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Systematic Literature Review on Stimulant use and HIV (A)

Part 4 /5

New Psychoactive Substances
Risk and Transmission

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This report is part of a series of five documents:

A. Stimulant use: HIV risk and transmission

1. Systematic Literature Review on HIV and Stimulant use: Methodology and summary of the findings of
2. Systematic Literature Review on HIV and Stimulant use: ATS and HIV Risk and Transmission
3. Systematic Literature Review on HIV and Stimulant use: Cocaine use and HIV Risk and Transmission
4. Systematic Literature Review on HIV and Stimulant use: NPS and HIV Risk and Transmission

B. Prevention of HIV, HCV & HBV and treatment

5. Systematic Literature Review on HIV and Stimulant use: Treatment and Prevention of HIV, HCV & HBV and treatment

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1. Overview

New Psychoactive Substances (NPS) are substances of abuse which may cause harm, but that are not controlled by the 1961 Single Convention on Narcotic Drugs or the 1971 Convention on Psychotropic Substances (UNODC, 2013). NPS, also known as 'designer drugs' or 'legal highs', emerged in the European drug scene in mid-2000 with several reports indicating an increase prevalence in the use of these drugs (Brandt, King, & Evans-Brown, 2014; Duffert, 2014; Favretto, Pascali, & Tagliaro, 2013; Gonzalez, Ventura, Caudevilla, Torrens, & Farre, 2013; Institoris et al., 2015; McNamara, Stokes, & Coleman, 2010; Regan, Mitchelson, & Macdonald, 2011; Szily & Bitter, 2013; Van Hout & Brennan, 2011). NPS have also been reported in Australia (Burns et al., 2014) and in the United States to a lesser extent (Maxwell, 2014; Spiller, Ryan, Weston, & Jansen, 2011; Stogner & Miller, 2013).

A variety of NPS have been designed and manufactured in laboratories and sold cheaply online or in headshops (Bruno, Poesiat, & Matthews, 2013; Cinosi et al., 2014; van Amsterdam, Nabben, Keiman, Haanschoten, & Korf, 2015). Initially, these drugs were legally sold as they were labelled 'not for human consumption' (Davidson, 2012; Musselman & Hampton, 2014). Many of these novel drugs have now been controlled or scheduled, but the arrival of new NPS is rapid. The EMCDDA is currently monitoring more than 450 new psychoactive substances, 101 of these were reported only in 2014 (EMCDDA, 2015). The control of NPS has proven difficult, as new drugs rapidly appear in the drug market to substitute recently scheduled ones (De Paoli, Maskell, & Pounder, 2011; Durham, 2011; Papaseit, Farre, Schifano, & Torrens, 2014; Watson, 2012; A. Winstock, Mitcheson, & Marsden, 2010).

There are a number of different types of NPS with different molecular structures aiming to imitate the effects of well-known drugs of abuse such as cannabis, cocaine, MDMA, benzodiazepines and opioids (L. A. Johnson, Johnson, & Portier, 2013). But the majority of NPS are either synthetic cannabinoids or synthetic cathinones (EMCDDA, 2014; Thornton & Baum, 2014). Synthetic cannabinoids have similar molecular structure to cannabis (Rosenbaum, Carreiro, & Babu, 2012), while synthetic cathinones have similar molecular structure to cathinone, which is found in the Khat plant (*Catha edulis*) (Cottencin, Rolland, & Karila, 2014; Iversen, White, & Treble, 2014; Valente, Guedes de Pinho, de Lourdes Bastos, Carvalho, & Carvalho, 2014). Synthetic cathinones have alike effect to some stimulant drugs, such as amphetamines, cocaine and MDMA (German, Fleckenstein, & Hanson, 2014; Gerona & Wu, 2012; Glennon, 2014), and for this reason this review will focus on NPS that fall under this group.

A number of synthetic cathinones, also known as 'bath salts', have been identified in the drug market in recent years (De Felice, Glennon, & Negus, 2014; Fass, Fass, & Garcia, 2012; Gunderson, Kirkpatrick, Willing, & Holstege, 2013; Prosser & Nelson, 2012; Winder, Stern, & Hosanagar, 2013; Zawilska, 2014). The most commons are mephedrone, pentedrone, methylone, methcathinone, MDPV, alpha-PVP, 4-MEC (Katz et al., 2014; Kyle, Iverson, Gajagowni, & Spencer, 2011; Wieland, Halter, & Levine, 2012).

Mephedrone is from the cathinones family and its structure is similar to amphetamine and MDMA (Dargan, Sedefov, Gallegos, & Wood, 2011; den Hollander et al., 2014; Green, King, Shortall, & Fone, 2014; Schifano et al., 2011; A. R. Winstock, Marsden, & Mitcheson, 2010; A. R. Winstock et al., 2011;

Wood & Dargan, 2012). Mephedrone has a longer effect of action than cocaine and MDMA and produces similar stimulant-like effects to these drugs, such as elated mood and increase in sexual drive, as well as cardiovascular and psychiatric side effects (Dybdal-Hargreaves, Holder, Ottoson, Sweeney, & Williams, 2013; Hohmann, Mikus, & Czock, 2014; Imam et al., 2013; James et al., 2011; Mas-Morey, Visser, Winkelmoen, & Touw, 2013; A. Winstock et al., 2011). Mephedrone has also been found to cause cognitive impairment, such as acute working memory impairment (Freeman et al., 2012). A number of case-reports highlighted the possible health-related consequence of mephedrone use (Garrett & Sweeney, 2010; Kasick, McKnight, & Klisovic, 2012; Khullar, Jain, & Sattari, 2014; Levine, Levitan, & Skolnik, 2013; Luciano & Perazella, 2014; Maan & D'Souza, 2012; Nicholson, Quinn, & Dodd, 2010; Omer & Doherty, 2011; Smith, Williams, & Shaikh, 2013). Fatalities following mephedrone use have also been reported (Kesha et al., 2013; Lusthof et al., 2011; Maskell, De Paoli, Seneviratne, & Pounder, 2011; Schifano, Corkery, & Ghodse, 2012; Torrance & Cooper, 2010). Mephedrone was initially sold legally via the internet and it has been added to the repertoire of 'party drugs', particularly among the gay community (Moore, Dargan, Wood, & Measham, 2013; Wood, Hunter, Measham, & Dargan, 2012). In the UK, mephedrone use also became prevalent among school and college/university students prior to being scheduled in April 2010 (Dargan, Albert, & Wood, 2010).

Mephedrone is consumed intranasal or orally, but intravenous use has been recently reported (EMCDDA, 2015). There is a risk of mephedrone use being linked to possible increases in HIV rates among people who inject drugs (PWID). Its short duration of action induces higher frequency of injection. It has also been suggested that mephedrone might be associated with risky sexual practices, particularly among MSM (Hunter, Dargan, Benzie, White, & Wood, 2014; Yamamoto, Kawsar, Ramsey, Dargan, & Wood, 2013). A survey among socially active young adults in nightlife venues in New York City found that 8.2% reported use of synthetic cannabinoids and 1.1% reported the use of mephedrone (Kelly et al., 2013). This study also found that sexual minority identity was associated with mephedrone use and younger age and Latino ethnicity are associated with synthetic cannabinoid use.

Recent outbreaks of HIV among PWID have been documented in some countries in Europe (Hedrich, 2013 ; Pharris, 2011) and in Israel. The outbreaks identified were in: Romania 2011, Hungary 2011, Greece 2012, Israel 2012-2013, Ireland 2015 and Glasgow in 2015. An increase in HCV and HIV co-infections has also been reported in Wales. The outbreaks in Greece and Glasgow were reported among heroin users, and factors other than NPS use might be associated with those outbreaks (Kentikelenis et al., 2011). However, there is some indication that the outbreaks in Romania, Hungary, Ireland, Israel and Wales were associated to changes in drug consumption patterns, more specifically traditional opioid users switching to injecting synthetic cathinones, such as mephedrone, α -PVP and MDPV. In Hungary, a study with 183 PWID from a large NEP found that during 2011 nearly half of the former amphetamine injectors had switched to MDPV as had 41.7% of the former heroin injectors and 78.6% of those using other substances (cocaine and mephedrone) (Csák, Demetrovics, & Rácz, 2013).

The 2011 reduction in heroin availability in the drug market might have triggered the initial experimentation of synthetic cathinones. Additionally, the drug effect, the low cost, the easy availability and the temporary legality might have made drugs, such as mephedrone, an attractive substitute to heroin. The combination of unsafe injecting practices and unprotected sex might

increase the risk and transmission of infectious virus among PWID using synthetic cathinones. The present review aimed to gather evidence from the scientific and grey literature on the association between synthetic cathinone and HIV, HCV and HBV risk and transmission.

2. Results

The methodology of the present review followed the same procedures detailed in the methods section of this literature review; except that no exclusion criteria have been set for study design. NPS is a fairly novel topic in the scientific literature and it was important to identify any emerging issues related to synthetic cathinone and HIV, HCV and HBV risk and transmission. A total of 15 publications reporting outcomes related to HIV, HCV, HBV, injecting risk behaviour or sexual risk behaviour were identified and included in the present review. Only three papers were identified through screening the original scientific literature retrieved for this review (out of 1,048 full texts), while the other publications were identified through screening reference lists and grey literature.

The publications identified were: cross-sectional surveys, one case-control study, qualitative studies, exploratory mix-method study, national reports, description/commentary and a conference abstract. The majority of publications (11) were European, two were from the United States and one was from Israel. One study was published in 2009 and the all the others were published between 2012 and 2015.

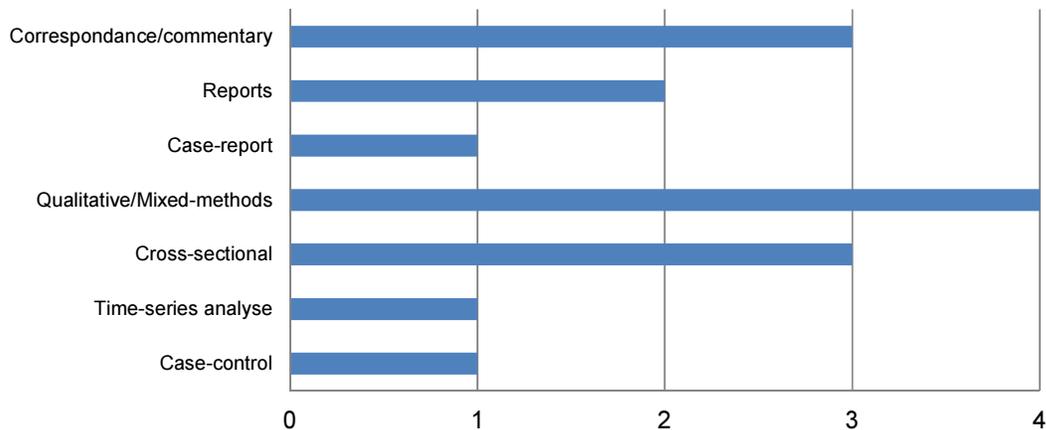


Figure 1: Study Designs

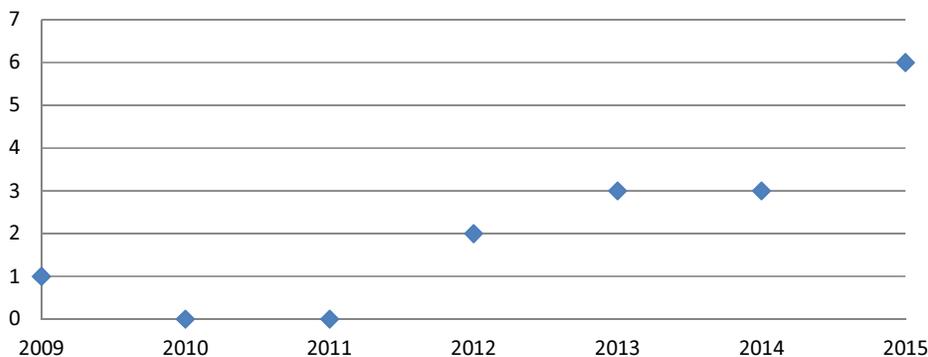


Figure 2: Number of publications per year



Figure 3: Countries in which the studies took place

France

Study 1 (Peyriere et al., 2013): A case-report described the case of three MSM in France who made use of mephedrone. The three individuals acquired viral and bacterial infections associated with their mephedrone use. One case described frequently injecting mephedrone and sharing syringes. This patient, who was already HIV-1 infected, acquired HCV while frequently injecting mephedrone. The second case described a patient who used mephedrone intranasal and frequently engaged in sexual risk behaviour. This patient acquired HIV and HCV. The third patient presented bacterial infection (staphylococcal) in sites used to inject mephedrone.

United Kingdom

Study 2 (Public Health England 2015): reported an increase in the number of people injecting stimulants, particularly mephedrone. One-in-eight people who inject drugs reported mephedrone injection. In England, Wales and Northern Ireland, the proportion of people who reported injecting ATS as their main drug tripled from 3.9% in 2004 to 12% in 2014. The number of people reporting injecting amphetamine during the past month increased from 18% in 2010 to 24% in 2014 (of these 5.9% injected mephedrone). Mephedrone injecting is a recent practice which occurs mainly among people who have a history of injecting drug use, and among people who have switched from snorting mephedrone. People injecting stimulants report higher levels of risk behaviours such as sharing and reusing needles and syringes, and sharing filters, mixers and containers. In England, Wales and Northern Ireland, those who reported that they had injected mephedrone during the past year were more likely to have HIV, to have antibodies to hepatitis C virus, and to report having had an injection site infection the past year. This publication also reports that Public Health Wales has identified a sharp rise in new hepatitis C diagnoses among PWID, as well as a small group of

individuals newly diagnosed with HIV and hepatitis C co-infection in south west Wales¹. It is suggested that this problem is linked to an opioid injecting population starting to inject stimulants, specifically NPS. An increase in the number of people who mainly inject stimulants has also been seen in Wales. This publication also reports that an outbreak of HIV among people who inject drugs in Glasgow is currently being investigated, but this outbreak has been reported among heroin users.

Study 3 (Bourne, 2014): The Chemsex Study was an exploratory, mixed-method study that explored drug use in sexual settings among gay and bisexual men living in Lambeth, Southwark and Lewisham (LSL). Men living in LSL were significantly more likely to use cocaine, mephedrone, GHB/GBL and crystal methamphetamine than men living elsewhere in England. Two thirds of men in LSL who used crystal meth in the last 4 weeks had diagnosed HIV. A third of participants had recently injected crystal meth or mephedrone. Injection drug use was generally safe with no evidence of needle sharing. But there were four frequent situations reported of drug use and sexual risk taking: (1) More than a quarter of participants (all HIV positive) had decided to engage in unprotected anal intercourse with a sero-concordant man (2) Nearly a third of men found it difficult to control their behaviour while under the influence of drugs and engaged in HIV/STI transmission risk behaviour. (3) A small sample of men sought out risky sex and felt that this was facilitated by the drugs they took. (4) Approximately one in four participants frequently engaged in 'chemsex' but felt in control of their actions and mostly engaged in safe sex.

Study 4 (Stuart, 2013): A description of unpublished data from a drug service from London. The publication describes the observed rise in the use of drugs such as crystal methamphetamine, mephedrone and GHB/GBL by MSM for use in sexual context. The paper mentioned the use of online sites and mobile apps by MSM to find partners willing to take part in 'chem-sex' or 'slamming'. The author mentioned the decrease in heroin use and the sharp rise in people reporting mephedrone use in the UK since 2006. This change was reflected in the service's presentations: crystal meth, mephedrone and GHB/GBL were responsible for 3% of all presentations in 2005 and for 85% of all presentations in 2012. The great majority reported using these drugs to facilitate sex and 70% reported needle sharing. More concerning, 75% of these drug users are HIV-positive. They often report difficulty adhering to ART and the vast majority attributed their HIV/HCV diagnosis to drug or alcohol use. This small group of men might be highly infectious and they often engage in unprotected sex with a significant number of men.

Study 5 (Gilbart, Simms, Gobin, Oliver, & Hughes, 2013): In-depth interviews that explored the lifestyle and sexual behaviour of 12 MSM diagnosed with *Shigella flexneri* serotype 3a. Mephedrone, ketamine, crystal methamphetamine, and γ -butyro-lactone had been used by most MSM (nine of 12) during sexual encounters. 'Slamming' occurred at sex parties and was reported by two. Condom use was rare, and most encounters were anonymous and arranged through internet sites. Most men (nine) were HIV positive (two who were negative are retesting), reported high numbers of sexual

¹ Also reported in the following personal communications: Smith et al. Reversing the tide: The impact of and responses to injecting New Psychoactive Substances in South Wales. Drug-related Infectious Diseases Annual Expert Meeting 15-16 June 2015 - Lisbon

partners in the past year (median 60), and had had gonorrhoea (nine) and chlamydia (seven). A small number of infections of syphilis, lymphogranuloma venereum, and hepatitis C were also identified.

Ireland

Study 6 (Giese et al., 2015): In Ireland, an unexpected increase in cases of acute HIV infection among people who inject drugs (PWID) associated with the injection of the synthetic cathinone alpha-PVP was reported in February 2015. This study compared drug and risk behaviours among 15 HIV cases and 39 controls. Injecting a synthetic cathinone (snow blow) was associated with recent HIV infection (AOR: 49; $p = 0.003$).²

Study 7 (Van Hout & Bingham, 2012): This study described the experiences of a group of Irish injecting drug users who were injecting mephedrone. The findings describe the abuse potential of these mephedrone when used by intravenous injection. Although participants were aware of risks and safe injecting practises, compulsive re-injecting with excessive binge use over long periods of time was common. Participants reported cognitive, psychological and physical harms associated to mephedrone injection. Multi and serial drug injecting with heroin was used to manage the intense rush and avoid unpleasant comedown. Participants reported limb abscesses, vein clotting, damage and recession resulting from product toxicity, crystallisation of the products when diluted and flushing practises. Seven participants were homeless and groin and street injecting were common. Following legislative changes, use of mephedrone products declined due to closure of headshops, increased street prices, concerns around contamination and the emergence of new street stimulant drugs.

Ukraine

Study 8 (Chintalova-Dallas, Case, Kitsenko, & Lazzarini, 2009): *Boltushka* is a home-made ATS-drug containing cathinone. The use of this drug was reported in Odessa, Ukraine in 2005 and this study carried out a further qualitative study to explore the use of this substance among ten users. The study revealed that *Boltushka* is injected and users engage in high levels of injecting risk behaviours and also in sexual risk behaviour post use. Injectors are young, poor and the vast majority are already HIV-positive. Some users reported little concern for acquiring HIV.

Hungary

Study 9 (Tarján et al., 2015): This study analysed recent quantitative national and subnational data from the period of 2011–2012 regarding HCV prevalence and injecting-related risk behaviours, with a special focus on NPS injecting. The study estimated the effects of heroin shortage and appearance of NPS among PWID and the impact of austerity times. The study found that the proportion of primarily opioid injectors decreased from 86.7% in 2006 to 50% in 2011, while proportion of stimulant injectors increased from 13.3% to 50% in those same years. In 2011, 17.1% of stimulant injectors mentioned injecting primarily NPS. Reported needles/syringes, and sharing any injecting

² Also reported in: Increase in diagnoses of recently acquired HIV in people who inject drugs. *Epi – Insight*, 2015, Vol 16, issue 7, July <http://ndsc.newsweaver.ie/epiinsight/w30o8zinms4> [Accessed: 10/12/15]

equipment also increased significantly, particularly among stimulant injectors. The mean number of injection times on the last day of injecting and the mean number of reuses of the last syringe were the highest among NPS injectors. There was no significant change in the overall prevalence of HCV infection between 2006 and 2011. However, HCV rates decreased among opioid injectors and increased among stimulant injectors. A probable HCV serosorting has taken place, by many PWID who are HCV infected switching over from injecting opioids to injecting amphetamines or NPS. In 2012, the number of syringes distributed dropped by 35% due to austerity measures.

Study 10 (Rácz, Gyarmathy, & Csák, 2015): this paper is an analytical commentary of new HIV cases detected among PWID recruited at a large NEP in Hungary. 167 PWID were recruited, of these 92 were tested for HIV. A third of the sample was female and the mean age was 33.8 years. The most common drug injected was pentadone (48%), followed by an unknown drug called 'music' (23%). Participants reported injecting in average 6 times per day and often reusing syringes. Injecting risk behaviour (sharing filters and syringes) was frequent. Two new cases of HIV infection were detected in PWIDs in Budapest in May 2014 (one of them among the sample surveyed and another case prior to this survey). These new cases may indicate an unfolding HIV outbreak among PWIDs. The paper also discuss the dangerous combination of the emergence of new designer drugs that require frequent injection, the cuts in harm reduction services and the re-criminalization of drug use.

Study 11 (Rácz, Csák, & Lisznyai, 2015): Since 2010, the members of a 'social micro segregate' community in Budapest changed their drugs use from "old" drugs (heroin, amphetamines) to new, "designer" drugs. The transition was studied with qualitative interviews. Data from life narrative interviews with 17 mephedrone users were collected (8males and 9 females). Data underline the supply driven drug transitions took place. All participants reported that the frequency of use and amount increased since they started injecting mephedrone. The new, more harmful injecting drug use pattern of injecting has emerged among this group moving from public places to flats.

Romania

Study 12 (Botescu, 2012): a sharp increase of newly diagnosed HIV infections among IDUs during 2011 was reported in Romania. While reporting three to five cases annually from 2007 to 2009, HIV infections among IDUs increased to 12 cases in 2010 to 129 in 2011. Until the end of June 2012, 102 new cases were registered, which is over three times the number of cases reported for the same period in 2011 (30 cases). Routine monitoring performed at registration for drug treatment services indicated an increase in HIV-positive cases among IDUs tested 1.1% in 2008, 3.3% in 2009 and 4.2% in 2010 and 11.6% in 2011. Unpublished data from the 2012 behavioural surveillance survey among IDUs (n=417) in Bucharest reported that the HIV prevalence among IDUs reached 52.5%. In 2010, there were reports of changes in drug use patterns from 2009, where 97% of respondents reported heroin as the main drug of injection, to 2010, where 67% reported heroin and 31% reported amphetamine-type stimulants, mostly synthetic cathinones, as the main drug of injection. Stimulant use is associated with more frequent injection and there are reports of increased syringe sharing. In 2012 significant changes were seen in drug use patterns. The main drugs of injection were new amphetamine type stimulants for 49.4% of the IDUs. The HIV outbreak among IDUs in 2011

coincided with a significant reduction of harm reduction service provision due to the ending of funding.

United States

Study 13 (P. S. Johnson & Johnson, 2014): 113 individuals in the U.S. reporting use of bath salts completed an anonymous, online survey characterizing demographic, experiential, and psychological variables. Respondents were more often male, 18– 24 years old, and Caucasian/white with some college education. Past year use was typically low (≤ 10 days), but marked by repeated dosing. Intranasal was the most frequently reported administration route (IV route not mentioned) and subjective effects were similar to other stimulants (e.g., cocaine, amphetamines). Bath salts use was associated with increased sexual desire and sexual HIV risk behaviour. 21% used to improve sexual experience and 48% took more sexual risks than normal after using bath salts.

Study 14 (Wagner et al., 2014): This is cross-sectional survey on synthetic drug use among a cohort of 485 PWID in San Diego, California. Seven percent of participants reported ever using synthetic cathinones and 30% reported ever using synthetic cannabinoids. In multivariate logistic regression, age and recent hospitalization were significantly associated with odds of synthetic cathinones and synthetic cannabinoids. Use of methamphetamine and use of club drugs in the past six months were significantly associated with synthetic cathinones use. Synthetic cathinones was used via injectable route by 48% of the sample. 462 participants were tested for HIV: 12.9% of synthetic cathinones users were HIV-positive while 8.6% of non- synthetic cathinones users were HIV-positive ($p= 0.34$). 462 participants were tested for HCV: 58.1% of synthetic cathinones users were HCV-positive while 67.8% of non-synthetic cathinones users were HCV-positive ($p= 0.27$). No significant differences were found in number of casual/regular partners and condom use.

Israel

Study 15 (Katchman, 2013): this conference abstract described a large-scale outbreak of primary HIV infection (PHI) in IDU in Tel Aviv, Israel, and its relation to changes in illicit drug use practices. The rate of PHI diagnosed in one centre increased six-fold after May 2012 (outbreak period; 5.9 versus 1.0 cases per month, $P < 0.0001$). PHI during the outbreak period was associated with injecting drug use (50.7% versus 0%, $P=0.0001$). Severe bacterial co-infections were frequent and comprised the most common reason for hospitalisation. All IDUs with PHI were co-infected with HCV and 33% were co-infected with HBV. The mortality rate was 7.5% three months after diagnosis of PHI. All HIV isolates were a variant of subtype A/CRF01 AE; phylogenetic analysis showed a tight clustering suggesting a single source of infection. All IDUs with PHI interviewed had recently switched from heroin use to injecting combinations of cathinone and buprenorphine, and reported increased frequency of injections, sharing of non-sterile containers and no need for boiling due to the high solubility of the new compounds. No cases of PHI were diagnosed in IDUs who continued to inject heroin.

3. Summary of the Findings

The present review identified 15 publications on NPS and reporting the outcomes of interest (HIV, HCV, HBV rates or sexual risk behaviour or injecting risk behaviour). Only five of these were quantitative studies published in peer-reviewed journals (three cross-sectional surveys, one time-series analysis and one case-control study). There were two national reports (from the UK and Romania) and 4 qualitative studies. Most of the studies were from Europe and most published between 2014 and 2015. Therefore, the evidence gathered in this review is limited, recent and weak. The findings from the included studies should be taken as an indication of the link between NPS use and HIV and other factors affecting this relationship should be considered.

This review focused on synthetic cathinones as they induce a stimulant-like effect similar to MDMA, cocaine and amphetamines. The uses of these drugs seem to be most common in Europe, although they have been reported in Australia and in the US. A large cross-sectional survey in night clubs in New York concluded that synthetic cannabinoids and mephedrone among adults remains relatively low in comparison with European nightlife scenes (Kelly et al., 2013).

ATS injecting has risen sharply in the last decade in the UK, and mephedrone injecting has become more common among PWID (Public Health England, 2015). The groups that seem to be at higher risk of initiating synthetic cathinone injecting are: people who already inject drugs, people who snort synthetic cathinones, homeless people, men who have sex with men and sex workers.

Some of the studies included in the present review indicated that a shift seems to have happened among PWID in their drug of choice and drug use patterns. The studies from the UK, Ireland, Hungary, Romania and Israel suggested that a significant proportion of PWID have switched to injecting synthetic cathinones in recent years (Botescu, 2012; Csák et al., 2013; Giese et al., 2015; Katchman, 2013; Public Health England, 2015; Rácz, Csák, et al., 2015; Tarján et al., 2015; Van Hout & Bingham, 2012). Some of the reasons for this change were the shortage in heroin supply, low price and easy availability (Van Hout & Bingham, 2012).

However, the use of synthetic cathinone seems to place users in a higher risk of acquiring blood-borne viruses, compared to heroin injecting. The short duration of action of some synthetic cathinones, like mephedrone and α -PVP, might lead to compulsive injection, as reported in Van Hout & Bingham (2012). Frequent injecting might bring users to share and reusing needles and syringes, and sharing filters, mixers and containers. In the UK, these behaviours were reported more frequently among mephedrone users than among other PWID (Public Health England, 2015). This pattern has also been seen with home-made ATS, such as 'Boltushka' in Ukraine. 'Boltushka' injectors engage in high levels of injecting risk behaviours and also in sexual risk behaviour post use. These injectors are young, poor and the vast majority are already HIV-positive. Some users reported little concern for acquiring HIV (Chintalova-Dallas et al., 2009).

The increase in high risky stimulant injecting might have contributed to some of the sharp rises in HIV rates documented in some places in Europe (EMCDDA, 2014; Pharris, 2011). In Ireland, an unexpected increase in cases of acute HIV infection among people who inject drugs (PWID) associated with the injection of the synthetic cathinone alpha-PVP was reported in February 2015 (Giese et al., 2015). This study compared drug and risk behaviours among 15 HIV-positive cases and 39 HIV-negative controls. Injecting a synthetic cathinone (snow blow) was associated with recent HIV infection (AOR: 49; $p = 0.003$). However, a study in the US tested 462 PWID for HIV and HCV and no

significant differences were identified between synthetic cathinone users and users of other drugs (Wagner et al., 2014). In this study, only 7% of the sample used synthetic cathinones and about half used it intravenously.

It is important to consider that synthetic cathinone use is a recent problem and there is little and weak evidence to support a reliable association between NPS use and increase HIV rates. The financial crisis and the impact of austerity measures in the health budget should not be ignored (Kentikelenis et al., 2011; Sypsa et al., 2015). Hungary has suffered severe cuts to their needle exchange programmes which resulted in the closure of centres, reductions in staff numbers, reductions in needles and syringes distributed and reductions in HIV screenings (Rácz, Gyarmathy, et al., 2015). So even if HIV rates do not rise in the future, it could be that cases are not been detected due to reduced testing facilities for PWID.

The sexual route of transmission might also be an issue among synthetic cathinone users. Over 20% of 'bath salts' users in the sample described by P. S. Johnson & Johnson (2014) used these drugs to improve sexual experience and 48% of them took more sexual risks than normal after using bath salts (P. S. Johnson & Johnson, 2014). The risk of HVI transmission through sexual risk contact might be particularly elevated among MSM. Mephedrone use seems to have risen among MSM in London and many are using it to facilitate sex (Stuart, 2013). Although some MSM might engage in 'chemsex' safely, some people might find difficult to have safe sex under the influence of stimulant drugs and other might voluntarily engage in unprotected sex (Bourne, 2014; Gilbert et al. 2013). In France, Peyriere et al. (2013) reported the cases of three MSM mephedrone users. One probably acquired HIV through injecting risk behaviour, another acquired HIV most likely through sexual risk behaviour and a third acquired bacterial infection at injecting sites. There is a concern that this subgroup of MSM who engage in chemsex on a regular basis might have higher prevalence of HIV, be highly virulent (if poor adherence to ART) and engage in unprotected sex frequently. This combination of factors might lead to an increase in HIV rates.

The risk and transmission of HIV, HCV and HBV among people who inject synthetic cathinone should be carefully monitored and measured should be taken to prevent future sharp rises. Web monitoring networks, such as the ones already in place (Corazza et al., 2013; Deluca et al., 2012), are important tools to identify new drugs in the market, changes in drug use patterns and health risk. Increase awareness of the health risks, including blood-borne virus transmission, is also important (Corazza, Simonato, Corkery, Trincas, & Schifano, 2014). The risk of HIV transmission should be emphasised among people who inject synthetic stimulants and also among those who treat this population.

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Author, Year	Country	Design	Drug	Relevant findings
1. Peyriere, 2013	France	Case-report	Mephedrone	Viral and Bacterial Risks Associated with Mephedrone Abuse in HIV-Infected Men Who Have Sex with Men: A case-report described the case of three MSM in France who made use of mephedrone. The three individuals acquired viral and bacterial infections associated with their mephedrone use. One case described frequently injecting mephedrone and sharing syringes. This patient, who was already HIV-1 infected, acquired HCV while frequently injecting mephedrone. The second case described a patient who used mephedrone intranasal and frequently engaged in sexual risk behaviour. This patient acquired HIV and HCV. The third patient presented bacterial infection (staphylococcal) in sites used to inject mephedrone.
2. Public Health England 2015	United Kingdom	National report	Mephedrone	Shooting up: infections among people who inject drugs in the United Kingdom: reported an increase in the number of people injecting stimulants, particularly mephedrone (Public Health England, 2015). One-in-eight people who inject drugs reported mephedrone injection. In England, Wales and Northern Ireland, the proportion of people who reported injecting ATS as their main drug tripled from 3.9% in 2004 to 12% in 2014. The number of people reporting injecting amphetamine during the past month increased from 18% in 2010 to 24% in 2014 (of these 5.9% injected mephedrone). Mephedrone injecting is a recent practice which occurs mainly among people who have a history of injecting drug use, and among people who have switched from snorting mephedrone. People injecting stimulants report higher levels of risk behaviours such as sharing and reusing needles and syringes, and sharing filters, mixers and containers. In England, Wales and Northern Ireland, those who reported that they had injected mephedrone during the past year were more likely to have HIV, to have antibodies to hepatitis C virus, and to report having had an injection site infection the past year. This publication also reports that Public Health Wales has identified a sharp rise in new hepatitis C diagnoses among PWID, as well as a small group of individuals newly diagnosed with HIV and hepatitis C co-infection in south west Wales. It is suggested that this problem is linked to an opioid injecting population starting to inject stimulants, specifically NPS. An increase in the number of people who mainly inject stimulants has also been seen in Wales. This publication also reports that an outbreak of HIV among people who inject drugs in Glasgow is currently being investigated, but this outbreak has been reported among heroin users.

3. Bourne, 2014	United Kingdom	exploratory , mixed-method study	Cocaine, mephedrone , GHB/GBL and crystal methamphetamine	The Chemsex Study: drug use in sexual settings among gay and bisexual men in Lambeth, Southwark and Lewisham: explored drug use in sexual settings among gay and bisexual men living in Lambeth, Southwark and Lewisham (LSL). Men living in LSL were significantly more likely to use cocaine, mephedrone, GHB/GBL and crystal methamphetamine than men living elsewhere in England. Two thirds of men in LSL who used crystal meth in the last 4 weeks had diagnosed HIV. A third of participants had recently injected crystal meth or mephedrone. Injection drug use was generally safe with no evidence of needle sharing. But there were four frequent situations reported of drug use and sexual risk taking: (1) More than a quarter of participants (all HIV positive) had decided to engage in unprotected anal intercourse with a sero-concordant man (2) Nearly a third of men found it difficult to control their behaviour while under the influence of drugs and engaged in HIV/STI transmission risk behaviour. (3) A small sample of men sought out risky sex and felt that this was facilitated by the drugs they took. (4) Approximately one in four participants frequently engaged in ‘chemsex’ but felt in control of their actions and mostly engaged in safe sex.
4. Stuart, 2013	United Kingdom	Descriptive narrative	Crystal methamphetamine, mephedrone and GHB/GBL	Sexualised drug use by MSM: background, current status and response. A description of unpublished data from a drug service from London. The publication describes the observed rise in the use of drugs such as crystal methamphetamine, mephedrone and GHB/GBL by MSM for use in sexual context. The paper mentioned the use of online sites and mobile apps by MSM to find partners willing to take part in ‘chem-sex’ or ‘slamming’. The author mentioned the decrease in heroin use and the sharp rise in people reporting mephedrone use in the UK since 2006. This change was reflected in the service’s presentations: crystal meth, mephedrone and GHB/GBL were responsible for 3% of all presentations in 2005 and for 85% of all presentations in 2012. The great majority reported using these drugs to facilitate sex and 70% reported needle sharing. More concerning, 75% of these drug users are HIV-positive. They often report difficulty adhering to ART and the vast majority attributed their HIV/HCV diagnosis to drug or alcohol use. This small group of men might be highly infectious and they often engage in unprotect sex with a significant number of men.
5. Gilbert, Simms, Gobin, Oliver, & Hughes 2013	United Kingdom	Qualitative	Mephedrone , ketamine, crystal methamphetamine, and γ -butyro-lactone	High-risk drug practices in men who have sex with men In-depth interviews that explored the lifestyle and sexual behaviour of 12 MSM diagnosed with Shigella flexneri serotype 3a. Mephedrone, ketamine, crystal methamphetamine, and γ -butyro-lactone had been used by most MSM (nine of 12) during sexual encounters. ‘Slamming’ occurred at sex parties and was reported by two. Condom use was rare, and most encounters were anonymous and arranged through internet sites. Most men (nine) were HIV positive (two who were negative are retesting), reported high

				numbers of sexual partners in the past year (median 60), and had had gonorrhoea (nine) and chlamydia (seven). A small number of infections of syphilis, lymphogranuloma venereum, and hepatitis C were also identified.
6. Giese et al., 2015	Ireland	Case-control	Synthetic cathinone (snow blow)	Injection of new psychoactive substance snow blow associated with recently acquired HIV infections among homeless people who inject drugs in Dublin, Ireland, 2015 In Ireland, an unexpected increase in cases of acute HIV infection among people who inject drugs (PWID) associated with the injection of the synthetic cathinone alpha-PVP was reported in February 2015. This study compared drug and risk behaviours among 15 HIV cases and 39 controls. Injecting a synthetic cathinone (snow blow) was associated with recent HIV infection (AOR: 49; p = 0.003).
7. Van Hout & Bingham, 2012	Ireland	Qualitative	Mephedrone injection	"A costly turn on": patterns of use and perceived consequences of mephedrone based head shop products amongst Irish injectors This study described the experiences of a group of Irish injecting drug users who were injecting mephedrone. The findings describe the abuse potential of these mephedrone when used by intravenous injection. Although participants were aware of risks and safe injecting practises, compulsive re-injecting with excessive binge use over long periods of time was common. Participants reported cognitive, psychological and physical harms associated to mephedrone injection. Multi and serial drug injecting with heroin was used to manage the intense rush and avoid unpleasant comedown. Participants reported limb abscesses, vein clotting, damage and recession resulting from product toxicity, crystallisation of the products when diluted and flushing practises. Seven participants were homeless and groin and street injecting were common. Following legislative changes, use of mephedrone products declined due to closure of headshops, increased street prices, concerns around contamination and the emergence of new street stimulant drugs.
8. Chintalova-Dallas, 2009	Ukraine	Case-report	Home-made AST	Boltushka: a Homemade Amphetamine-Type Stimulant and HIV Risk in Odessa, Ukraine: Boltushka is a home-made ATS-drug containing cathinone. The use of this drug was reported in Odessa, Ukraine in 2005 and this study carried out a further qualitative study to explore the use of this substance among ten users. The study revealed that Boltushka is injected and users engage in high levels of injecting risk behaviours and also in sexual risk behaviour post use. Injectors are young, poor and the vast majority are already HIV-positive. Some users reported little concern for acquiring HIV.
9. Tarján et al., 2015	Hungary	Time series analysis	NPS	Emerging Risks Due to New Injecting Patterns in Hungary During Austerity Times: This study analysed recent quantitative national and subnational data from the period of 2011–2012 regarding HCV prevalence and injecting-related risk behaviours, with a special focus on NPS injecting. The

				<p>study estimated the effects of heroin shortage and appearance of NPS among PWID and the impact of austerity times. The study found that the proportion of primarily opioid injectors decreased from 86.7% in 2006 to 50% in 2011, while proportion of stimulant injectors increased from 13.3% to 50% in those same years. In 2011, 17.1% of stimulant injectors mentioned injecting primarily NPS. Reported needles/syringes, and sharing any injecting equipment also increased significantly, particularly among stimulant injectors. The mean number of injection times on the last day of injecting and the mean number of reuses of the last syringe were the highest among NPS injectors. There was no significant change in the overall prevalence of HCV infection between 2006 and 2011. However, HCV rates decreased among opioid injectors and increased among stimulant injectors. A probable HCV serosorting has taken place, by many PWID who are HCV infected switching over from injecting opioids to injecting amphetamines or NPS. In 2012, the number of syringes distributed dropped by 35% due to austerity measures.</p>
10. Rác, Gyarmathy, et al., 2015	Hungary	Analytical commentary	Pentedrone and 'music' (unknown drug)	<p>New cases of HIV among PWIDs in Hungary: False alarm or early warning? This paper is an analytical commentary of new HIV cases detected among PWID recruited at a large NEP in Hungary. 167 PWID were recruited, of these 92 were tested for HIV. A third of the sample was female and the mean age was 33.8 years. The most common drug injected was pentedrone (48%), followed by an unknown drug called 'music' (23%). Participants reported injecting in average 6 times per day and often reusing syringes. Injecting risk behaviour (sharing filters and syringes) was frequent. Two new cases of HIV infection were detected in PWIDs in Budapest in May 2014 (one of them among the sample surveyed and another case prior to this survey). These new cases may indicate an unfolding HIV outbreak among PWIDs. The paper also discuss the dangerous combination of the emergence of new designer drugs that require frequent injection, the cuts in harm reduction services and the re-criminalization of drug use.</p>
11. Rác, Csák, & Lisznyai, 2015	Hungary	Qualitative	Mephedrone	<p>Transition from "old" injected drugs to mephedrone in an urban micro segregate in Budapest, Hungary: a qualitative analysis: Since 2010, the members of a 'social micro segregate' community in Budapest changed their drugs use from "old" drugs (heroin, amphetamines) to new, "designer" drugs. The transition was studied with qualitative interviews. Data from life narrative interviews with 17 mephedrone users were collected (8males and 9 females). Data underline the supply driven drug transitions took place. All participants reported that the frequency of use and amount increased since they started injecting mephedrone. The new, more harmful injecting drug use pattern of injecting has emerged among this group moving from public places to flats.</p>

12. Botescu, 2012	Romani a	Report	Synthetic cathinones	<p>HIV/AIDS among injecting drug users in Romania. Report of a recent outbreak and initial response policies: A sharp increase of newly diagnosed HIV infections among IDUs during 2011 was reported in Romania. While reporting three to five cases annually from 2007 to 2009, HIV infections among IDUs increased to 12 cases in 2010 to 129 in 2011. Until the end of June 2012, 102 new cases were registered, which is over three times the number of cases reported for the same period in 2011 (30 cases). Routine monitoring performed at registration for drug treatment services indicated an increase in HIV-positive cases among IDUs tested 1.1% in 2008, 3.3% in 2009 and 4.2% in 2010 and 11.6% in 2011. Unpublished data from the 2012 behavioural surveillance survey among IDUs (n=417) in Bucharest reported that the HIV prevalence among IDUs reached 52.5%. In 2010, there were reports of changes in drug use patterns from 2009, where 97% of respondents reported heroin as the main drug of injection, to 2010, where 67% reported heroin and 31% reported amphetamine-type stimulants, mostly synthetic cathinones, as the main drug of injection. Stimulant use is associated with more frequent injection and there are reports of increased syringe sharing. In 2012 significant changes were seen in drug use patterns. The main drugs of injection were new amphetamine type stimulants for 49.4% of the IDUs. The HIV outbreak among IDUs in 2011 coincided with a significant reduction of harm reduction service provision due to the ending of funding.</p>
13. P. S. Johnson & Johnson, 2014	US	Cross-sectional survey	'Bath Salts': mephedrone, methylone, and MDPV	<p>Investigation of "bath salts" use patterns within an online sample of users in the United States: 113 individuals in the U.S. reporting use of bath salts completed an anonymous, online survey characterizing demographic, experiential, and psychological variables. Respondents were more often male, 18– 24 years old, and Caucasian/white with some college education. Past year use was typically low (≤ 10 days), but marked by repeated dosing. Intranasal was the most frequently reported administration route and subjective effects were similar to other stimulants (e.g., cocaine, amphetamines). Bath salts use was associated with increased sexual desire and sexual HIV risk behaviour. 21% used to improve sexual experience and 48% took more sexual risks than normal after using bath salts.</p>
14. Wagner et al., 2014	US	Cross-sectional survey	synthetic cathinones and cannabinoids	<p>Use of synthetic cathinones and cannabimimetics among injection drug users in San Diego, California: This is cross-sectional survey on synthetic drug use among a cohort of 485 PWID in San Diego, California. Seven percent of participants reported ever using synthetic cathinones and 30% reported ever using synthetic cannabinoids. In multivariate logistic regression, age and recent hospitalization were significantly associated with odds of synthetic cathinones and synthetic cannabinoids. Use of methamphetamine and use of club drugs in the past six months were significantly associated with synthetic cathinones use. Synthetic cathinones was used via</p>

				<p>injectable route by 48% of the sample. 462 participants were tested for HIV: 12.9% of synthetic cathinones users were HIV-positive while 8.6% of non-synthetic cathinones users were HIV-positive ($p= 0.34$). 462 participants were tested for HCV: 58.1% of synthetic cathinones users were HCV-positive while 67.8% of non-synthetic cathinones users were HCV-positive ($p= 0.27$). No significant differences were found in number of casual/regular partners and condom use.</p>
15. Katchman, 2013	Israel	Cross-sectional survey (conference abstract)	Cathinone and buprenorphine combination	<p>An Outbreak of Primary HIV Infection among Injecting Drug Users in Tel Aviv, Israel Associated with Changes in the Illicit Drug Use Practices: this conference abstract described a large-scale outbreak of primary HIV infection (PHI) in IDU in Tel Aviv, Israel, and its relation to changes in illicit drug use practices. The rate of PHI diagnosed in one centre increased six-fold after May 2012 (outbreak period; 5.9 versus 1.0 cases per month, $P < 0.0001$). PHI during the outbreak period was associated with injecting drug use (50.7% versus 0%, $P=0.0001$). Severe bacterial co-infections were frequent and comprised the most common reason for hospitalisation. All IDUs with PHI were co-infected with HCV and 33% were co-infected with HBV. The mortality rate was 7.5% three months after diagnosis of PHI. All HIV isolates were a variant of subtype A/CRF01 AE; phylogenetic analysis showed a tight clustering suggesting a single source of infection. All IDUs with PHI interviewed had recently switched from heroin use to injecting combinations of cathinone and buprenorphine, and reported increased frequency of injections, sharing of non-sterile containers and no need for boiling due to the high solubility of the new compounds. No cases of PHI were diagnosed in IDUs who continued to inject heroin.</p>