068 (58%)				
	OR (95% CI)	*p*	AOR (95% CI)	*p*
Injected NPS in the Last 6 Months				
No	1.00		1.00	
Yes	1.40 (1.05–1.87)	0.023	1.71 (1.23–2.38)	0.001
Region of Scotland				
Rest of Scotland	1.00		1.00	
Lothian	0.61 (0.49–0.75)	< 0.001	0.48 (0.38–0.62)	< 0.001
Age (Per Year Increase)	1.06 (1.04–1.07)	< 0.001	1.06 (1.05–1.08)	< 0.001
Gender				
Female	1.00		1.00	
Male	1.01 (0.83–1.23)	0.897	0.89 (0.72–1.10)	0.297
Homeless in the Last 6 Months				
No	1.00		1.00	
Yes	1.49 (1.21–1.84)	< 0.001	1.66 (1.32–2.08)	< 0.001
Currently on Methadone				
No	1.00		1.00	
Yes	1.43 (1.17–1.73)	< 0.001	1.36 (1.10–1.68)	0.005
Average Injecting Frequency in the Last 6 Months				
Less than daily	1.00		1.00	
1–3 times a day	1.24 (1.04–1.49)	0.017	1.15 (0.94–1.39)	0.166
4 or more times a day	2.23 (1.58–3.14)	< 0.001	2.39 (1.63–3.50)	< 0.001
Shared Needles/Syringes in the Last 6 Months				
No	1.00		1.00	
Yes	1.45 (1.02–2.06)	0.041	1.39 (0.94–2.06)	0.095
Average Needle Reuse in the Last 6 Months				
Never	1.00		1.00	
Once or twice	1.37 (1.11–1.69)	0.003	1.33 (1.06–1.66)	0.012
3–5 times	1.47 (1.11–1.93)	0.006	1.36 (1.01–1.82)	0.044
5+ times	1.44 (1.10–1.88)	0.008	1.31 (0.98–1.76)	0.071
Used Contraception in the Last 6 Months				
Yes	1.00		1.00	
No	1.30 (1.07–1.59)	0.008	1.13 (0.91–1.40)	0.267

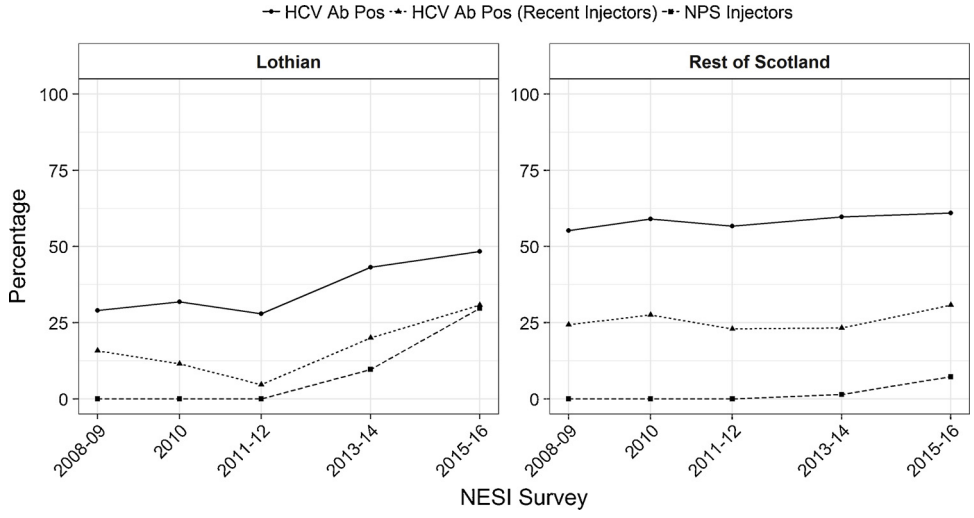

Fig. 1. HCV prevalence and NPS injecting prevalence, Scotland and Lothian NHS Board, 2008–2016.

Table 4
Factors associated with aggregate HCV antibody prevalence among PWID reporting injecting in the previous six months, Lothian NHS Board, 2008–2016.

	OR	95% CI	*p*	AOR	95% CI	*p*
NESI Year	1.14	1.09–1.19	< 0.01	1.07	0.97–1.19	0.19
% NPS injectors	1.03	1.02–1.03	< 0.01	1.01	0.99–1.03	0.21

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Table 5
Trends in demographics, OST engagement and injecting risk behaviours among PWID in Lothian NHS Board, 2008–2016.

		NESI year				
		2008–09	2010	2011–12	2013–14	2015–16
Number recently infected[a]		1	3	2	0	7
HCV incidence	*per 100 person-years*	3.4	8.2	7.3	n/a	18.4
	95% CI	0.0, 11.3	0.0, 18.0	0.0, 18.1	n/a	6.8, 31.1
Mean (SD) Age	*mean*	32.6	32.9	34.1	34.8	37.1
	SD	7.2	7.1	7.1	7.8	7.6
Male	*n*	202	254	157	184	324
	% within NESI year	76.2%	77.7%	77.3%	74.8%	75.7%
Homeless in the last six months	*n*	88	94	45	89	151
	% within NESI year	33.2%	28.7%	22.2%	36.2%	35.3%
Currently on methadone	*n*	170	236	123	142	241
	% within NESI year	75.2%	81.1%	73.7%	69.3%	64.1%
Injected Heroin in the last six months	*n*	257	322	194	223	386
	% within NESI year	97.0%	98.5%	95.6%	90.7%	90.2%
Ever been in prison	*n*	141	174	102	141	240
	% within NESI year	53.2%	53.5%	50.2%	57.6%	56.5%
Shared Needles/Syringes in the last six months	*n*	24	36	22	23	42
	% within NESI year	9.1%	11.0%	10.8%	9.3%	9.8%
Shared paraphernalia in the last six months	*n*	107	129	67	57	122
	% within NESI year	40.4%	39.4%	33.0%	23.2%	28.5%
Reused Needles/Syringes 5+ times, on average, in the last six months	*n*	10	51	42	42	84
	% within NESI year	3.8%	15.6%	20.7%	17.1%	19.6%

[a] In the very early stages of HCV infection, individuals have high levels of HCV virus (RNA) before developing antibodies (anti-HCV); recent infections therefore refer to individuals who are anti-HCV negative and HCV RNA positive.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.drugpo.2019.01.008.

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